Co-occurring Anxiety and Alcohol Use: Advancing Prevention and Early Intervention

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Abstract

Associations between anxiety and alcohol use have been widely examined in psychological research, with evidence suggesting that their co-occurrence is relatively common. This comorbidity has been linked to more complex symptomatology, clinical presentations, and poorer outcomes. Despite substantial research to date, the specific mechanisms driving this comorbidity remain poorly understood. Moreover, important gaps persist in how best to prevent these co-occurring conditions and intervene early to reduce long-term harm. This thesis aimed to advance understanding of anxiety-alcohol comorbidity by i) disentangling the relationship between anxiety and alcohol use, and ii) enhancing early interventions for co-occurring anxiety and alcohol problems.

Study 1 was the first systematic review and meta-analysis to synthesise mediating and moderating factors in the anxiety-alcohol relationship. Drawing on 315 unique effects from 55 studies, the findings highlight potential targets for prevention and intervention, including age, externalising symptoms, perceptions of peer alcohol use, and positive family experiences. Study 2 examined the relationship between anxiety and hazardous alcohol use across seven timepoints from early adolescence through to young adulthood. Moderating factors across developmental stages were also tested. Across early- to middle-adolescence (up to age 16), consistent positive associations were observed between anxiety and hazardous alcohol use within the same developmental stage. While these relationships were moderated by externalising symptoms, drinking motives, and sex cross-sectionally, no consistent longitudinal moderation effects were detected during early adolescence. Study 3 employed causal inference methods to identify mechanisms of change in the first online intervention for youth with co-occurring anxiety and alcohol use. Emotion regulation and alcohol use did not mediate social anxiety outcomes, and emotion regulation and positive alcohol expectancies and motives did not mediate alcohol outcomes. Study 4 used a mixed-methods approach to identify barriers and enablers to engagement with online treatment among young adults with co-occurring anxiety and alcohol use concerns. Results indicated that individual factors, rather than program-related factors, were the primary barriers to engagement.

Collectively, this thesis advances understanding of co-occurring anxiety and alcohol use, offering critical evidence to inform prevention, early intervention, and treatment approaches, particularly among youth. The findings also delineate clear avenues for future research to better elucidate the causal mechanisms driving anxiety-alcohol comorbidity.

Statement of originality

This is to certify that the content of this thesis is my own work. This thesis has not been submitted for any other degree or purpose.

I certify that the intellectual content of this thesis is the product of my own work, and that all assistance received in preparing this thesis and all sources have been acknowledged.

Tara Gückel

18th December 2025

I would like to acknowledge the Gadigal People of the Eora Nation, Traditional Custodians of the land on which this thesis was written.

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Authorship attribution statement

The research presented in this thesis has resulted in two published papers, two manuscripts currently under review, and one manuscript that is ready for submission to a peer-reviewed journal. On all publications I am the first and corresponding author, reflecting my substantial contribution to all aspects of these studies. Citations are provided on page xvi.

Chapter 2 reports on content published in one journal, a protocol for a systematic review published in *JMIR Research Protocols,* and a systematic review currently under review in *Behaviour Research and Therapy.* The authors of the protocol are Tara Gückel (TG), Katrina Prior (KP), Nicola Clare Newton (NCN), and Lexine Ann Stapinski (LAS). TG conceptualised the study with support from KP, NCN and LAS. TG wrote the original manuscript. All authors critically revised the manuscript and approved the final versions. The authors of the systematic review are TG, KP, NCN, Eyal Karin (EK), Kathryn Soltis Gex (KSG), Jayden Sercombe (JS) and LAS. TG conducted all article screening, data extractions, developed the quality appraisal tools, conducted risk of bias, completed the narrative synthesis, prepared data for meta-analyses, and drafted the manuscript. EK assisted with the meta-analysis providing statistical advice on the appropriate analytical approaches. KSJ and JS double screened a subset of titles and abstracts and dual-reviewed the risk of bias assessments. All authors critically revised the manuscript and approved the final version. This manuscript has undergone one round of peer review and has been revised for resubmission.

Chapter 3 is under review in *Behaviour Research and Therapy* as part of a special issue entitled "*Understanding the nature and treatment of comorbid emotional disorders and substance use disorders".* The authors are TG, NCN, KP and LAS. TG conceptualised the study with support from NCN, KP and LAS. TG conducted all analyses and drafted the manuscript. All authors critically reviewed the manuscript and approved the final submitted version.

Chapter 4 is published in *Behaviour Research and Therapy* as part of a special issue entitled *"Predictors, moderators, and mediators of online treatments for psychological disorders"*. TG led the development of the study using data from the Inroads RCT. The authors are TG, KP, NCN, Andrew Baillie (AB), Maree Teesson (MT) and LAS. TG, KP, NCN and LAS conceptualised the study. NCN, AB, MT and LAS secured funding for the Inroads RCT. KP and LAS were responsible for ethics and governance of overall trial administration. TG developed the methodology and conducted the formal analysis. TG wrote the original manuscript. All authors critically revised the manuscript and approved the final version.

Chapter 5 is an unpublished manuscript, prepared for submission to *Internet Interventions.* TG led the development of the study using data from the Inroads naturalistic trial. The contributors are TG, KP, NCN, and LAS. TG conceptualised the study with support from KP, NCN and LAS. TG, NCN and LAS secured funding for the naturalistic trial. TG, KP and LAS led updates to the intervention. TG and KP were responsible for trial management with oversight from LAS. TG conducted 100% of qualitative interviews. TG developed the methodology and conducted the formal quantitative and qualitative analysis. TG wrote the original manuscript. All authors critically revised the manuscript and approved the final version.

I confirm that all of the work in this thesis is my own, and any contribution made by others has been explicitly acknowledged.

Tara Gückel

18th December 2025

As supervisors for the candidate upon which this thesis is based, we can confirm that the author attribution statement above is correct.

Lexine Stapinski

18th December 2025

Katrina Prior

18th December 2025

Nicola Newton

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Generative AI statement

During the preparation of the thesis the author used OpenAI for assisting with editing and refining text (e.g., sentence structure, paraphrasing, improving clarity of expression) and for code checking with the statistical program R. The author confirms that where text was modified by generative AI, the content was carefully reviewed for possible errors, inaccuracies, and bias. The author takes full responsibility for the submitted thesis and ensures their work is their own and has used generative AI in accordance with University of Sydney's guidelines and policies.

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Abbreviations

ABS: Australian Bureau of Statistics

AIHW: Australian Institute of Health and Welfare

AUD: alcohol use disorder

AUDIT: alcohol use disorders identification test

AGReMA: A Guideline for Reporting Mediation Analyses

BSI: Brief symptom inventory

CBT: cognitive behaviour therapy

CI: confidence interval

DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition

GABA: Gamma-Aminobutyric Acid

GAD: generalised anxiety disorder

GRADE: Grading of Recommendations Assessment, Development, and Evaluation

NHMRC: National Health and Medical Research Council

MAR: missing at random

MCAR: missing completely at random

Mediation PNDE: mediation pure natural direct effect

Mediation TNIE: mediation total natural indirect effect

Mediation TE: mediation total effect

MICE: Multivariate Imputation by Chained Equations

PEO: population, exposure, outcome

PRSIMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

LGBTQIA+: lesbian, gay, bisexual, transgender, gender diverse, intersex and queer

SAD: social anxiety disorder

S.E: standard error

SD: standard deviation

SUD: substance use disorder

SURPS: substance use risk profile scale

TLFB: timeline follow back

RCT: randomised controlled trial

WHO: World Health Organisation

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Publications associated with this thesis

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Additional publications arising during candidature

Peer reviewed publications

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Government reports

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Policy submissions

Bower, M., Donohoe-Bales, A., Grummitt, L., **Gückel, T**., Smout, S. & Teesson, M. (2023). *Submission in Response to the National Health and Climate Strategy.*

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Rowe, A.L., Buncuga, A., Gray, M., **Gückel, T**. Egan, L., Bailey, S., Barrett, E., Newman, P., Ross, K., Stapinski, L., Grager, A., & Routledge, K. (2022). Diversity and Inclusion Makers and Shapers Award. *Faculty of Medicine and Health, The University of Sydney.*

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Chapter 1

General introduction

Preface

Anxiety and alcohol use commonly co-occur, and their interplay can create a mutually reinforcing cycle that leads to escalating difficulties over time. Although substantial research has documented the prevalence and interconnected nature of anxiety and alcohol use, far less attention has been directed toward *prevention* or *early intervention* for this comorbidity.

Given the considerable individual, societal, and economic burden associated with both anxiety and alcohol use, there is a critical need to identify effective approaches to intervene before these concerns progress. Ideally, such efforts should begin in adolescence or young adulthood, when anxiety symptoms and patterns of alcohol use commonly emerge, and when developmental trajectories are most malleable.

Several theoretical models exist which begin to explain the interrelationship between anxiety and alcohol use. As outlined throughout this introductory chapter though, evidence regarding the directionality, developmental onset, and mechanisms underlying this association remain inconclusive. These knowledge gaps limit our ability to design and implement prevention and early intervention approaches that effectively reduce harm. Compounding this challenge is the need to ensure that interventions can be delivered at scale, reaching the young people who need them most while achieving meaningful public health impact.

This thesis aims to address these gaps by i) disentangling the anxiety-alcohol relationship and ii) enhancing early intervention for co-occurring anxiety and alcohol use concerns. These aims are addressed through the following four research objectives:

1. Systematically review the evidence identifying factors that longitudinally a) *mediate* and b) *moderate* the bidirectional relationship between anxiety → alcohol use and alcohol use → anxiety.
2. Examine developmental associations between, and moderators of, anxiety and hazardous alcohol use across multiple timepoints from early adolescence through to young adulthood.

3. Investigate the causal mechanisms responsible for reducing social anxiety and hazardous drinking within an efficacious online early intervention program for young adults.
4. Identify barriers and enablers to the delivery of, and user engagement with, an online intervention for young adults experiencing co-occurring anxiety and hazardous alcohol use.

To contextualise these objectives, this introductory chapter outlines the prevalence of anxiety and varying patterns of alcohol use, as well as their co-occurrence. It overviews dominant theoretical perspectives explaining this comorbidity, including the current state of research on underlying factors or mechanisms (mediators and moderators) that may drive the association. Approaches to treating co-occurring anxiety disorders and alcohol use disorder (AUD) are then discussed, including the shortcomings of treatments that focus on single disorders. Lastly, the chapter outlines the role of prevention and early intervention in addressing co-occurring anxiety and alcohol use concerns. Current evidence, particularly regarding the scalability of online interventions is reviewed, before introducing the four novel empirical chapters that address the research objectives.

1.1 Prevalence of anxiety, alcohol use, and their co-occurrence

1.1.1 Anxiety prevalence and associated harms

Anxiety disorders are the most prevalent mental disorders affecting approximately 30% of people in their lifetime (Bandelow & Michaelis, 2015). This equates to more than 301 million people living with an anxiety disorder globally (Yang et al., 2021). Prevalence estimates vary by type of anxiety disorder, with specific phobia, social anxiety disorder (SAD), and generalised anxiety disorder (GAD) typically more common than panic disorder, separation anxiety disorder, agoraphobia, or selective mutism (Bandelow & Michaelis, 2015). Despite global trends showing a rise in anxiety disorder incidence over the past three decades, geographical disparities persist (Javaid et al., 2023; Yang et al., 2021). High-income countries, such as Australia, tend to report higher prevalence rates compared to low- and middle-income countries (Javaid et al., 2023; Yang et al., 2021). Recent national data from Australia indicates that one in six Australians (15.7%) aged 16-85 have experienced an anxiety disorder in the past

12 months (Slade et al., 2025). In addition to regional differences, sociodemographic patterns are evident. Women are consistently 1.3-2.4 times more likely to experience anxiety disorders compared to men (McLean et al., 2011; Penninx et al., 2021). Anxiety is also more common among adolescents and young adults (Baxter et al., 2013; Wu et al., 2025), LGBTQIA+ individuals (Australian Bureau of Statistics, 2022; Ross et al., 2018), and those who have experienced childhood maltreatment (Li et al., 2016). At a subthreshold level anxiety is even more common, and represents a significant risk factor for developing a clinical disorder (Haller et al., 2014; Zhong et al., 2024).

While presentations vary, anxiety is consistently characterised by excessive worry, fear, or avoidance in response to perceived threats, whether external (e.g., social situations) or internal (e.g., bodily sensations) (Craske & Stein, 2016). Anxiety can cause considerable functional, social, and occupation impairment in an individual's life, with the severity of this impact increasing as symptoms become more chronic (McKnight et al., 2016). Importantly, anxiety often follows a persistent and recurrent course, with symptoms that can fluctuate yet remain unresolved for years without appropriate treatment or support (Craske & Stein, 2016). Collectively, these symptoms contribute to the substantial harms and overall burden of disease associated with anxiety. Globally, anxiety disorders rank as the sixth leading cause of disability, with the greatest burden observed among individuals aged 10-24 years (Vos et al., 2020). In Australia, anxiety disorders account for the highest burden of disease among all mental and substance use disorders (SUD), contributing 3.9% to the nation's total disease burden (Australian Institute of Health and Welfare [AIHW], 2025b). A recent systematic review and meta-analysis has also demonstrated a significant relationship between clinical anxiety and impacts to functional impairment and quality of life among children and adolescents (Dickson et al., 2024). Given the burden and chronicity of anxiety symptoms and related disorders, preventing their onset and escalation as early as possible is paramount; ideally during adolescence and young adulthood when these concerns most commonly emerge.

1.1.1.1 Spotlight on anxiety in young people

Not only are anxiety disorders the most common mental disorder globally, they are also the most common disorders among young people[1] (Rapee et al., 2023). Across all anxiety disorders there is a mean age of onset of 21 years, however, earlier onset is seen for some disorders

[1] The term 'young people' is used in this introduction to broadly capture the age periods across adolescence (typically ages 10-19 years), youth (typically ages 15-24 years), and emerging adulthood (typically ages 17-30 years) (Sawyer et al., 2018).

(Lijster et al., 2017). Typically, separation anxiety disorder and specific phobias are the first to emerge, at ages 10.6 and 11 years respectively (Lijster et al., 2017). Whilst SAD can also be diagnosed in early life, early to middle adolescence (ages 10-15 years) is the peak age of onset (Lijster et al., 2017; Solmi et al., 2022). The age of onset for GAD is more variable. Estimates indicate early 30s as the mean age of onset (Lijster et al., 2017; Solmi et al., 2022), however, manifestations of generalised anxiety symptomology often begin earlier (Köcher et al., 2021; Rapee et al., 2023) and adolescents are more likely to present with subthreshold GAD compared to other ages (Haller et al., 2014). In Australia, 7% of 4-17-year-olds and 32% of 16-24 year-olds have experienced and anxiety disorder in the past 12-months (ABS 2022; AIHW 2025c). Modelling of future global anxiety disorder prevalence indicates that by 2025, prevalence among 15-19 year olds will exceed that of all other age groups, highlighting the importance of prevention efforts during early adolescence (Chen et al., 2025).

1.1.2 Alcohol use prevalence and associated harms

Alcohol consumption and AUD are also highly prevalent. Globally, more than 2.5 billion people aged 15 years and above consume alcohol, with the highest prevalence observed in high-income regions such as Australasia and Europe (World Health Organization [WHO], 2024). At a clinical level, AUD is the most common SUD globally, affecting an estimated 400 million people, or approximately 7% of the world's population aged 15 years and above (WHO, 2024). AUD is characterised by a persistent pattern of problematic alcohol use that leads to clinically significant impairment or distress. AUD is diagnosed as mild, moderate, or severe depending on the number of symptoms e.g., craving alcohol, present in the past 12-months (*Diagnostic and statistical manual of mental disorders : DSM-5™*, 2013). Similar to anxiety disorders, clear gender differences in prevalence estimates exist, with AUD more common among men than women (9.3% versus 4.8%, respectively) (WHO, 2024). Beyond formal diagnostic thresholds, research has identified patterns of alcohol use that confer substantial harm despite not meeting the clinical threshold for AUD (Morris et al., 2025). Terms such as harmful drinking, hazardous drinking, heavy episodic drinking, risky drinking, binge drinking, and problem drinking are frequently used, sometimes interchangeably, to describe these patterns and their related consequences. The primary focus of this thesis is these harmful and hazardous patterns of alcohol use. While these patterns of use may not reach the diagnostic

threshold for AUD, they meaningfully elevate the risk for AUD, adverse physical health outcomes, and psychosocial harms (MacKillop et al., 2022).

In Australia, two-thirds (69%) of the population aged 14 years and over have consumed alcohol in the previous 12 months, and 31% of individuals have drunk at levels which place themselves or others at risk of harm (i.e., risky drinking) (AIHW, 2025a). In this case, risky drinking was defined as exceeding the Australian national health guidelines of >10 drinks per week on average and/or 4 drinks in a single day at least once a month over the previous year (National Health and Medical Research Council, 2020). Men are more likely than women to engage in this pattern of risky drinking (39% versus 23% respectively). There are also other risk factors for harmful alcohol use and subsequent AUD which span biological, psychosocial, and environmental domains. Examples include genetic predisposition (Tawa et al., 2016), early life stressors and adversity (Enoch, 2011; Hughes et al., 2017), and experiencing greater socioeconomic disadvantage (Collins, 2016).

The individual, societal, and economic harms associated with alcohol use and AUD are vast and burdensome. Worldwide, 2.6 million deaths each year are attributable to alcohol use (WHO 2024). Alcohol consumption is associated with more than 200 different diseases and conditions (Im et al., 2023; Shield et al., 2013). In Australia, alcohol use is the 6th highest contributor to the country's burden of disease (AIHW, 2025a). The estimated societal cost of this burden for 2022-2023 alone was $75 billion from use of health services and decreased productivity (Gadsen et al., 2023). At an individual level, alcohol-related harms include an increased risk of chronic diseases, mental disorders and suicide, risk of acute injury, lower performance at school or work, and negative impacts on social relationships due to factors such as an increase in aggressive behaviour (Brain, 2023; Iranpour & Nakhaee, 2019; Isaacs et al., 2022; Shield et al., 2013). In addition, almost half of Australian adults have been affected by others' drinking, with women and younger people disproportionally affected (AIHW, 2025a; Laslett et al., 2025). Such harms can include verbal, physical, or sexual abuse from someone under the influence of alcohol, impacts on the community including noise and vandalism, and workplace disruptions including absenteeism and accidents or injuries while under the influence of alcohol (Karriker-Jaffe et al., 2018; Laslett et al., 2025). The harms associated with alcohol use are not distributed equally across those who drink, rather, earlier age of drinking initiation is associated with greater alcohol related harms (Clare et al., 2025). Similarly, earlier age of drinking onset is a strong predictor of later drinking habits and risk of an AUD (DeWit et al., 2000; Gardner et al., 2024; Sjödin et al., 2024).

1.1.2.1 Spotlight on alcohol use in young people

Alcohol use and related harms among young people are prevalent and pervasive. Although the age of first drink differs across nations, alcohol use during adolescence and young adulthood is relatively common in high-income countries (WHO, 2024). Globally, 22% of 15-19-year-olds (WHO, 2024), and 31% of 14-17-year-olds in Australia have consumed alcohol in the past year (AIHW, 2024). Harmful patterns of alcohol use are often more prevalent among young people than in the broader population. In Australia, 42% of 18-24-year-olds consume alcohol at risky levels, with higher rates observed among me than women (45% versus 40% respectively) (AIHW, 2024). Consistent with this pattern, recent Australian data indicate that young people aged 16-25 have the highest prevalence of AUD (5.7%) compared to other age groups (Slade et al., 2025). This prevalence is again higher among young men than young women (Danpanichkul et al., 2025; Slade et al., 2025). Beyond gender differences, a systematic review has identified externalising symptoms (e.g., aggression and impulsivity) and illicit drug use as predictors of AUD among young adults (Meque, Salom, et al., 2019).

Despite the ubiquity of alcohol use in young people's lives, there has been a decreasing trend of alcohol consumption in high-income countries across the past two-decades among younger age groups, which has not been observed across the general population (Caluzzi et al., 2022; Vashishtha et al., 2021). Arguments for such reductions include a de-normalisation of drinking and normalisation of non-drinking, substitution with other illicit substances, changes in parental practices, impacts of stronger alcohol policies, increased investment in prevention and health promotion within schools and communities, overall shifts in leisure time, and increasing use of digital technology (Caluzzi et al., 2022; Kraus et al., 2020; Vashishtha et al., 2020). However, these declines are not uniform across all young people. In Australia, potential rebound effects in drinking are being observed for young women. Specifically, 28% of women aged 14-17 years had consumed alcohol in the past 12-months in 2019, with this rising to 35% in 2022-2023 (AIHW, 2024). This rebound, coupled with persistently high rates of risky alcohol use among 18-24-year-olds, indicates that high risk subgroups of young people remain despite broader downward trends. Given these patterns, adolescence and young adulthood continue to represent a critical developmental window for alcohol-related prevention. Intervening during this period not only reduces immediate harms but also plays a pivotal role in preventing risky use from escalating into a chronic, entrenched AUD.

1.1.3 Co-occurring anxiety and alcohol use and associated harms

Not only are anxiety and alcohol use highly prevalent in isolation, they also commonly co-occur (also known as 'comorbidity'). Estimates of this comorbidity differ across settings, with a higher prevalence observed in clinical or treatment seeking samples compared with community-based samples. A meta-analysis of national epidemiological surveys found that, in the general population, 20-40% of individuals with anxiety will also experience an AUD in their lifetime (Lai et al., 2015). Conversely, among individuals with an AUD, the odds of also having an anxiety disorder are approximately 30% higher than in the general population (Glantz et al., 2020; Grant et al., 2015). Recent Australian population data among adults aged 16-85 years further illustrate this comorbid relationship, which varies across anxiety disorder. The probability of having an AUD given the presence of GAD was 8.7%, panic disorder 5.8%, and SAD 3.2% (Sunderland et al., 2025). When examined in the opposite direction, conditional probabilities were higher: the probability of SAD given an AUD was 19.3%, GAD given an AUD 10.7%, and panic disorder given an AUD 9.7% (Sunderland et al., 2025). In treatment settings, prevalence estimates are even higher, with up to one in three people receiving treatment for an AUD or a SAD experiencing both disorders (Bakken et al., 2005; Burns et al., 2005) and one in two people experiencing both AUD and GAD (Smith & Book, 2010). Co-occurrence with AUD tends to differ depending on the specific anxiety disorder, with twin studies demonstrating that SAD has the strongest association with AUD, over and above that of other anxiety disorders (Torvik et al., 2019). Beyond clinical or diagnostic thresholds, there is also evidence that elevated levels of anxiety sensitivity are consistently associated with patterns of harmful alcohol use including hazardous drinking and alcohol-related problems (DeMartini & Carey, 2011; Paulus et al., 2017; Schmidt et al., 2007; Taylor, 1999). Gender differences in anxiety-alcohol use comorbidity have been explored, with evidence to suggest women are more likely than men to experience both disorders (Kessler et al., 1997; Smith & Randall, 2012). Women have also been shown to engage in stress-related alcohol use (i.e., self-medication) more often than men (Johannessen et al., 2017; Peltier et al., 2019).

Compared with individuals who have either an anxiety disorder or AUD alone, co-occurring anxiety and AUD are associated with greater clinical complexity. Comorbid presentations are linked to more severe symptoms of both conditions, greater functional impairment, poorer quality of life, and increased risk of additional emotional disorders, particularly depression (Bartoli et al., 2021; Kushner et al., 2000). Moreover, co-occurrence is associated with poorer treatment response, more complicated management, and worse overall prognosis compared

with either disorder in isolation. (Anker & Kushner, 2019; Kushner et al., 2000; Smith & Randall, 2012; Wolitzky-Taylor et al., 2011). Greater health service utilisation is also seen among those with co-occurring conditions as well as a greater loss to productivity and subsequent economic burden (Burns et al., 2005; Souêtre et al., 1994). Clinical studies and reviews have also documented a poorer response to AUD treatment among individuals with anxiety, including a higher return to drinking post-treatment (Burns et al., 2005; Driessen et al., 2001; Kushner et al., 2005; Schellekens et al., 2015; Stapinski et al., 2024; Tonigan et al., 2010; Wolitzky-Taylor et al., 2011). The impacts of subthreshold anxiety within alcohol treatment settings have also been documented. Among AUD treatment seeking samples, higher rates of sub-clinical anxiety are associated with greater alcohol use during and up to one year post-treatment (Hurlocker et al., 2023). In contrast, impacts of alcohol use on individuals seeking treatment for anxiety are less well-documented. There is evidence to suggest that pre-treatment problem drinking is predictive of poorer social interaction anxiety outcomes but not social performance or panic anxiety outcomes (McEvoy & Shand, 2008). Presence of alcohol problems (vs. no problems) at baseline may also impact long-term, but not short-term, anxiety treatment outcomes (Wolitzky-Taylor, Brown, et al., 2015). During treatment follow-up, AUD has also been associated with a greater recurrence of anxiety disorders (Bruce et al., 2005). Thus, although both anxiety and alcohol use can be debilitating in and of themselves, their combination is particularly pernicious, representing a significant public health concern. Preventing the onset of this comorbidity, which typically develops early in life is paramount.

1.1.3.1 Spotlight on co-occurring anxiety and alcohol use in young people

Robust estimates of co-occurring anxiety disorders and AUD among young people are scarce, yet both alcohol use and anxiety symptoms typically escalate and peak across adolescence and young adulthood (Grant et al., 2015; Legerstee et al., 2019; Lijster et al., 2017). Given the earlier age of onset for anxiety disorders, they often precede the development of AUD, with anxiety estimated to precede alcohol problems in up to 75% of co-occurring cases (Buckner et al., 2013; Kushner et al., 1990; Stapinski, Sannibale, et al., 2021). Adolescent samples also indicate potential comorbidity even at subthreshold levels, with 22% of adolescents with subthreshold anxiety also meeting criteria for subthreshold AUD (Lewinsohn et al., 2004).

Early onset anxiety disorders, during adolescence, have also been associated with earlier first use of alcohol (Birrell et al., 2015; Kaplow et al., 2001), faster progression from first use to

regular use, and increased risk of transition to AUD (Christie et al., 1988; Conway et al., 2016; Johannessen et al., 2017; Kushner et al., 1999; Zimmermann et al., 2003). In contrast to evidence that anxiety increases the risk of later alcohol use and related harms, a smaller body of research suggests the opposite: that anxiety may act as a protective factor against alcohol use during adolescence (Kaplow et al., 2001; Peeters et al., 2024; Wills et al., 1999). For example Peeters et al. (2024) found that higher anxiety symptoms predicted lower heavy drinking during adolescence, though these associations were no longer evident in young adulthood at ages 22 or 25. Protective effects of anxiety have been attributed to increased fear of authority, reluctance to engage in illegal or risky activities, discomfort in social situations, and heightened concern about negative consequences of alcohol use. Among adolescents these attitudes appear more pronounced among girls than boys (Pardini et al., 2007; Rieselbach et al., 2023).

The findings of anxiety as both a risk and protective factor underscore the complexity of the anxiety-alcohol relationship, and justify the need to examine this association across finer-grained developmental periods spanning early adolescence to young adulthood. Within these developmental periods there are key stages as outlined in Table 1.1 (Arnett et al., 2014; Sawyer et al., 2018; WHO, 2014). In this thesis, the term 'young people' is used inclusively to capture this range of developmental stages.

Table 1.1: Developmental periods of adolescence and young adulthood

Developmental period and related terms	**Age range**
Adolescence	10 -19
Early adolescence	10-12
Middle adolescence	13-15
Late/older adolescence	16-19
Young adulthood/ emerging adulthood	18 - ~30
Youth	15-24
The 'new' adolescence	10-25

These developmental periods encompass rapid social, cognitive, and emotional changes, during which the meaning, function, and consequences of anxiety can shift markedly across these stages (Sawyer et al., 2018). Anxiety related factors that appear protective of alcohol use in early adolescence may weaken, disappear, or even reverse by young adulthood. For example, Colder et al. (2017) reported that generalised and social anxiety symptoms were protective

against alcohol use in early and middle adolescence, but this effect diminished with age particularly among young people with elevated social anxiety. By young adulthood, most studies report that elevated anxiety sensitivity is linked to greater hazardous drinking in community samples (McKenzie et al., 2011; Paulus & Zvolensky, 2020; Stewart et al., 2002). Interestingly, however, a meta-analysis of alcohol use in college students concluded that social anxiety was negatively related to alcohol use but positively related to alcohol-related problems (Schry & White, 2013). Together, these findings highlight that the anxiety-alcohol relationship is not static across development but varies by age, anxiety construct, and outcome examined. Examining associations both within and across distinct developmental windows is therefore critical, as broad age groupings risk obscuring when and how anxiety shifts from potentially functioning as a protective factor to a risk factor for alcohol-related harm. These developmental shifts underscore the need for theoretical frameworks that can account for when, why, and for whom anxiety and alcohol use become intertwined across adolescence and young adulthood.

1.2 Theoretical models of the anxiety-alcohol relationship

The nature and interrelationship between anxiety and alcohol use is complex, with several theories proposed to explain how these two concerns develop and interact. Broadly, three pathways have been identified to explain the onset and maintenance of comorbid anxiety and alcohol use concerns, as outlined below (Santucci, 2012; Smith & Randall, 2012; Stewart & Conrod, 2008). Pathways one and two may be direct (i.e., causal) or indirect via intermediatory factors (Marel et al., 2022).

1. **Anxiety as a risk factor for alcohol use (anxiety → alcohol)**
   Elevated anxiety may lead individuals to use alcohol to manage or cope with distress, which over time can contribute to and/or exacerbate patterns of harmful or problematic alcohol use.
2. **Alcohol use as a risk factor for anxiety (alcohol → anxiety)**
   Alcohol consumption, particularly heavy or prolonged use, can induce or exacerbate anxiety symptoms, creating a cycle in which alcohol's effects heighten vulnerability to anxiety.
3. **Shared underlying factors influence both anxiety and alcohol use**
   Common psychological, biological, or environmental influences may increase risk for both anxiety and alcohol involvement, giving rise to their frequent co-occurrence.

These pathways are not necessarily mutually exclusive, with evidence of a bidirectional anxiety-alcohol relationship also observed. Once established co-occurring anxiety and alcohol use can exacerbate each other in a feed-forward cycle, aptly referred to as the "vicious cycle of comorbidity" in prior work (George et al., 1990; Kushner et al., 2000; Stewart & Conrod, 2008). This cycle helps explain the persistence and mutually reinforcing nature of anxiety-alcohol comorbidity. The three onset and developmental pathways of co-occurring anxiety-alcohol are outlined below (subsection 1.2.1 to 1.2.3), followed by a discussion of theoretical models that explain the bidirectional and mutually maintaining processes underlying this comorbidity (subsection 1.2.4 and 1.2.5).

1.2.1 Anxiety as a risk factor for alcohol use pathway

Evidence for the first pathway, whereby anxiety increases risk for alcohol use, has received the greatest empirical attention to date. Several influential models support this pathway including the self-medication hypothesis (Khantzian, 1985, 1997; Quitkin et al., 1972), tension-reduction theory (Conger, 1956; Greeley & Oei, 1999), and the stress response dampening model (Sher & Levenson, 1982). Collectively, these frameworks share a central premise: individuals consume alcohol to alleviate or "cope" with anxiety symptoms. In the tension-reduction hypothesis, alcohol is used to reduce a state of "tension", operationalised as the subjective emotional experience of stress often accompanied by objective physiological indices such as increased heart rate (Greeley & Oei, 1999). This conceptualisation was refined by the stress-response dampening model, which emphasised the role of perceived stress as a subjective component of tension (Dvorak et al., 2018; Sher & Grekin, 2007). Central to these models are positive cognitive beliefs and expectancies regarding alcohol's anxiolytic effects on emotion, behaviour, or mood (De Boer et al., 1993). For example, an individual with elevated anxiety may expect alcohol to reduce feelings of nervousness and therefore drink in social situations to manage anxiety.

Across these models, a key mechanism underpinning this pathway is alcohol's short-term anxiolytic or stress dampening effect. Pharmacologically, alcohol acts as a central nervous system depressant by enhancing Gamma-Aminobutyric Acid (GABA) activity and reducing amygdala reactivity, temporarily lowering anxiety and physiological arousal (Roberto et al., 2021). These acute effects can provide immediate relief from distress, thereby negatively

reinforcing alcohol consumption as a coping strategy (Blume et al., 2000). Over time, repeated use of alcohol for its anxiolytic properties can lead individuals to increasingly rely on drinking as a coping strategy. This escalation not only increases vulnerability to hazardous patterns of alcohol use but also heightens the risk of developing an AUD (Blume et al., 2000; Smith & Randall, 2012).

The use of alcohol to cope or self-medicate is well documented among individuals with elevated anxiety, and higher prevalence is observed in clinical over community samples (Smith & Randall, 2012). Further support for this pathway comes from the temporal patterns of onset. As outlined in subsection 1.1.3.1, anxiety disorders typically emerge earlier in life than AUD (Buckner et al., 2013), and prospective longitudinal studies consistently show that primary anxiety predicts subsequent development of AUD (Turner et al., 2018). More recently, research has increasingly focused on identifying the mechanisms that mediate or moderate this relationship to better understand the nature of this potential causal pathway.

Hypothesised mechanisms underlying the anxiety → alcohol use pathway span cognitive, behavioural, and psychosocial domains. Constructs that have received substantial empirical attention include drinking motives, alcohol outcome expectancies, repetitive negative thinking, emotion dysregulation, and distress intolerance (DeMartini & Carey, 2011; Sloan et al., 2017; Wolitzky-Taylor, Guillot, et al., 2015; Wolitzky-Taylor et al., 2016). Across studies, these mediating mechanisms have been shown to contribute to the association between anxiety and alcohol use. However, the diversity in anxiety and alcohol constructs measured across different studies has made it challenging to isolate the specific effects of individual mechanisms. Ultimately, no single mechanism is likely to account for the anxiety → alcohol pathway. Instead, a combination of psychological, cognitive, and biological processes would be expected to contribute to both the development and maintenance of this association. To date these mechanisms have not been systematically synthesised.

1.2.2 Alcohol use as a risk factor for anxiety pathway

The opposite pathway, whereby alcohol use induces or increases anxiety has also been proposed. The dominant theory in support of this pathway is the substance-induced anxiety model (Kushner et al., 2000; Smith & Randall, 2012) and the kindling/stress hypothesis (Breese et al., 2005). In the short-term, alcohol can heighten anxiety through both physiological rebound effects and situational or cognitive responses following drinking (Ehlers et al., 2019;

Marsh et al., 2019). Physiologically, increases in anxiogenic symptoms are well documented during hangover and alcohol withdrawal states (Brady et al., 2007; Johnston et al., 1991; Rothman et al., 2025). The term "hangxiety" has been coined for this next-day anxious state (Marsh et al., 2019). While hangxiety can be situational, stemming from worries about what one said or did while intoxicated, there are also potential neurobiological responses underlying these effects (Marsh et al., 2019; Smith & Randall, 2012). Specifically, gamma-aminobutyric acid type A ($GABA_A$) receptors play a fundamental role in the short- and long-term effects of alcohol (ethanol) on the body's central nervous system (Davies, 2003). During alcohol intoxication, there is increased activity of the neurotransmitter $GABA_A$ which can result in anxiolytic and calming effects. With chronic alcohol use, however, neuroadaptation occurs, including downregulation of $GABA_A$ receptors and compensatory upregulation of excitatory systems. This can result in heightened anxiety, particularly during periods of reduced intake or withdrawal (Most et al., 2014). Relatedly, the kindling/stress hypothesis proposes that repeated withdrawals from chronic alcohol use contribute to a progressive development of persisting neuro-adaptive changes (i.e., kindling) that sensitises withdrawal-induced anxiety and allows stress to evoke symptoms associated with negative affect during abstinence (Breese et al., 2005). These neurobiological processes also help contextualise commonly reported anxiety symptoms following alcohol use, such as hangxiety. Although post-drinking anxiety symptoms appear relatively common (Rothman et al., 2025), alcohol-induced anxiety disorders are relatively rare (Stewart & Conrod, 2008). Accurate estimates of alcohol-induced anxiety disorders are scarce, however, estimates of prevalence for substance-induced anxiety disorders more broadly are approximately 1-2% (Grant et al., 2004; Torrens et al., 2011). Nonetheless, even sub-clinical anxiety symptoms during withdrawal or abstinence may reinforce ongoing alcohol use as a maladaptive coping strategy.

Further to these neurobiological processes, the psychosocial impacts of chronic alcohol use and AUD may in part explain why alcohol use can increase anxiety (Smith & Randall, 2012). Repeated heavy and prolonged alcohol consumption can lead to cumulative problems across interpersonal relationships, employment, study, and finances (Collins, 2016; Klingemann & Gmel, 2001). Interference with daily functioning and responsibilities, is in fact, one of the diagnostic criteria for an AUD. These psychosocial impacts may activate and intensify stress or anxiety among already vulnerable individuals. However, specific causal mechanisms underlying this pathway have been less investigated compared to mechanisms of the anxiety → alcohol use pathway.

1.2.3 Shared underlying factors influence both anxiety and alcohol use pathway

Rather than a direct causal relationship between anxiety and alcohol use, the alternative view is that comorbidity is a result of a common or shared "third" factor. This "common factor" model suggests there is no causal relationship between the anxiety and alcohol use, but rather an underlying vulnerability which contributes to the onset of both (Smith & Randall, 2012; Stewart & Conrod, 2008). Shared genetic risk factors for both anxiety disorders and AUD have been identified in twin and familial studies (Lahey et al., 2017; Nelson et al., 2000; Nurnberger et al., 2004; Tambs et al., 1997) and molecular genetic studies (Cerdá et al., 2010; Hodgson et al., 2016). Using a longitudinal, population twin study Torvik et al. (2019) found that positive associations between AUD and anxiety disorders (other than SAD) were fully explained by shared genetic risk factors. For SAD, however, biometric modelling favoured a direct causal relationship from SAD to AUD above models with shared genetic and environmental risk factors.

Further to hypotheses of a shared genetic basis for anxiety and alcohol, is the potential of common personality traits or psychopathology contributing to their association. Anxiety sensitivity is a key candidate and has been linked to the incidence of both anxiety disorders and AUD (DeMartini & Carey, 2011; Smith & Randall, 2012). Other potential contributors include socioeconomic status, history of trauma and/or adverse childhood experiences, and a general tendency towards psychopathology, often conceptualised as the p factor (Caspi et al., 2014; Collins, 2016; de Aguiar & Bloc, 2024; Elmore & Crouch, 2020; Forbes et al., 2019; Kirkbride et al., 2024; Lynch et al., 2024; Rehan et al., 2017). The p factor may explain, or even drive, variation across multiple forms of psychopathology, providing a potential account for comorbid associations such as the co-occurrence of anxiety and alcohol concerns (Caspi et al., 2014; Forbes et al., 2019). Evidence that a specific mechanism operates in both the anxiety → alcohol and alcohol → anxiety pathways would further support the role of common underlying factors. However, conclusive evidence for these candidates remains scarce. Investigating mediators and moderators of the bidirectional anxiety-alcohol association is therefore critical, as these analyses can clarify both the processes and conditions under which co-occurring anxiety and alcohol use emerge and persist. Identifying such third variables would be particularly

advantageous for prevention as interventions targeting a single common factor could, in theory, prevent both anxiety disorder and AUD onset or escalation.

1.2.4 Bidirectional relationship between anxiety and alcohol use

The aforementioned hypothesised pathways to the onset and exacerbation of anxiety and alcohol use comorbidity suggest this relationship may be bidirectional. Previously, investigations of a potential bidirectional relationship were limited to cross-sectional designs, prohibiting conclusions about the temporal onset (Kushner et al., 2000). A limited number of longitudinal studies have explored this bidirectional relationship within the same sample with mixed results. In a Dutch study, anxiety disorders at baseline were more likely to predict a first-incident AUD during the 3-year follow up, but individuals with an AUD at baseline had no higher risk for an anxiety disorder at follow-up (Marquenie et al., 2006). The opposite was seen in a different Dutch study where anxiety disorders in the past year did not predict a first incidence of substance use disorder (AUD and drug use disorders), whereas SUD did predict a first-incident anxiety disorder (de Graaf et al., 2013). In contrast, other studies do support a bidirectional or reciprocal relationship. A population-based study in the United States identified predictive associations in both-directions over 3 years between GAD and AUD (B. F. Grant et al., 2009). More recently a Dutch population-based study saw comparable results where individuals with an AUD had a higher risk of developing anxiety disorders, and vice versa. These results were robust to adjustment for sociodemographic factors (Ummels et al., 2022). Beyond clinical classifications, there is also support that anxiety symptoms are positively associated with alcohol use quantity and vice versa, as demonstrated in a longitudinal sample of Australian adults (D'Aquino et al., 2025).

1.2.5 The mutual maintenance of anxiety and alcohol concerns

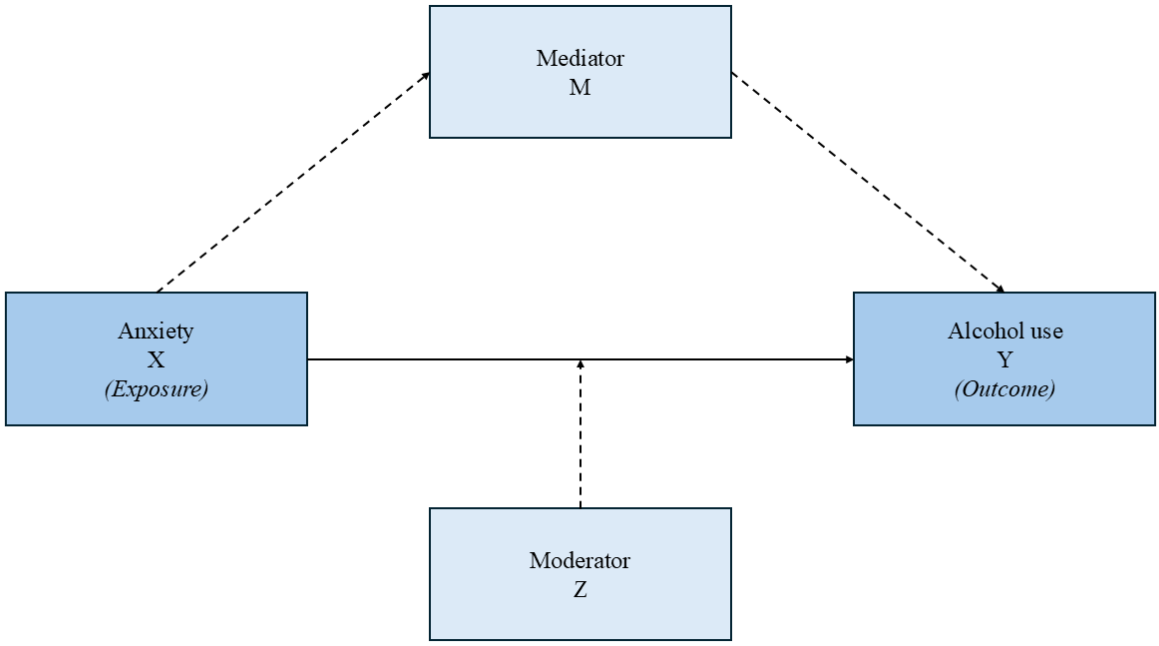
Regardless of the initial onset or temporal sequencing of anxiety and alcohol use concerns, once established, they are widely understood to mutually maintain and exacerbate one another (Stewart & Conrod, 2008). As introduced in subsection 1.2, this dynamic relationship is often described as a 'vicious cycle', that operates in a feed-forward manner. For example, a person with elevated social anxiety who uses alcohol in social situations may experience short-term relief from their anxiety, which negatively reinforces alcohol use and strengthens the belief that

reducing drinking would worsen their anxiety. Over time, greater reliance on alcohol can contribute to more intense withdrawal effects (e.g., hangxiety), further entrenching this cycle. Together, this cycle outlines how both the self-medication and alcohol-induced intensification of anxiety processes contribute to the maintenance of comorbidity. This reciprocal relationship emphasises the necessity of understanding features which contribute to anxiety-alcohol maintenance so they can be targeted in prevention and intervention approaches.

1.2.6 Causal mechanisms underlying pathways of anxiety and alcohol use.

The prior sections outlined the significant body of work to date which has focused on estimating the prevalence of co-occurring anxiety and alcohol use, and the theoretical models for the basis of this comorbidity. Potential mediators and moderators were also introduced in the context of these pathways. To further advance the theoretical understanding and disentangle the anxiety and alcohol relationship, mediators and moderators must be investigated to elucidate mechanisms within this relationship. Conceptually, a mediator or moderator is a third variable which is thought to account for the relationship between an independent/exposure and outcome variable. A mediator can help explain *how* or *why* something occurs, as it lies on the causal sequence between two variables. Moderators are not part of the causal sequence but instead influence the *strength* or *direction* of the association between the exposure and outcome of interest (Baron & Kenny, 1986). Figure 1.1 illustrates these concepts in the context of the anxiety → alcohol pathway using a direct acyclic graph (DAG).

Figure 1.1: Direct acyclic graph of a mediating and moderating variable in the anxiety → alcohol relationship



Despite the theoretical and clinical importance of understanding mechanisms underlying the anxiety-alcohol relationship, to date, mediating or moderating factors have not been systematically reviewed. One existing review focused specifically on drinking motives in the relationship between anxiety sensitivity and alcohol use, which highlighted several methodological limitations of the literature identified as well as the need to evaluate gender-related patterns further (DeMartini & Carey, 2011). A comprehensive synthesis of the fragmented literature on mediators and moderators is therefore needed. Given that prior reviews of individual factors, such as drinking motives and gender differences, have yielded inconsistent findings, clarification is required as to whether these factors represent viable targets for prevention, early intervention, or treatment.

1.3 Treating co-occurring anxiety and alcohol use concerns

The prevalence of co-occurring anxiety and alcohol use concerns has prompted efforts to identify effective treatments for this common clinical presentation. As noted earlier, individuals with co-occurring anxiety and AUD typically experience poorer outcomes when receiving conventional single-disorder psychological and behavioural treatments targeting either anxiety or alcohol use alone (McHugh, 2015; Stapinski et al., 2024; Wolitzky-Taylor et al., 2011). The

efficacy of single-disorder treatments among people with both an anxiety disorder and AUD have been more extensively documented for AUD-focused rather than anxiety-focused treatments. Across multiple AUD treatment trials, individuals with co-occurring anxiety disorders demonstrate poorer treatment efficacy and reduced long-term maintenance of gains (Stapinski et al., 2024). Inferior alcohol outcomes have been observed among those with co-occurring GAD (Farris et al., 2012; Smith & Book, 2010), panic disorder (Kushner et al., 2005), SAD/social phobia (Kushner et al., 2005; Tonigan et al., 2010), and anxiety symptoms more broadly (Burns et al., 2005; Driessen et al., 2001). SAD in particular has been shown to predict relapse to drinking, especially early relapse, above and beyond other anxiety or mental disorders (Kushner et al., 2005; Schellekens et al., 2015). Contrary to these inferior outcomes, a small number of studies have found no significant differences in alcohol treatment outcomes between individuals with and without anxiety disorders. For example, Tómasson and Vaglum (1996) reported no association between anxiety disorders and alcohol consumption at a 15-month follow-up, nor with likelihood of abstinence at 28 months, although only 16% of participants remained abstinent by that point. A more recent study has shown that comorbid GAD, panic disorder, nor social phobia affected alcohol treatment outcomes (frequency and intensity of drinking) (Mellentin et al., 2015). Similarly, a secondary analysis of an online proactive "e-alcohol" therapy trial found no evidence that moderate-severe anxiety symptoms at baseline modified the effect of treatment initiation, compliance, or alcohol intake at the 3- and 12- month follow-up (Egan et al., 2025). Despite these mixed findings, the prevailing consensus remains that alcohol-focused treatments alone are insufficient for individuals with co-occurring anxiety disorders (Haber et al., 2021; Marel et al., 2022).

Evidence of the contrary, an AUDs impact on anxiety-focused treatment, is limited. This knowledge gap likely reflects the common exclusion of participants with alcohol or substance use problems from psychotherapy trials for anxiety disorders (Marel et al., 2016; Morris et al., 2005). Among the limited evidence available, one study of cognitive behavioural therapy (CBT) for panic disorder and social phobia found that higher pre-treatment alcohol use did not predict change in panic symptoms, but was associated with poorer improvement in social interaction anxiety among an adult sample in the United States (McEvoy & Shand, 2008). Conversely, Subotic-Kerry et al. (2021) found no effect of pre-treatment alcohol *consumption* on SAD treatment response; however, presence of a comorbid AUD was weakly associated with poorer social anxiety symptom scores at follow-up. Longitudinal data also suggest enduring effects. In a 12-year prospective study, the presence of an alcohol or other substance

use disorder reduced the likelihood of recovery from GAD by nearly fivefold and increased the likelihood of GAD recurring over fourfold (Bruce et al., 2005). Though no such association was found for the recovery or recurrence of social phobia or panic disorder. Alcohol use during treatment for anxiety may also increase treatment drop-out, as seen in a 12-week outpatient CBT treatment for panic disorder and agoraphobia (Martinsen et al., 1998). Overall, while efficacious psychological treatments exist for anxiety and alcohol use disorders when treated separately, comorbid presentations often lead to poorer outcomes. This likely reflects the mutually reinforcing nature of the two disorders, which is not adequately addressed in single-disorder treatment approaches (Kushner, 2014; Stapinski et al., 2024; Wolitzky-Taylor, 2023).

The adverse outcomes observed when treating anxiety or alcohol use in isolation can be partly attributed to structural barriers in treatment delivery. Mental health and substance use services are often siloed, resulting in a comorbidity "roundabout" in which individuals are referred back and forth between services, required to repeatedly retell their story to different providers, fall through service gaps, or are excluded from care altogether (Kay-Lambkin et al., 2004; Marel et al., 2022). These limitations highlight the need for treatment approaches which address both anxiety and alcohol concerns simultaneously.

1.3.1 Dual-focused treatments delivered sequentially or concurrently/in parallel

One approach to improve treatment outcomes for individuals with co-occurring anxiety disorders and AUD is the delivery of *concurrent* or *dual-focused* treatments. In this format, anxiety-focused and alcohol-focused interventions are delivered either in parallel or sequentially, but not necessarily by the same treatment professional, at the same time, or within the same facility (Randall et al., 2008). In a seminal trial targeting co-occurring SAD and AUD, Randall et al. (2001) randomised participants to either a 12-week alcohol-only treatment or dual-focused treatment in which each session was divided equally between alcohol-focused CBT and SAD-focused CBT. Contrary to expectations, at the 3-month follow up, the dual-focused treatment group demonstrated poorer drinking outcomes, including fewer days abstinent, a higher percentage of heavy drinking days, and higher total number of drinks consumed, relative to the alcohol-focused treatment group. Similarly, Bowen et al. (2000) found no additional benefit of a sequential dual-focused panic and alcohol treatment compared to an alcohol-focused treatment alone for either anxiety or alcohol-related outcomes. For

anxiety symptoms, however, some additional benefits from dual-focused treatment have been reported. In one randomised controlled trial (RCT), Schadé et al. (2005) compared 32 weeks of alcohol-focused treatment to the same treatment supplemented with twelve, weekly anxiety-focused CBT sessions and optional pharmacotherapy. The sequential dual-focused group showed greater reductions in social anxiety and agoraphobic symptoms, although no additional improvements in alcohol outcomes were observed. Overall, support for parallel and sequential dual-focused treatments remains limited, and sometimes outcomes are inferior to single-disorder approaches. The lack of therapeutic and physical integration between anxiety and alcohol treatments may place additional cognitive demands on clients and, in some instances, increase exposure to alcohol-related settings or drinking as a coping response during anxiety exposure tasks (Randall et al., 2008). The mixed evidence from single-disorder and dual-focused approaches underscores the importance of addressing anxiety disorder and AUD simultaneously, along with the underlying mechanisms that mutually reinforce their connection.

1.3.2 The case for fully integrated anxiety-alcohol treatment

To address the limitations of single-disorder and dual-focused treatments, integrated treatment models for anxiety disorders and AUD have garnered significant attention in the past two decades (Hesse, 2009; Kushner et al., 2006; Wolitzky-Taylor, 2023). Broadly, integrated treatments are underpinned by a central idea to target both anxiety disorders and AUD concurrently, whilst also considering and addressing factors which contribute to the mutually reinforcing nature of anxiety-alcohol comorbidity highlighted earlier. There is now clear empirical and clinical support for the efficacy of integrated anxiety-alcohol treatments as the most efficacious way to treat co-occurring anxiety disorders and AUD, as evidenced by reviews on the treatment and management of co-occurring anxiety and alcohol concerns (Baillie & Sannibale, 2007; Farchione et al., 2017; Stapinski et al., 2024; Stapinski et al., 2015; Wolitzky-Taylor, 2023). Several psychotherapy clinical trials to date have now examined the efficacy of such integrated treatments across varying anxiety disorders and co-occurring AUD.

Early work from Kushner et al. (2006) demonstrated that integrated CBT treatment for panic disorder and AUD resulted in superior clinical reductions in panic disorder symptoms compared to an alcohol-focused control at the 4-month follow up. The percentage of individuals who relapsed was similar between groups, although the integrated group were less

likely to meet alcohol dependency criteria at follow-up (Kushner et al., 2006; Kushner, Sletten, et al., 2009). Building upon this, the integrated treatment was expanded to include SAD and GAD (Kushner et al., 2013). A RCT compared the transdiagnostic, integrated CBT for AUD and anxiety to an AUD-only control condition (AUD residential treatment plus a Progressive Muscle Relaxation Training program). Superior benefits for all alcohol outcomes (i.e., relapse, binge drinking, drinks per month) were demonstrated in the integrated treatment group. Both groups experienced comparable anxiety reductions post-treatment, with the integrated treatment group sustaining reduction at the 4-month follow-up. Similar results were found in a study comparing routine alcohol-focused counselling to an integrated CBT treatment for alcohol and anxiety and/or depression in an outpatient hospital setting (Morley et al., 2016). Superior benefits of the integrated treatment were seen for most alcohol outcomes (i.e., number of days to relapse and days abstinent); however, reduction in anxiety and depression symptoms were comparable across the two groups. Lastly an integrated treatment for comorbid anxiety and SUD adapted an efficacious anxiety-focused CBT program to be suitable for use with individuals who have co-occurring anxiety and SUD (Wolitzky-Taylor, Krull, et al., 2018). The adapted, integrated anxiety and substance use treatment was delivered in a group format and compared to usual SUD-only outpatient care. At the 6-month follow-up, individuals in the integrated treatment had superior reductions in anxiety symptoms and alcohol drinking days relative to individuals in the SUD-only treatment.

The effectiveness of integrated treatment for AUD and SAD specifically has been evaluated across two RCTs (Stapinski, Sannibale, et al., 2021; Wolitzky-Taylor et al., 2022). Stapinski, Sannibale, et al. (2021) compared 10 individual alcohol-focused CBT sessions to integrated SAD and alcohol sessions. Both treatments similarly reduced alcohol consumption and severity across the 6-month follow-up, however greater improvements were seen in SAD symptoms, depression, and quality of life for the integrated group. Comparable outcomes were seen in another study comparing an integrated SAD and AUD treatment to a usual outpatient CBT alcohol-focused treatment (Wolitzky-Taylor et al., 2022). By the 6-month follow-up, the integrated treatment demonstrated superior improvements on the number of drinking days in the past 30 days, and social anxiety severity, however, both groups saw comparable reductions for alcohol related problems.

1.3.2.1 Levels of integrated treatment approaches

Evidently there are therapeutic advantages to integrated treatments, with the aforementioned studies demonstrating some difference on anxiety, alcohol, and/or broader quality of life related

outcomes. These differences in outcomes may be a reflection of differences in the design and theory underpinning the level of therapeutic "integration". As integrated treatment becomes more common place, a model has been proposed to conceptualise the levels (or tiers) of treatment integration within the context of comorbid anxiety and SUDs (Wolitzky-Taylor, 2023). A three-level integration model is proposed which outlines the level of integration, but not necessarily superiority of one level over the other. Level 1 involves integration at the content level, with additional content usually added into an existing treatment for one problem as an adjunctive, tailored treatment. This level aligns with the previously described intergraded SUD and anxiety disorder treatment by Wolitzky-Taylor and colleagues which adapted their efficacious CBT protocol for anxiety disorders (Coordinated Anxiety Learning and Management for Addiction Recovery Centers; CALM ARC) for use in patients with co-occurring anxiety disorder and SUD (Wolitzky-Taylor, Krull, et al., 2018). Level 2 integration involves a stand-alone treatment specifically designed for comorbidity, with components directly targeting both concerns. Such interventions incorporate evidence-based principles from anxiety and alcohol treatments, alongside strategies that explicitly address the mutual maintenance of both concerns (Stewart & Conrod, 2008). An integrated treatment for SAD and AUD that targets their reciprocal relationship is an example of this level of integration. Lastly, level 3 integration involves a stand-alone treatment that targets processes or mechanisms underlying both problems. This includes integration at the content, delivery, and mechanism level whereby treatment components targeting malleable factors underlying both anxiety and substance use are addressed, particularly transdiagnostic factors. As highlighted earlier, a significant body of work has begun exploring the malleable factors which potentially mediate the anxiety-alcohol relationship; however, to date no synthesis of these potential mechanisms has been conducted. RCTs at this level of treatment integrating have more commonly focused on samples with high risk or hazardous alcohol use, rather than diagnosed AUD. From the small number of studies applying this transdiagnostic integrated approach, there is preliminary efficacy in reducing drinking motives and emotional relief alcohol expectancies (Watt et al., 2006). Whether this approach is efficacious for individuals with co-occurring anxiety and alcohol concerns at a *disorder* level still requires further investigation. Importantly, the success of such integrated interventions depends on a clear understanding of malleable mediating mechanisms related to both anxiety and alcohol use symptom reduction.

Together, the varying levels of integrated treatment have demonstrated efficacy above and beyond single-disorder or dual-focused treatments across multiple settings (Kushner et al.,

2013; Stapinski et al., 2024; Wolitzky-Taylor, 2023). Despite these advances, such treatments are often sought long after anxiety disorders and AUD first emerge during youth. Across the aforementioned integrated anxiety and AUD treatment trials, the lowest mean age of participants was 36 years old, as seen in the study from Stapinski and colleagues (2021). Evidently, this is long after typical disorder onset and entrenchment of the mutual-maintenance cycle of comorbid anxiety disorders and AUD. Such prolonged delays in seeking treatment are common; with Australian national surveys showing individuals with an AUD wait on average 10-18 years after the onset of symptoms to seek treatment (Birrell, Prior, et al., 2025; Chapman et al., 2015) and individuals with an anxiety disorder wait an average of 11 years after symptom onset to access treatment (Birrell, Prior, et al., 2025). To reduce unnecessary years of impairment, efforts should be channelled into interventions to engage youth when these concerns first emerge during adolescence and young adulthood.

1.4 Preventing and intervening early to reduce harm

Although anxiety and alcohol use concerns are highly prevalent, both individually and in co-occurrence, they are highly preventable (Bienvenu & Ginsburg, 2007; Lawrence et al., 2017; MacKillop et al., 2022; Sánchez-Puertas et al., 2022). The prevention of, and early-intervention for, co-occurring anxiety and alcohol use holds considerable potential to reduce the individual, economic, and societal harms outlined in subsection 1.1.3. The most effective interventions for comorbid anxiety disorder and AUD start early, ideally during adolescence and young adulthood before onset and escalation typically occurs (Morris et al., 2005). Preventing disorder onset is particularly paramount within the context of co-occurring concerns given the additional barriers to care and treatment individuals with co-occurring conditions often experience (Priester et al., 2016).

Prevention approaches are commonly conceptualised along a continuum that targets different stages of "disease" onset, development, or progression. Within this framework three stages of prevention are typically distinguished: primary, secondary (i.e. early intervention), and tertiary (i.e., treatment) (Baumann & Karel, 2013; Caplan & Grunebaum, 1967).

1.4.1 Primary prevention

The aim of primary prevention is to prevent the onset of anxiety symptoms and hazardous alcohol use before they emerge, and reduce or modify upstream risk factors that contribute to their co-occurrence. Primary prevention strategies may be delivered to a whole population (i.e., universal prevention) or targeted at a sub-group of the population (i.e., selective or indicated prevention) (Gordon, 1983).

1.4.1.1 Universal primary prevention

Universal prevention for both anxiety and alcohol use alone have received considerable attention to date. Universal alcohol prevention approaches are often delivered in school settings, with evidence to support their effectiveness in several reviews (Foxcroft & Tsertsvadze, 2012; Mewton et al., 2018; Teeson et al., 2012). For instance, a review of universal alcohol prevention strategies for alcohol use across multiple settings in Australia concluded that in addition to schools, there is evidence to support their efficacy in family settings (Mewton et al., 2018). An earlier review also supported the efficacy of some school, family, and multi-component universal interventions in preventing alcohol use in young people (Foxcroft & Tsertsvadze, 2012).

Evidence for universal prevention of anxiety symptoms and disorders has historically been less favourable, and the role of universal school-based prevention for mental health remains a point of active debate (Andrews & Foulkes, 2025; Birrell, Grummitt, et al., 2025; Werner-Seidler et al., 2021). A recent systematic review concluded that universal CBT did not demonstrate significant prevention benefits for anxiety across age groups in childhood/adolescence nor adulthood (Bermudez et al., 2025). In addition to limited efficacy, some school-based universal interventions have been associated with iatrogenic increases in anxiety symptoms (Guzman-Holst et al., 2025). This is contrasted by other evidence suggesting universal, school-based approaches have small effects in reducing anxiety with CBT principles favoured over mindfulness or other prevention theories (Hayes et al., 2025).

Few universal approaches exist that aim to prevent *both* anxiety and alcohol use simultaneously. One exception is the Australian *Climate Schools Combined (CSC)* program, now known as the *OurFutures* suite of programs (Teesson et al., 2014). This program sequentially delivered a universal substance use prevention program followed by a universal mental health prevention program. In a large RCT, students who received the combined CSC program showed greater alcohol- and mental-health knowledge, lower odds of drinking, and

smaller increases in anxiety symptoms at 12- and 30-month follow-up compared to control (education as usual) (Teesson et al., 2020). Nonetheless, the limitations, and potential harm, for the universal prevention of anxiety disorders suggest selective and indicated approaches may be more suitable for the prevention of anxiety concerns, and thus comorbid anxiety and alcohol more broadly (Bienvenu & Ginsburg, 2007; Lau & Rapee, 2011).

1.4.1.2 Targeted primary prevention (i.e. selective and indicated approaches)

The other forms of primary prevention (selective and indicated) are considered targeted prevention approaches (Stephan et al., 2025). Broadly, targeted prevention involves intervening with individuals or subgroups of the population whose risk of developing a disease is significantly higher than average, as evidenced by biological, psychological, or social risk factors (Gordon, 1983). In the context of co-occurring anxiety and alcohol use, targeted prevention depends on the temporal associations between the two conditions and the underlying risk factors. As discussed in subsection 1.2, multiple pathways and risk factors have been proposed to explain this comorbid relationship. Depending on the order of onset, targeted prevention could involve intervening with young people who have anxious traits or elevated anxiety symptoms (to prevent the development of anxiety disorders and subsequent alcohol problems), adolescents at risk of early alcohol initiation (to delay first drink and reduce later alcohol-related harms and subsequent anxiety), or groups characterised by shared risk factors for both anxiety and alcohol use.

While there are several pathways to the onset of anxiety-alcohol comorbidity, anxiety disorders typically precede problems with alcohol, demonstrating the importance of targeting known risk factors of anxiety in young people. There is an extensive body of work on risk and protective factors for anxiety (Blanco et al., 2014; Cabral & Patel, 2020; Drake & Ginsburg, 2012; Zimmermann et al., 2020) with evidence-based interventions developed based on these targets (Rapee et al., 2009; Stockings et al., 2016). Risk factors commonly targeted include individuals with heightened worry, repetitive negative thinking or rumination, and temperamental or behavioural inhibition. Interventions include targeting these risk factors directly with the individual using CBT or via parenting or family-based programs for younger children and adolescents (Johnco et al., 2019; Morgan et al., 2016; Rapee et al., 2005). Compared to universal approaches, these targeted programs have demonstrated larger effects on anxiety prevention (Werner-Seidler et al., 2021; Zbukvic et al., 2024). Targeted prevention can also include indicated intervention among people with mild symptoms of anxiety e.g., worry, panic or social anxiety who have already begun experimenting with alcohol. While there is evidence

for indicated interventions for prevention of anxiety disorders, most trials do not typically capture alcohol use and related outcomes (Hugh-Jones et al., 2021).

One targeted, selective intervention with demonstrated benefits for both anxiety and alcohol prevention is the personality-based program, *Preventure. Preventure* aims to reduce risk of substance use by targeting key personality risk factors, one of which is anxiety sensitivity (Conrod et al., 2008). Although primarily developed as a substance use prevention program, trials have shown significant reductions across multiple alcohol-related outcomes, including drinking quantity and frequency, binge drinking, and problem drinking symptoms (Edalati & Conrod, 2018). In Australia, a long-term follow-up of an RCT demonstrated that compared to controls, adolescents who received *Preventure* at age 13 had reduced alcohol related harms up to 7 years post-delivery (Newton, Debenham, et al., 2022). Secondary benefits on anxiety symptom reduction have also been demonstrated among adolescents who receive the *Preventure* program (Edalati & Conrod, 2018; Newton et al., 2020).

Overall, few targeted approaches exist which specifically aim to prevent co-occurring anxiety disorder and AUD. Designing effective prevention requires understanding both the developmental sequence and the progression of these concerns, including the critical windows during which anxiety and alcohol use interact or mutually exacerbate one another. However, as outlined in subsection 1.1.3.1, there is discrepant evidence on whether anxiety is a risk or protective factor for alcohol use during adolescence. This uncertainty complicates the delivery of appropriately timed interventions. Alternatively, addressing shared risk factors for both anxiety and alcohol use is another way for targeted interventions to prevent disorder onset. While some evidence suggests common genetic predispositions or adverse childhood experiences contribute to both concern (subsection 1.2.3) these factors are less amendable to intervention efforts. Identifying modifiable risk or protective factors, particularly those that moderate the anxiety-alcohol relationship, would provide actionable targets for prevention efforts. Such approaches, focused on high-risk youth and critical developmental windows, have the potential for greater impact than universal interventions. Without examining these moderators and developmental shifts, broad conclusions about the anxiety-alcohol relationship risk obscuring important nuances among subgroups, which are crucial for guiding primary prevention *before* disorder onset. Clarifying the developmental nature and temporal associations between anxiety and alcohol use is therefore essential for informing targeted prevention strategies.

1.4.2 Secondary prevention (early intervention)

The aim of secondary prevention in the context of co-occurring anxiety and alcohol use is to detect and intervene early when symptoms of anxiety and risky alcohol use first emerge, to prevent progression into comorbid or chronic conditions (Colizzi et al., 2020). This level of prevention is broadly synonymous with 'early intervention'. Rather than responding to established disorders, early intervention focuses on disrupting emerging, reciprocal patterns between anxiety and alcohol use at a stage when symptoms are milder and more amenable to change. Whilst there may be some overlap between secondary prevention and targeted primary prevention, secondary prevention is distinct in targeting early or milder presentations that may have met diagnostic threshold. Aligning with the age of onset for anxiety disorders and AUD, secondary prevention is ideally provided during young or "emerging" adulthood (Arnett et al., 2014). Early intervention among anxious youth may halt or dampen the development of maladaptive patterns of coping related to alcohol use, reducing the risk of progression to a clinically diagnosable AUD.

Like primary prevention, there is a substantial body of work on secondary prevention approaches for anxiety and alcohol alone. Early interventions for anxiety, especially in youth, typically focus on halting the trajectory to a clinical disorder (Hirshfeld-Becker & Biederman, 2002; Rapee et al., 2009). Evidence supports both individually focused psychosocial interventions delivered directly to young people (Fisak et al., 2023; Howes Vallis et al., 2020), as well as parent-based interventions designed to reduce the risk of anxiety disorder onset (Fisak et al., 2023; A. J. Morgan et al., 2017). For alcohol concerns, early intervention is typically focused on screening and detecting alcohol-related problems at an early stage and providing brief intervention as needed (Moyer & Finney, 2004). Multiple settings are proposed to deliver such brief interventions, including in hospitals, college or university, and community based settings such as criminal justice services (Platt et al., 2016). There is also evidence to support digital based alcohol brief- or early- intervention approaches as evidenced by several reviews (Kaner et al., 2017; Nair et al., 2015; Ndulue & Naslund, 2024; Woliansky et al., 2025).

Again, despite the work focusing on early intervention for anxiety and alcohol in isolation, limited work has addressed early interventions for co-occurring anxiety and alcohol concerns. To prevent the progression from anxiety and alcohol symptoms to disorder onset, psychoeducation and therapy which challenges positive expectancies around alcohol's

perceived and potential anxiolytic effects are paramount (Labbe & Maisto, 2011). Importantly, such approaches need to be implemented early, before anxiety-alcohol use becomes an entrenched coping strategy (Stewart & Conrod, 2008). One intervention which shows promise in scalable early intervention for co-occurring anxiety and hazardous drinking is the online *Inroads* program.

1.4.2.1 Inroads: An online early intervention program for anxiety and alcohol use

Inroads is the first early intervention to simultaneously target anxiety and hazardous alcohol use, delivered online to increase accessibility and scalability (Stapinski et al., 2019). Co-designed for youth with youth, the program explicitly addresses the interconnections between anxiety and alcohol to interrupt the trajectory toward co-occurring anxiety and AUD. The programs' content is based on the in-person, integrated CBT treatment for co-occurring social anxiety and AUD which, as highlighted earlier in subsection 1.3.2, demonstrated efficacy in treating adult samples (Stapinski et al., 2015; Stapinski, Sannibale, et al., 2021). The *Inroads* program involves five self-guided modules with content aimed at challenging positive alcohol expectancies and developing skills to manage anxiety and hazardous alcohol use. Modules are approximately 30-45 minutes in length and become available at a rate of one per week to allow time for skill practice and consolidation. Alongside written text, the program modules also incorporate images, videos, infographics, interactive forms, case vignettes as "real-life" examples, and quizzes.

To date the *Inroads* program has been evaluated in one pilot RCT (Stapinski, Prior, et al., 2021) and one naturalistic single-arm trial (Gückel, Radmall et al., 2025), with a subsequent long-term efficacy and cost-effectiveness RCT underway (Prior et al., 2024). In the first RCT, 124 young adults aged 17-24 years with transdiagnostic anxiety symptoms (social, generalised, or panic) and hazardous alcohol use were randomised to either i) the *Inroads* self-guided online program plus brief psychologist support or ii) an alcohol psychoeducation control group. Therapist support consisted of weekly emails and a 30-minute telephone or chat session after modules 1 and 4. Results showed that this integrated, early-intervention program resulted in significantly greater reductions in both general and social anxiety post-intervention, with improvements in social anxiety sustained at 6-months. Superior benefits were seen for the *Inroads* group in hazardous alcohol use reduction both post-intervention and at the 6-month follow up. Additionally, while both groups reduced their alcohol consumption and binge

drinking post-intervention, only the *Inroads* group sustained these reductions at the 6-month follow-up, suggesting a rebound in the control group (Stapinski, Prior, et al., 2021) .

The demonstrated efficacy of the program led to it being made available as part of a naturalistic, single-arm trial during the COVID-19 pandemic. During this time there was a need for access to evidence-based programs to help individuals who reported increased drinking, especially to cope with increasing anxiety related to the pandemic (Stanton et al., 2020). To increase scalability and long-term implementation, the program was updated to be fully self-guided without psychologist support. Program updates centred additional features to encourage engagement including weekly summary emails with personalised feedback and email and SMS reminders. During the trial 115 young Australian's aged 17-30 met eligibility criteria and were provided access to the fully self-guided version of the *Inroads* program. Significant reductions in hazardous alcohol use, binge drinking frequency, and social anxiety symptoms were observed at both the 2- and 6-month follow-up compared to baseline (Gückel, Radmall, et al., 2025). Whilst these positive reductions were observed, adherence was considerably lower compared to the previous psychologist supported trial (Stapinski, Prior, et al., 2021). Understanding the factors that affect engagement and retention of youth to *Inroads* and other digital interventions is paramount for enhancing the scalability and reach of early intervention approaches for co-occurring anxiety and alcohol use.

1.4.3 Tertiary prevention (treatment)

The final stage in the prevention framework is tertiary prevention, targeting the stage after disorder onset. This stage is often synonymous with treatment. Within the context of co-occurring anxiety disorders and AUD, this level of prevention aims to reduce the impact of established comorbidity on an individual's functioning, quality of life and longevity though treatment and psychosocial supports. As detailed in subsection 1.3.2 effective, integrated treatments exist for individuals with co-occurring anxiety disorders and AUD. These treatments have demonstrated benefits and can reduce harm and improve quality of life. Approaches to tertiary prevention also centre around relapse prevention, which has been highlighted as a crucial component of integrated anxiety-alcohol treatments (Buckner, Ledley, et al., 2008; Stapinski et al., 2024). Alcohol relapse prevention and withdrawal management may require additional medical support or pharmacotherapy among clients with more moderate to severe AUD (Haber et al., 2021). Benzodiazepines are considered the gold-standard for alcohol

withdrawal management (Sachdeva et al., 2015) and acamprosate or naltrexone are recommended to manage alcohol craving and aid relapse prevention (McPheeters et al., 2023). More broadly, tertiary prevention can include macro level approaches that influence socioecological factors (Latimore et al., 2023). This may include campaigns aimed at reducing mental health or substance use related stigma and discrimination and ensuring there is accessible and affordable access to health care services (Latimore et al., 2023). Online or digitally delivered interventions are one avenue offering great promise for providing accessible and affordable approaches to care.

1.5 The potential of online scalability to advance intervention approaches

Contemporary approaches to prevention, early-intervention, and treatment must be accessible and scalable, with digital innovations offering substantial potential for this (McGorry et al., 2024). Recent reviews highlight that online interventions are particularly promising for access to psychotherapeutic care, especially in regions with limited services or for young people who face barriers to treatment, allowing for early, low-threshold interventions before crises escalate and become chronic (Löchner et al., 2025). Ensuring sustainable delivery is imperative for the individual, societal, and economic benefits of prevention to be reaped, with online approaches particularly offering promise for youth (McGorry et al., 2024).

Despite the ever growing and evolving body of work on digital mental health interventions, comorbid mental and substance use concerns, particularly comorbid anxiety and alcohol use, have received relatively less attention. Individuals with co-occurring conditions face additional barriers to accessing care, in part because mental health and substance use services are often siloed. Online interventions may therefore be particularly advantageous for providing integrated, coordinated care in the context of co-occurring conditions (Priester et al., 2016). As such, understanding the utility of online interventions for co-occurring anxiety and alcohol use concerns, as well as the barriers and enablers to engagement among individuals with co-occurring anxiety and alcohol use concerns is paramount.

One crucial aspect for the scalability of online interventions is not only understanding *if* interventions work but *how* they work. This aligns with a growing call in the development and evaluation of psychological therapies to understand the mechanisms of change i.e., mediators

of intervention and treatment effects (Hofmann & Hayes, 2019; Kazdin, 2007; Windgassen et al., 2016). Given the efficacy of the *Inroads* program, and its potential to prevent escalation of co-occurring anxiety disorders and AUD, it is critical to investigate the mechanisms that drive its effects. One previous study has examined mechanisms of change in the context of a face-to-face CBT-based treatment for anxiety and SUD (Wolitzky-Taylor, Drazdowski, et al., 2018). In this clinical context, reductions in anxiety sensitivity were found to mediate decreases in drinking days among individuals with comorbid anxiety disorders and SUD. While this offers preliminary insight, it primarily reflects a downstream effect of reduced anxiety symptoms. Further work is needed to identify mechanisms that operate *prior* or in addition to general reductions in anxiety. Namely, the processes that shape changes in anxiety itself. These may include cognitive shifts central to anxiety-alcohol comorbidity, such as reductions in positive beliefs about alcohol's anxiolytic effects. Investigating mediation is important both for the advancement of psychological theory underpinning anxiety-alcohol comorbidity and refinement of prevention, early intervention, and treatment approaches. By pinpointing mediating mechanisms, therapeutic processes may be refined to focus on specific aspects of therapy that lead to improvements in outcomes, with the possibility of discarding aspects that are less relevant (Kazdin, 2007).

Another crucial consideration for scalable online interventions is understanding factors that influence user engagement among individuals with co-occurring anxiety and alcohol use concerns. While research has examined barriers and facilitators to engagement with digital mental health programs in general (Berardi et al., 2024; Borghouts et al., 2021; Cross et al., 2025), the perspectives of young people with both anxiety and alcohol concerns remain largely unexplored. Gaining insight into the experiences of young adults who participate in these programs, including what facilitates or hinders their ability to complete them, will strengthen usability and enhance scalable impact, particularly for self-guided interventions. This is particularly important given the widespread issues of poor engagement and high attrition in digital mental health interventions more broadly (Fleming et al., 2018; Smith et al., 2025). Despite the promise of online interventions for providing timely and accessible care, benefits cannot be realised if users are not engaged. Understanding how to engage and retain users is therefore essential for optimising design and maximising their full potential. Taken together, identifying both the mechanisms that drive change in online interventions, as well as the barriers and enablers that shape engagement among individuals with co-occurring anxiety and

alcohol concerns, can support the development of more effective, efficient, and economically sustainable interventions for this common comorbidity.

1.6 Summary of knowledge gaps

In response to the gaps and limitations identified in the literature reviewed above, a summary of the knowledge gaps addressed by this thesis in the subsequent chapters are presented in Table 1.2.

Table 1.2: Summary of knowledge gaps.

Knowledge gap	Summary of key limitations of the existing literature
1a) Insufficient understanding of underlying *mediating* factors driving the bidirectional anxiety-alcohol association.	• There has been *no systematic synthesis* of studies examining mediators in the bidirectional relationship between anxiety and alcohol use. • The only existing review, focused narrowly on drinking motives, was not systematic and included cross-sectional work precluding causal inference to be drawn. • This review also examined only the anxiety → alcohol pathway, despite evidence suggesting a *bidirectional* association. • It remains unclear whether mediating factors differ across distinct anxiety constructs (e.g., social anxiety, general anxiety) and alcohol outcomes (e.g., frequency, binge drinking, AUD symptoms). • Overall, there is no consolidated overview of mediators studied to date, the strength of evidence for each, or whether any show consistent mediating potential.
1b) Lack of synthesis for factors which *moderate* the bidirectional anxiety-alcohol association.	• No systematic review has examined moderating factors in the anxiety-alcohol relationship. • Existing reviews typically summarise the association itself, rather than identifying *for whom* and *under what conditions* this relationship strengthens or weakens. • Findings on key moderators (e.g., gender, drinking motives) are inconsistent across individual studies, preventing conclusions about their role as risk or protective factors.
2) Lack of clarity around the anxiety-alcohol relationship across distinct developmental periods in adolescence through to young adulthood.	• Evidence is inconsistent on whether anxiety serves as a risk or protective factor for alcohol use during adolescence. • Most studies focus on a single developmental stage, missing important transitions from early adolescence through to young adulthood. • Longitudinal studies that do span multiple developmental periods often collapse windows spanning several years, despite rapid developmental changes occurring over short intervals.

Knowledge gap	Summary of key limitations of the existing literature
3) Insufficient evidence regarding the mechanisms that mediate effective early intervention for social anxiety and hazardous drinking.	• Mechanisms of change in anxiety-alcohol interventions have received almost no empirical investigation. • It remains uncertain whether hypothesised therapeutic targets (e.g., coping skills, cognitive change, expectancy modification) actually drive improvements in anxiety or alcohol use. • No studies have examined mechanisms of change in *online* interventions for co-occurring anxiety and alcohol concerns. • *Causal* mediation methods have not yet been applied to understand pathways of change in any anxiety-alcohol intervention trial.
4) Lack of evidence regarding factors that influence engagement and retention to online interventions among youth with co-occurring anxiety and hazardous alcohol use concerns.	• Little is known about preferences and needs of young people with co-occurring anxiety and alcohol concerns when accessing online interventions. • No research has examined barriers and enablers to engagement in a *self-guided* online intervention tailored to this comorbidity. • Implementation studies of digital mental health programs often rely on deductive approaches, whereas qualitative methods offer greater nuance and insight into individual experiences.

1.7 Thesis aims and outline

This thesis aims to address the identified knowledge gaps with the overarching aim of advancing the theoretical and clinical understanding of anxiety and alcohol use comorbidity to improve prevention and early intervention approaches for these co-occurring concerns.

To achieve these aims, this thesis has the following four objectives:

1. Systematically review the evidence identifying factors that longitudinally a) *mediate* and b) *moderate* the bidirectional relationship between anxiety → alcohol use and alcohol use → anxiety.
2. Examine developmental associations between, and moderators of, anxiety and hazardous alcohol use across multiple timepoints from early adolescence through to young adulthood.
3. Investigate the causal mechanisms responsible for reducing social anxiety and hazardous drinking within an efficacious online early intervention program for young adults.
4. Identify barriers and enablers to the delivery of, and user engagement with, an online intervention for young adults experiencing co-occurring anxiety and hazardous alcohol use.

These four objectives are addressed across four novel empirical chapters (**Chapters 2-5** of this thesis), with the overall findings and broader implications of this work synthesised in the discussion (**Chapter 6**). A brief overview of each empirical chapter is provided below.

Chapter 2 presents the first systematic literature review examining mediators and moderators of the relationship between anxiety and alcohol use. This review comprehensively synthesises evidence across the bidirectional association and encompasses the full spectrum of potential biological, psychological, and socio-environmental factors that may shape these pathways. Fifty-five studies reporting 315 unique effects were identified. The review provides several novel insights into risk and protective factors for co-occurring anxiety and alcohol concerns and offers an evidence map summarising the current state of mediation and moderation research in this field.

Chapter 3 examines the association between anxiety symptoms and hazardous alcohol use across seven distinct developmental periods spanning early adolescence to young adulthood

(aged 13.4-20.5 years). Associations are assessed both within the same developmental window and longitudinally, while also testing the potential moderating role of sex, depressive symptoms, drinking motives, and externalising symptoms. Identifying *when* the association between anxiety and hazardous alcohol use emerges, and *for whom* risk is heightened, is critical for optimally timing and targeting prevention and early intervention efforts.

Chapter 4 presents the first study to apply causal mediation analysis to identify mechanisms of change in an early intervention program targeting co-occurring anxiety and hazardous alcohol use. Using data from a RCT involving sub-clinical youth aged 17-24 years, separate multiple mediation models were conducted to examine hypothesised psychological mechanisms underlying reductions in social anxiety symptoms and hazardous drinking, respectively.

Chapter 5 reports a mixed-methods study exploring the barriers and enablers to engaging with a self-guided online early intervention for co-occurring anxiety and hazardous drinking. This chapter provides in-depth insight into young adults' experiences using the intervention in a naturalistic context. Quantitative data were triangulated with qualitative interviews (n = 11) to ensure participants' perspectives were captured with sufficient nuance and depth. Findings regarding factors influencing engagement and retention are critical for informing the scalable delivery of effective interventions targeting co-occurring anxiety and alcohol use.

Chapter 2

Exploring Mediators and Moderators in the Relationship Between Anxiety and Alcohol Use: A Systematic Review

Preface

Despite numerous reviews on the association between anxiety and alcohol use, none have synthesised evidence on the mediating and/or moderating factors that underpin this relationship. This chapter addresses this gap by presenting the first comprehensive and systematic synthesis of mediators and moderators underlying the anxiety-alcohol association. Given evidence of a bidirectional relationship between anxiety and alcohol use, as outlined in **Chapter 1**, this review examined factors influencing both the anxiety → alcohol and alcohol → anxiety pathways. No restrictions were placed on the types of factors considered; biological, psychological, and socio-environmental mediators and moderators were all eligible for inclusion.

Understanding these factors is critical for advancing theoretical models of co-occurring anxiety and alcohol use, particularly regarding the mechanisms that drive their interrelationship. Such insights can also inform targets for prevention, early intervention, and treatment. In addition to the systematic synthesis, this chapter presents two novel, evidence-based risk-of-bias tools designed to address the limitations of existing tools in assessing mediation- and moderation-specific biases.

This chapter addresses the first objective of this thesis, which is to:

Systematically review the evidence identifying factors that longitudinally a) mediate and b) moderate the bidirectional relationship between anxiety → alcohol use and alcohol use → anxiety.

This systematic review is currently under review in *Behaviour Research and Therapy* and was revised aligned with reviewer comments following a first round of review. It is under review as:

Gückel, T., Prior, K., Newton, N. C., Karin, E., Gex, K. S., Sercombe, J., & Stapinski, L. A. Exploring mediators and moderators in the relationship between anxiety and alcohol use: a systematic review. *Behaviour Research and Therapy*.

Supplementary materials for **Chapter 2** are provided in Appendix A. The risk of bias assessment tool for mediation studies is provided in Appendix B and the risk of bias assessment tool for moderation studies is provided in Appendix C.

The accompanying protocol for this study is available in Appendix D and has been published as:

Gückel, T., Prior, K., Newton, N. C., & Stapinski, L. A. (2023). Mediators and moderators in the co-occurring anxiety and alcohol use relationship: protocol for a systematic review and meta-analysis. *JMIR Research Protocols*, *12*, e48875. https://doi.org/10.2196/48875.

Abstract

This systematic review provides the first synthesis of mediating and moderating factors in the bidirectional relationship between anxiety and alcohol use and related problems. Six electronic databases were searched for longitudinal studies that assessed a mediator and/or moderator in the anxiety → alcohol or alcohol → anxiety pathway. Risk of bias was assessed with two quality assessment tools developed to assess biases pertaining to mediation and moderation studies, respectively. Of the 14,776 records identified, 55 were eligible, from which effects from 315 unique models were extracted. Effects included 30 mediation analyses, 258 moderation analyses, and 27 other complex analyses (e.g. multiple mediation or three-way moderation). Identified mediating and moderating factors were categorised in line with the biopsychosocial model, with subsequent subtheme classification (e.g. sex, drinking motives). Further to the narrative synthesis, fourteen moderation subthemes provided sufficient data for meta-analysis. Results of the meta-analysis of moderators suggest age (Fisher's *z*: 0.065 95% CI: 0.017, 0.113), externalising factors (Fisher's *z*: -0.186, 95% CI: -0.222, -0.150), perceptions of peer alcohol use (Fisher's *z* : -0.076, 95% CI: -0.119, -0.033), positive family experiences (Fisher's *z*: -0.081, 95% CI: -0.098, -0.064), and experimental manipulation of anxiety (Fisher's *z*: 0.242. 95% CI: 0.103, 0.382) significantly moderated the relationship between anxiety and alcohol. Narrative synthesis of other moderating subthemes and all mediation subthemes yielded inconsistent evidence which did not demonstrate conclusive moderated or mediated effects. Across studies, methodological quality was suboptimal, with future directions for research discussed.

2.1 Introduction

Despite clear evidence that anxiety and alcohol use commonly co-occur, the specific factors and mechanisms driving this relationship are still poorly understood. It is estimated that among individuals with an anxiety disorder, 20-40% will also experience an AUD in their lifetime (Lai et al., 2015; Sunderland et al., 2025). Similarly, the prevalence of anxiety disorders is higher among individuals with an AUD than in the general population, with approximately one in two individuals with an AUD also meeting diagnostic criteria for GAD (Smith & Book, 2010; Zech et al., 2024) and one in eight meeting diagnostic criteria for SAD (Glantz et al., 2020; Grant et al., 2004). The impacts of this co-occurring relationship are not only significant on a personal and clinical level (Hurlocker et al., 2023; Schellekens et al., 2015), but also on a societal and economic level (Manthey et al., 2021; Yang et al., 2021).

2.1.1 Previous reviews on anxiety and alcohol

Systematic and critical reviews to date have proposed several explanations and pathways for the bidirectional nature of anxiety and alcohol use comorbidity (Anker & Kushner, 2019; Kushner et al., 2000; Smith & Randall, 2012; Susan et al., 2010). Within these reviews, three models are commonly used to explain the co-occurrence of anxiety and alcohol use: the self-medication model, the substance induced model, and the common-factor model. The self-medication hypothesis proposes an anxiety → alcohol relationship whereby individuals consume alcohol in an attempt to alleviate or 'self-medicate' anxiety symptoms, leading to a reliance on drinking (Khantzian, 1985, 1997). If left unmanaged, over time this negatively reinforcing coping strategy can lead to an AUD (Quitkin et al., 1972; Robinson et al., 2009; Smith & Randall, 2012). The opposite is theorised in the substance-induced model which proposes an alcohol → anxiety relationship. Acute alcohol use over a prolonged period has significant neurobiological impacts, including the depletion of neurotransmitters such as GABA which can induce anxiety symptoms, particularly during alcohol withdrawal (Kushner et al., 2000; Nuss, 2015). Both hypotheses propose a causal effect of one disorder on the other, via direct and indirect causal pathways (Anker & Kushner, 2019; Smith & Randall, 2012). These causal pathways are likely to be mediated and/or moderated by additional mechanisms such as cognitive, affective, and behavioural factors, which contribute to the development and maintenance of the comorbidity (Sabourin & Stewart, 2008). Lastly, the common factor model presumes there is not a causal relationship between anxiety and alcohol use, but rather there is

a third “common factor” variable which can account for the joint presentation of both disorders (Kushner et al., 2000). Genetic or environmental mechanisms are often positioned as common factors, with family and twin studies providing some supporting evidence for this model (Nelson et al., 2000; Nurnberger et al., 2004; Tambs et al., 1997). There is also evidence, however, that these directional relationships may not be mutually exclusive. In fact, previous work has found support for a bidirectional association between anxiety and alcohol, whereby both variables influence the other (D'Aquino et al., 2024; Dyer, Easey, et al., 2019; Kushner et al., 2000).

2.1.2 Mediators and moderators in the anxiety and alcohol relationship

Given the extensive body of work on the prevalence and possible theoretical explanations for co-occurring anxiety and alcohol use, research has begun to probe this association further. Recent studies have focused on exploring potential mediators and moderators underlying and driving the co-occurrence of these two concerns. A mediator can lie on the causal pathway between the exposure and outcome, with the exposure influencing the mediator which in turn influences the outcome (Hall & Sammons, 2013). Moderators can affect the strength and/or direction of the relationship between the exposure and outcome (Hall & Sammons, 2013). Some variables have the potential to function as a mediator and/or moderator, with studies assessing their plausibility in both situations. Examples of such factors include drinking motives, alcohol outcome expectancies, and impulsivity. Gender and age, however, are examples of variables which would be expected to only function as potential moderators, as they would not lie on the causal pathway between anxiety and alcohol use. To date, there has been no systematic synthesis encompassing all potential mediating and moderating factors on the association between anxiety and alcohol use. A single critical review by DeMartini and Carey (2011) focused on drinking motives as a singular third variable, and found that drinking motives mediated the relationship between anxiety sensitivity (i.e., a fear of anxiety-related symptoms and sensations) and alcohol use, and gender moderated the association between anxiety sensitivity and drinking motives. Given that existing studies typically examine a single mediator or moderator, synthesising the body of evidence across studies is paramount. Identifying these mechanistic drivers (mediators) and effect modifiers (moderators) in the anxiety and alcohol relationship allows for targeted prevention, early-intervention, and treatment approaches which address both the underlying processes and conditions that drive

the connection between these two issues. Specifically, mediators and moderators of the *longitudinal* association between anxiety and alcohol are especially advantageous as they can aid understanding of the temporal and developmental processes driving these concerns.

2.1.3 The present study objectives

The purpose of this review is to systematically identify and synthesise evidence for mediators and moderators in the co-occurring anxiety and alcohol use relationship. Given the evidence for a bidirectional association between anxiety and alcohol use, factors mediating or moderating the relationship in either direction from anxiety → alcohol use or alcohol use → anxiety were of interest. Specifically, this review will address the following questions to develop an evidence map and provide an overview of the current state of the literature on the pathways and mechanisms connecting anxiety and alcohol use.

- What factors *mediate* the longitudinal relationship between i) anxiety and alcohol use/problems?
- What factors *mediate* the longitudinal relationship between ii) alcohol use/problems and anxiety?
- What factors *moderate* the longitudinal relationship between iii) anxiety and alcohol use/problems?
- What factors *moderate* the longitudinal relationship between iv) alcohol use/problems and anxiety?

2.2 Methods

2.2.1 Protocol and registration

This systematic review was designed, conducted, and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). The protocol for this review was published (Gückel et al., 2023) and registered prospectively with PROSPERO (CRD42023358402). Deviations from the protocol include limiting to longitudinal study designs only and revising the risk of bias tool to more appropriately capture biases specific to mediation or moderation analyses. These changes are further outlined below.

2.2.2 Eligibility criteria

The inclusion criteria was guided by the Population, Exposure, Outcome (PEO) framework developed for reviews of association (etiology) (Moola et al., 2020). In essence, studies were eligible if they met the below criteria and reported a test of moderation or mediation between anxiety and alcohol use, even if results were not statistically significant or effect sizes were missing. Full details of the eligibility criteria are provided in the protocol paper (Gückel et al., 2023) and summarised below.

Population: All human populations were of interest, and no limits were placed on study population or participant type. Both the exposure and outcome were required to be measured in the same individual, i.e. parent and offspring studies were excluded. Animal studies were also excluded.

Exposure and outcome: Depending on the direction of the relationship investigated in a study, both anxiety and alcohol could be either an exposure or outcome (see Figure 2.1 and Figure 2.2). As anxiety and alcohol are multifaceted constructs with no universal measure of each concept, a broad spectrum of anxiety and alcohol use measures were eligible in this review. Anxiety was conceptualised in line with the DSM-5, where anxiety disorders are differentiated from obsessive compulsive and related disorders, and trauma and related-stressor disorders (*Diagnostic and statistical manual of mental disorders : DSM-5™*, 2013). Studies measuring anxiety from disorder level (e.g. SAD) through to anxious traits (e.g. anxiety sensitivity) were of interest and included in the review. Similarly, studies measuring the full spectrum of alcohol use and related difficulties were of interest and included in the review (e.g., AUD, binge drinking, and average drinks per day).

Types of studies: All longitudinal study designs, including both observational and experimental designs were eligible. This is a deviation from the registered protocol where non-longitudinal designs (e.g. cross-sectional studies) had originally been planned for inclusion. However, a significantly greater number of studies were identified at the full-text stage than anticipated, so in the interests of feasibility we updated the inclusion criteria to longitudinal studies only. Restricting to longitudinal studies also enabled stronger conclusions to be drawn about the developmental association between anxiety and alcohol use, contributing further to their theoretical understanding and thus inform intervention approaches which target mediating and moderating factors (Caemmerer et al., 2024; Maxwell & Cole, 2007). Longitudinal study designs are also particularly pertinent for testing mediational hypotheses with temporal

ordering of variables to assess appropriate causal assumptions (Fairchild & McDaniel, 2017). No language or publication year restrictions were applied.

For synthesis, studies were grouped by their analysis type (i.e. mediation or moderation), direction of relationship (i.e., anxiety → alcohol or alcohol → anxiety), and the type of mediating or moderating factor tested (i.e. biological, psychological, or socio-environmental). This grouping of mediators and moderators is in line with the biopsychosocial model which provides a framework for understanding health and illness beyond the traditional biomedical model (Engel, 1977).

Figure 2.1: Diagram demonstrating the possible mediator (Me) and moderator (Mo) pathways between the exposure variable anxiety (X) and outcome variable alcohol (Y)

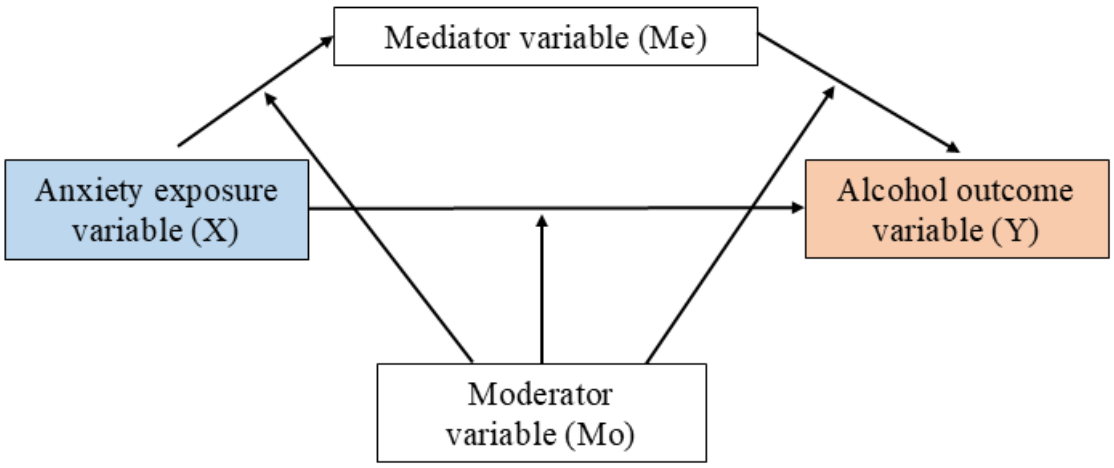
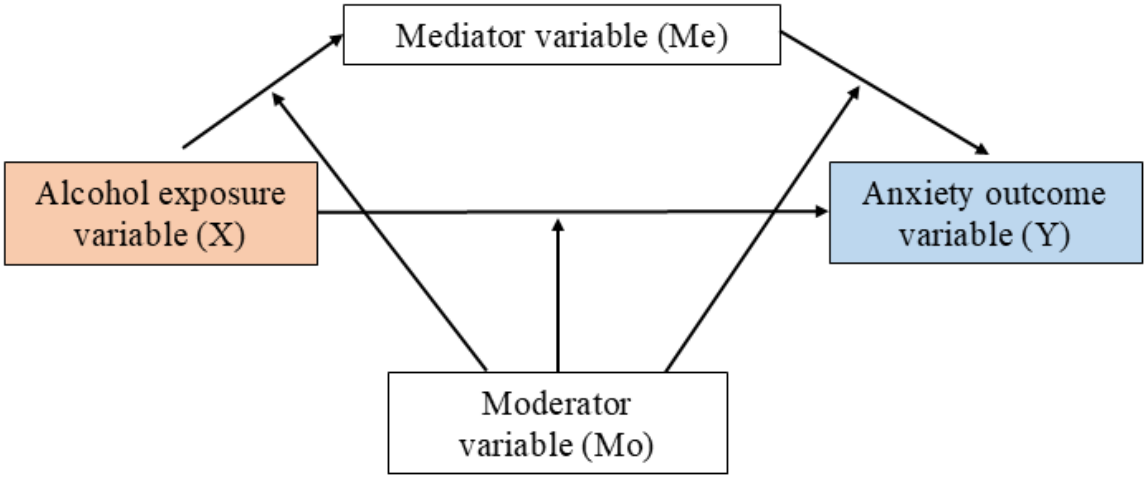


Figure 2.2: Diagram demonstrating the possible mediator (Me) and moderator (Mo) pathways between the exposure variable alcohol (X) and outcome variable anxiety (Y)



2.2.3 Information sources and search strategy

In September 2022, searches were conducted in six electronic databases: Medline (Ovid), PsycINFO (Ovid), Embase (Ovid), Cochrane Central Register of Controlled Trials (Ovid), Scopus, and Web of Science and re-run in November 2024 (and limited to publication between 2022 to 'current'). The overarching themes of anxiety, alcohol, and mediator or moderator guided the search strategy and structure of searches within each database. The full search strategies for each database can be seen in supplementary material (Appendix A: Table A1 to Table A6). Reference lists of included studies were also hand-searched to identify any additional studies.

2.2.4 Study selection and data extraction

All identified records were imported into EndNote software (Clarivate) for removal of duplicates, and subsequently imported into the web-based systematic review software, Covidence (Veritas Health Innovation). In Covidence, reviewer one (TG) independently screened 100% of titles and abstracts against the inclusion and exclusion criteria, while reviewers two (KG) and three (JS) independently double screened a random sample of 50%. The full text of remaining articles was then assessed for eligibility, with reviewer one assessing

100% and reviewers two and three each assessing 50%. Disagreements at each stage were resolved through discussion or a fourth reviewer (LAS) if required. Full-text screening inter-rater reliability was substantial, with Cohen's kappa ranging from 0.70-0.76 between reviewers from 87.5% - 88.3% agreement.

Data extraction for all studies was conducted independently by reviewer one using a purpose designed form in Microsoft Excel. Extracted data was reviewed by a second reviewer. The extracted data included: i) author and publication year, ii) study characteristics (i.e., aims, study design, follow-up time points, country), iii) study sample characteristics (i.e., age at baseline, gender, whether it was a general or clinical population), iv) the direction of relationship investigated, v) analysis type (i.e., single or multiple mediation, moderation analysis, moderated-mediation) and statistical approach used for the mediation/moderation analysis, vi) predictor variable information including the measurement tool, vii) outcome variable information including the measurement tool, viii) information on the mediator(s)/moderators(s) and how they were measured, and ix) if reported, statistical results including effect size and measure of variance. Where multiple analyses were reported within a singular study, we extracted all eligible results in line with the eligibility criteria. It was common for included studies to test multiple models with a range of mediators or moderators, or eligible outcomes (e.g., alcohol frequency, alcohol quantity, and alcohol related harms).

2.2.4.1 Data categorisation and themes for mediation and moderator variables

To assist with data synthesis of the extracted effects, we categorised each effect based on the mediating or moderating factor. Categorisation was aligned with the overarching biopsychosocial model themes (biological, psychological, socio-environmental). Given the breadth and number of mediators and moderators, subtheme categorisation, created through expert consensus between authors, was then used to further assist interpretation. An example of subtheme categorisation includes the moderating variables externalising symptoms, sensation seeking, and impulsivity which were categorised under the "externalising symptoms" subtheme. Examples of subthemes identified across the biopsychosocial domains included:

- Biological: age, gender/sex
- Psychological: drinking motives: drinking to cope, emotion dysregulation, perceptions of peer alcohol use
- Socio-environmental: peer social support, drinking context, positive family experiences

2.2.5 Data synthesis and analysis

Firstly, at the study level, all studies that met inclusion criteria were summarised in a study attributes table to provide an overview of the available literature. Studies were grouped by direction of effect investigated i.e., anxiety → alcohol, alcohol → anxiety, or both directions. Individual effects from the respective studies were then synthesised across several steps to provide an overview of the current state of research on mediating and moderating factors in the anxiety-alcohol association. These steps included i) a visual summation of identified mediating and moderating factors across subthemes, ii) a narrative synthesis across each mediator and moderator subtheme, iii) streamlining of effects into a common metric, and for moderation effects only due to data availability iv) meta-analysis

2.2.5.1 i) Visual summation of moderator and mediator effects identified

To capture the breadth of identified effects, a high-level visual summary was developed to depict the number and typology of subthemes examined across studies. Separate summaries were produced for mediation and moderation effects, separated by direction of relationship (anxiety → alcohol or alcohol → anxiety). The two figures illustrate the number of studies examining each mediator/moderator subtheme and the proportion of those studies reporting significant positive, significant negative, non-significant effects, or significant without value.

2.2.5.2 ii) Narrative synthesis

Further to the count summaries provided in the visual summation, each mediator and moderator subtheme was narratively synthesised. Narrative synthesis was grouped using the following levels i) model type (i.e., mediation, moderation, or other complex model), ii) direction of relationship, iii) biopsychosocial theme, and iv) subtheme. The aim of the narrative synthesis was to contextualise the relationships across mediator and moderator subthemes, particularly given the reviews broad inclusion criteria and subsequent diversity of study contexts and samples.

2.2.5.3 iii) Streamlining effects to a common metric

For both mediation and moderation studies there was a broad range of potential effect measures for the anxiety and alcohol outcomes (e.g., odds ratio, unstandardised coefficients, standardised coefficients). To streamline effects across study designs, analyses, and reporting styles we transformed all mediation and moderation effects into a single metric, the Fisher's *z* correlation, using established procedures recommended by the Campbell Initiative for data conversion (Polanin & Snilstveit, 2016) and as used previously for large-scale literature aggregation

(Kayrouz et al., 2025). In this process, odds ratios greater than one were converted into positive correlations (indicating a positive association), and values less than one into negative correlations (indicating a negative association). Where the effect size metric or magnitude was not directly reported, we used available information (e.g., standard errors, sample sizes, or standardised/unstandardised coefficients of interaction terms) to estimate an R-equivalent effect size, which was then transformed into Fisher's *z* (Rosenberg, 2010; Rosenthal & Rubin, 2003). Authors of mediation studies were contacted to provide additional data where possible. There were, however, some studies which reported no, numeric, statistical information. These studies and effects were still included in visual summaries and supplementary material on the basis of their descriptive reporting of a significant or non-significant effect. A full dataset is provided in supplementary material (Appendix A: Table A7 to Table A11), which list the original effect statistics alongside transformed effect estimates. We note that in some cases our estimates may differ from those reported by the original authors, as meta-analytical methods are generally more conservative than direct application of complex models (Kayrouz et al., 2025). Across our extraction and reporting, we prioritised reported over transformed data.

Further to transforming effects into a common metric, the magnitude of effect was determined based on common effect size classifications. Effect sizes for the common metric (Fisher's *z*) between 0.0 and 0.309 were considered small, 0.310 and 0.549 moderate, and above 0.6 as large (Lovakov & Agadullina, 2021). Significance (based on reported test in original study) and effects size classifications are provided in supplementary material (Appendix A: Table A12 to Table A16. Overall, across the analytical scope, our primary aim was to achieve broad coverage of the literature, with a secondary aim of incorporating partially reported and indirectly estimable effects.

2.2.5.4 iv) Meta analysis of moderation effects

The preregistered protocol had planned for meta-anlaysis of both mediation and moderation effects if sufficient data was available (Gückel et al., 2023). However, only a small number of mediation studies were identified, and individual subthemes predominantly comprised 1-3 effect sizes derived from the same study. This limited the independence of effects and precluded meaningful estimation of between-study variance using the methods outlined by Cheung (2021). As such, the available data were not considered sufficiently suitable for quantitative synthesis. Moderation effects which reported sufficient (numeric) data for effect transformation to the Fisher's *z* were eligible for meta-anlaysis. Meta-analysis was possible for 13 anxiety → alcohol and four alcohol → anxiety moderator subthemes. Effect size estimates were produced

for moderation studies, capturing the strength of the moderating relationships. A DerSimonian-Laird estimator was used as a common, default, estimator (Langan et al., 2019). Measures of meta-estimate heterogeneity were also reported within each subtheme, using the Q-test and I^2 statistic (Higgins & Thompson, 2002). The Q-statistic determines the presence or absence of heterogeneity, whereas the I^2 statistic quantifies the degree of heterogeneity. I^2 values of 25%, 50%, and 75% were interpreted as indicating a low, moderate, and large amount of heterogeneity (Higgins & Thompson, 2002). See supplementary materials for detailed meta-analysis results (Appendix A: Table A17 and Table A18).

Because of the diversity of study designs and models, some studies contributed more than one moderating effect, either within a subtheme or across subthemes. Most studies were thus represented multiple times contributing data across a range of extracted effects, also known as effect multiplicity (López-López et al., 2018). The decision to allow this overlap reflected both the limited number of studies available within many subthemes and the aim of capturing and mapping a wide range of findings across diverse conceptual areas.

2.2.6 Risk of bias assessment

Currently no validated or consensus-based tools exist for assessing the bias specific to mediation studies or moderation studies (Pincus et al., 2011; Vo et al., 2022). In the review protocol, the Joanna Briggs Institute Critical Appraisal Tools including the Checklist for Analytical Cross-Sectional Studies and the Checklist for Cohort Studies (Moola et al., 2020) were specified for quality and bias assessment. In light of the revision to exclude cross-sectional studies, the corresponding checklist was no longer required. Furthermore, at the point of data extraction, it was determined that the Cohort Studies Checklist would not sufficiently capture potential biases specific to mediation and/or moderation analyses, which are at the core of the review's questions of interest. As such, we developed two custom tools to assess individual study risk of bias for mediation and moderation studies in this review. Development of the risk of bias tool for mediation studies was guided by the overview of quality assessment practice in systematic reviews of mediation studies by Vo et al. (2022) and development of the risk of bias tool for moderation studies was guided by the Editorial on moderation by Memon et al. (2019).

The primary aim of the developed tools was to assess mediation-specific or moderation-specific biases of included studies. Secondary signalling questions were also included in both

tools to assess additional domains including study design biases (i.e. representativeness of the studies sample) and analysis biases (i.e., appropriate handling of missing data). Both tools cover four overarching bias domains: i) study design and selection bias, ii) measurement bias, iii) statistical and analytical bias, and iv) selection of the reported results bias. With the mediation tool including the additional domain: v) confounding bias, as recommended by Vo et al. (2022). The full 15 item mediation tool can be seen in Appendix B: *Risk of bias assessment tool for mediation studies*. The full 12 item moderation tool can be seen in Appendix C: *Risk of bias assessment tool for moderation studies.*

For both tools, each of the domains is scored and given an overall risk of bias judgement: low risk of bias, some concerns, or high risk of bias. Finally, an overall judgement about the study's risk of bias is given, with the criteria used to determine this judgement guided by existing Cochrane risk of bias tools (Higgins et al., 2019). Details on determining domain and overall risk of bias are provided within each tool (see Appendix B and Appendix C). Using these tools, two reviewers independently assessed the risk of bias for each included study. If a study contained both mediation and moderation analyses, the risk of bias was assessed with both risk of bias tools. Any discrepancies were resolved through discussion until consensus was reached.

2.2.7 Certainty of evidence

To draw conclusions about the certainty of evidence for results in the meta-analyses, we employed the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach (Balshem et al., 2011). GRADE assessments were provided at the subtheme level by one reviewer using the five GRADE considerations: study limitations, consistency of effect, imprecision, indirectness, and publication bias. The starting rating is typically defined as high-certainty for RCTs and low-certainty for non-randomised studies. Given high-quality observational studies are valid for testing mediators or moderators, we opted to give subthemes a starting rating of high certainty. Reasons for downgrading or upgrading the certainty of evidence was guided by existing frameworks (Schünemann et al., 2019). A final certainty of evidence classification of very low, low, moderate, or high was given to the subthemes. As meta-analyses were only possible for some moderator subthemes GRADE evaluations were only done on these subthemes with sufficient information. Further details on determining certainty of evidence classification and the full classification for the moderator subthemes are provided in supplementary material (Appendix A: Table A19).

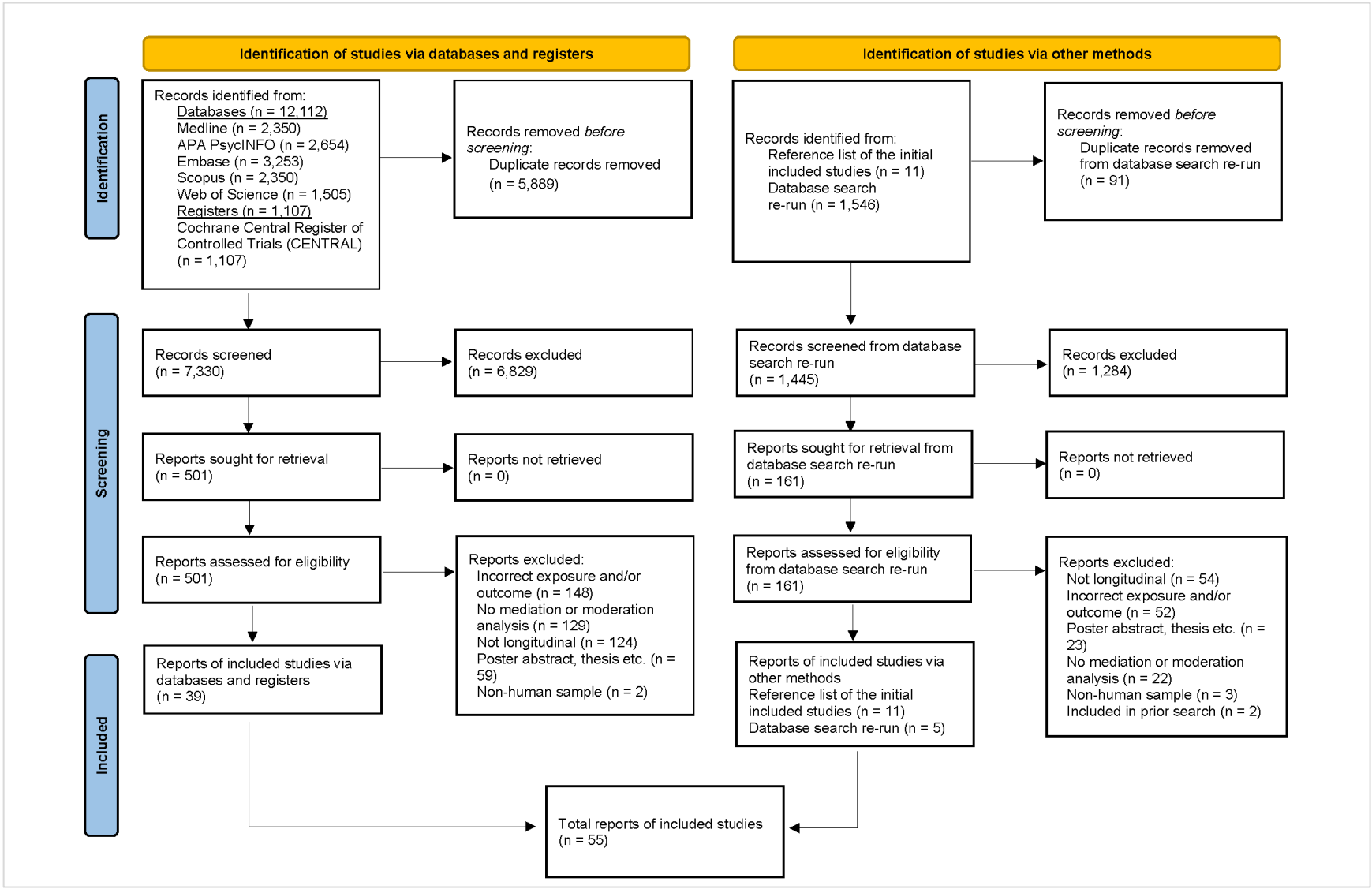
2.3 Results

2.3.1 Study selection

Initial database and register searches ran in October 2022 yielded 13,219 results. After removing duplicates, 7,330 records remained for title and abstract screening. Of these, 501 studies remained and had their full text assessed for suitability, with 338 being excluded. Among the remaining 163 studies, 124 were cross-sectional design and thus excluded, resulting in 39 studies eligible for inclusion. The subsequent search re-run in November 2024 identified 2,330 additional records. After removing duplicates, 1,445 records were screened, and 171 full-text articles assessed for eligibility. Of these, 5 studies met the inclusion criteria. Reference lists of included studies were also screened, with 11 additional studies fulfilling the eligibility criteria identified. Together, this yielded a total of 55 studies for inclusion in the review. Figure 2.3 provides a flow chart outlining the screening process including reasons for exclusion of articles at the full-text reviewing stage.

Studies were predominately excluded for being cross-sectional in their design, having an unsuitable exposure or outcome measure, or not including a mediation or moderation analysis. For example, several mediation or moderation studies looking at predictors of alcohol use examined repetitive negative thinking as the exposure variable. However, these studies were excluded as this was not deemed a specific enough measure of anxiety or related traits (Devynck et al., 2017; Hamonniere et al., 2020). Similarly, studies which utilised an alcohol outcome measure of desire to drink, alcohol craving, or drinking motives were excluded as these measures did not capture alcohol *use* or alcohol *problems* (Adams et al., 2019; Blumenthal et al., 2021; Dyer et al., 2020; Stewart et al., 2002). Lastly studies which only looked at mediators of treatment or intervention outcomes were excluded (Terlecki et al., 2021; Terlecki et al., 2012; Wu et al., 2018) .

Figure 2.3: PRISMA flow diagram



2.3.2 Study characteristics

Table 2.1 provides a summary of the 55 included studies in the review and their study characteristics, grouped by direction of effect. Across the 55 studies there were 315 effects extracted. The effects included 30 unique single mediation analyses, 258 unique single moderation analyses, and 27 other complex analyses such as moderated moderation (3-way interactions) or moderated mediation analyses. It was more likely for studies to investigate the relationship from anxiety to alcohol (39 studies, 70.9%) compared to alcohol to anxiety (13 studies, 23.6%), with three studies (5.5%) investigating the relationship in both directions. Most studies (72.7%) were published from 2010 onwards and were conducted in North America (85.5%). There were more cohort than experimental studies, with samples sizes ranging from 37 (Steele & Josephs, 1988) to 439,494 individuals (Cook et al., 2024). The samples were predominately non-clinical (94.5%), with a mean baseline age range of 18-49 (52.7%), followed by under 18 (43.6%).

Table 2.1: Characteristics of included studies grouped by direction of effect

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models[2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
Anxiety → Alcohol models									
(Abrams, Kushner, et al., 2002)	USA	44 (63.6%)	29	Experimental	1 other (three-way interaction)	a) Drink activity order b) Gender	a) Anxiety condition (anxiety speech challenge vs reading session)	a) Drink choice selection (weak, moderate, or strong alcoholic content)	High
(Armeli et al., 2008)	USA	458 (54.4%)	18.77	30-day daily diary	5 moderation	a) Drinking to cope motives (Drinking Motives Questionnaire Revised; DMQ-R)	a) Anxiety- daily mood b) Same day anxiety c) Sunday only anxiety d) Daily anxiety (Positive and Negative Affect Schedule and Mood Circumplex)	a) Weekly drinking onset b) Any drinking c) Heavy drinking (4+ women, 5+ men)	High
(Armeli et al., 2010)	USA	530 (52%)	18.76	Retrospective and daily diary reporting	12 moderation 6 other (three-way interaction)	a) Drinking to cope motives (DMQ-R) b) Drinking to socialise or enhance (DMQ-R)	a) Daily diary anxiety (items "worry" or "jittery") b) Retrospective anxiety (State-trait anxiety inventory state form; STAI)	a) Month-level drinking frequency b) Month-level drinking quantity c) Any drinking e) Drinks per drinking day	High
(Armeli, Erik, et al., 2014)	USA	844 (53%)	18.33	Prospective cohort	4 moderation 2 other (three-way interaction)	a) Drinking to cope motive (bespoke question) b) Past month mean drinking	a) Anxiety symptoms (mean) (STAI) b) Anxiety symptoms (monthly) (STAI)	a) Drinking related problems (Brief Young Adult Alcohol Consequences Questionnaire)	High
(Bekman et al., 2010)	USA	677 (0%)	N/A (~14-18)	Prospective cohort	4 mediation 2 other (multiple mediation)	a) Expectancies for not drinking b) Perceptions of peer alcohol use	a) Social anxiety symptoms (Social Avoidance and Distress-New Scale of the Social Anxiety Scales for Adolescence)	a) Drinking initiation	High
(Bilevicius et al., 2020)	Canada	297 (72%)	20.86	Prospective cohort	2 moderation	a) Trait impulsivity (Substance use risk profile; SURPS)	a) Social anxiety symptoms (Social Phobia Scale; SPS)	a) Weekly alcohol use (quantity x frequency)	High

[2] Note: total model count may not equal the sum of mediators/moderators, predictors, and outcomes as some studies reported multiple analytic models (e.g. unadjusted versus adjusted analyses).

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models [2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
								b) Alcohol problems (Rutgers Alcohol Problems Index; RAPI)	
(Borges et al., 2018)	USA	246 (44%)	13.06	Prospective cohort	1 moderation	a) Positive alcohol expectancies	a) Anxiety sensitivity (Childhood anxiety sensitivity index; CASI)	a) Quantity of alcoholic beverages (past year)	High
(Buckner & Turner, 2009)	USA	544 (100%)	N/A (18+)	Prospective cohort	1 mediation 6 moderation	a) Negative life events b) Family cohesion c) Adverse family relations d) Partner support e) Peer social support f) Positive parent support g) Friends alcohol use	a) SAD (Composite International Diagnostic Interview; CIDI)	a) Alcohol use disorder (CIDI)	High (mediation) High (moderation)
(Caumiant et al., 2023)	USA	48 (50%)	22.6	Ecological Momentary Assessment	5 moderation	a) Social familiarity (bespoke question)	a) Social anxiety symptoms total (Liebowitz Social Anxiety Scale; LSAS) b) Social anxiety symptoms- fear (LSAS-fear subscale) c) Social anxiety symptoms- avoidance (LSAS- avoidance subscale)	a) Estimated breath alcohol concentration (transdermal alcohol sensors)	High
(Cerdá et al., 2013)	USA	460 (0%)	6.7	Prospective cohort	4 Moderation	a) Age b) Race/ ethnicity	a) Anxiety symptoms (Child Behavior Checklist; CBCL, Youth Self Report; YSR, and Teacher Report Form; TRF)	a) Alcohol use initiation	Some concerns
(Cheng et al., 2004)	Taiwan	49 (69.7%)	N/A (~35)	Prospective cohort	2 moderation	a) Age (15-24 vs. >35) b) Age (25-34 vs. >35)	a) Anxiety disorder (Chinese version of the Clinical Interview Schedule)	A) Alcohol use disorder (Adapted version of the Chinese version of the Clinical Interview Schedule)	High

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models [2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
(Cloutier et al., 2019)	USA	104 (100%)	13.9	Experimental	2 moderation	a) Anticipatory anxiety (Subjective Units of Distress Scale; SUDS) b) Post task anxiety (SUDS)	a) Social anxiety- social phobia (RCADS)	a) Alcohol initiation onset	High
(Colder et al., 2017)	USA	387 (55%)	12.1	Prospective cohort	8 moderation 3 other (three-way interaction)	a) Externalising symptoms b) Age	a) Generalised anxiety symptoms (TRF, YSR)	a) Drinks per year b) Drinking problems (Young Adult Alcohol Consequences Questionnaire; YAACQ)	Some concerns
(Colder et al., 2019)	USA	387 (55%)	17.9	Prospective cohort	1 moderation	a) Gender	a) Social anxiety symptoms (Social Interaction Anxiety Scale; SIAS)	a) Alcohol use quantity	High
(Collins et al., 2018)	Canada	219 (72.6%)	20.59	Prospective cohort	5 mediation	a) Coping-anxiety drinking motives b) Coping depression drinking motives c) Enhancement drinking motives d) Conforming drinking motives e) Social drinking motives (five-factor Modified Drinking Motives Questionnaire Revised; Modified DMQ-R)	a) Social avoidance (LSAS-avoidance subscale)	a) Alcohol problems (RAPI)	High
(Dahne et al., 2014)	USA	277 (43.7%)	11	Prospective cohort	2 moderation	a) Time b) Gender	a) Social phobia (Revised Child Anxiety and Depression Scale; RCADS)	a) Any alcohol use	High
(Dvorak & Simons, 2014)	USA	100 (61%)	20.09	Ecological momentary assessment	4 other (three-way interaction)	a) Gender b) Set shifting (Computerized Wisconsin Card Sort Task 64)	a) Daytime anxious mood (Positive and Negative Affect Schedule)	a) Drinking likelihood b) Intoxication (derived from a composite of 4 items)	High

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models [2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
						c) Sustained attention (Connors' Continuous Performance Task)			
(Dyer, Heron, et al., 2019)	England	3,452 (N/A)	17.8	Prospective cohort	8 moderation	a) Drinking to cope motives (adapted from the DMQ-R)	a) GAD (Clinical Interview Schedule Revised; CIS-R)	a) Frequent drinking (age 18) b) Frequent bingeing (age 18) c) Hazardous drinking (age 18) d) Harmful drinking (age 18) e) Frequent drinking (age 21) f) Frequent bingeing (age 21) g) Hazardous drinking (age 21) h) Harmful drinking (age 21)	Some concerns
(Gohari et al., 2023)	Canada	1,901 (65.3%)	N/A (12-18)	Prospective cohort	12 moderation	a) Sex	a) Anxiety symptoms (Generalised Anxiety Disorder 7-item; GAD-7)	a) Alcohol consumption escalation (vs. maintenance) from pre to early pandemic b) Alcohol consumption reduction (vs. maintenance) from pre to early pandemic c) Alcohol consumption Initiation (vs. abstinence) from pre to early pandemic d) Alcohol consumption escalation (vs. maintenance) from early to ongoing pandemic	High

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models [2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
								e) Alcohol consumption reduction (vs. maintenance) from early to ongoing pandemic f) Alcohol consumption Initiation (vs. abstinence) from early to ongoing pandemic g) Binge drinking escalation (vs. maintenance) from pre to early pandemic h) Binge drinking reduction (vs. maintenance) from pre to early pandemic i) Binge drinking Initiation (vs. abstinence) from pre to early pandemic j) Binge drinking escalation (vs. maintenance) from early to ongoing pandemic k) Binge drinking reduction (vs. maintenance) from early to ongoing pandemic l) Binge drinking Initiation (vs. abstinence) from early to ongoing pandemic	
(Goldstein et al., 2019)	Canada	203 (54.03%)	21.01	Prospective cohort	2 mediation	a) Emotion dysregulation (Difficulties in	a) Anxious attachment (Experiences in Close	a) Alcohol problems (YAACQ)	High

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models[2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
						Emotion Regulation Scale; DERS) b) Interpersonal difficulties (DERS)	Relationships-Revised; ECR-R)		
(Gorka et al., 2014)	USA	817 (58%)	16.6	Prospective cohort	2 moderation	a) Maternal support (Conflict Behavior Questionnaire; CBQ) b) Paternal support (CBQ)	a) Anxiety disorder (DSM-III-R)	a) Alcohol use disorder (DSM-III-R)	High
(V. V. Grant et al., 2009)	USA	146 (77%)	Not reported	3-week daily diary study	5 Moderation	a) Coping-anxiety drinking motives b) Coping depression drinking motives c) Enhancement drinking motives d) Conforming drinking motives e) Social drinking motives (Modified DMQ-R)	a) Daily anxious mood (self-report mood scale)	a) Daily alcohol consumption	High
(Kaplow et al., 2001)	USA	936 (45%)	N/A (~9)	Prospective cohort	3 moderation	a) Sex	a) Overall anxiety (Child and Adolescent Psychiatric Assessment; CAPA) b) Generalised anxiety (CAPA) Separation anxiety (CAPA)	a) Initiation of alcohol use at follow-up	High
(Leis et al., 2012)	UK	12,824 (100%)	27.7	Prospective cohort	2 moderation	a) Alcohol use in the 1st trimester	a) Anxiety symptoms (Crown Crisp Experiential Index; CCEI anxiety subscale)	a) Alcohol use 32 weeks gestation b) Binge drinking 32 weeks gestation	Some concerns
(Littlefield et al., 2012)	USA	115 (57%)	N/A (~18-19)	8 week daily diary	6 moderation	a) Social & enhancement drinking motives (DMQ-R) b) Drinking to cope motives (DMQ-R)	a) Anxiety symptoms (Positive and Negative Affect Schedule)	a) Onset of drinking b) Onset of heavy episodic drinking c) Onset of intoxication	High
(Mackinnon et al., 2014)	Canada	302 (72.5%)	20.84	Prospective cohort	6 mediation	a) Coping-anxiety drinking motives	a) Anxiety sensitivity (SURPS)	a) Alcohol problems (RAPI)	High

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models [2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
						b) Coping depression drinking motives c) Conformity drinking motives			
(Marmorstein et al., 2010)	USA	503 (0%)	6.2	Prospective cohort	4 moderation	a) Time in study b) Delinquency (bespoke scale)	a) Generalised anxiety symptoms (CBCL, YSR, TRF) b) Social anxiety symptoms (CBCL, YSR, TRF)	a) Age of first use of alcohol	High
(Marmorstein, 2015)	USA	144 (50%)	11.9	Prospective cohort	2 moderation	a) Urgency (UPPS-R-Child Impulsivity Scale)	a) Generalised anxiety symptoms (Screen for Child Anxiety and Related Disorders; SCARED) b) Social anxiety symptoms (SCARED)	a) Alcohol use frequency	Some concerns
(McCarty et al., 2023)	USA	361 (7%)	33.56	Prospective cohort	3 mediation	a) Depressive symptoms (Inventory of Depression and Anxiety Symptoms-General Depression; IDAS-GD)	a) Anxiety sensitivity (ASI-3)	a) Alcohol use frequency b) Alcohol use quantity c) Alcohol use problems (Short Index of Problems; SIP)	High
(Nichter & Chassin, 2015)	USA	818 (0%)	16	Prospective cohort	18 moderation	a) Race/ethnicity b) Life-time non-drug related self-reported offending c) Proportion of supervised time	a) Worry (Revised Children's Manifest Anxiety Scale; RCMAS) b) Physiological anxiety (RCMAS)	a) Typical quantity of drinking b) Frequency of binge drinking c) Alcohol dependence symptoms	High
(O'Grady, Cullum, Armeli, & Tennen, 2011)	USA	476 (52.3%)	18.73	30-day daily diary	4 moderation	a) Embarrassing event	a) Social anxiety symptoms (SCS-R)	a) Same day drinking b) Same evening drinking c) Next day drinking d) Next evening drinking	High
(O'Grady, Cullum, Tennen, & Armeli, 2011)	USA	574 (50%)	18.77	30-day daily diary one a	1 other (three-way interaction)	a) Year b) Event specific drinking norms	a) Social anxiety symptoms (SCS-R)	a) Previous night alcohol consumption	High

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models [2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
				year for 4 years					
(Pardini et al., 2007)	USA	506 (0%)	13.9	Prospective cohort	4 moderation	a) Conduct disorder symptoms (DSM-III-R)	a) Anxiety/ withdrawal (CBCL, YSR, TRF)	a) Alcohol use disorder symptoms, count (Diagnostic Interview Schedule; DIS) b) a) Alcohol use disorder symptoms, Zero inflation (DIS) c) Alcohol abuse diagnosis (DIS) d) Alcohol dependence diagnosis (DIS)	Some concerns
(Pedersen et al., 2013)	USA	193 (33%)	16.64	Prospective cohort	1 moderation	a) Perceived peer drinking norms (bespoke single item)	a) Anxiety symptoms (Mental Health Inventory)	a) Alcohol related consequences (bespoke measure)	Some concerns
(Richton et al., 2017)	USA	537 (51.7%)	18.77	Longitudinal daily diary	12 moderation 1 other (3-way interaction)	a) Tension reduction alcohol expectancies (daily) b) Tension reduction alcohol expectancies (yearly) c) Impairment alcohol expectancies (daily) d) Impairment alcohol expectancies (yearly) e) sex	a) Social anxiety symptoms (Self-Consciousness Scale; SCS-R Social Anxiety subscale)	a) Any drinking	High
(Schleider et al., 2019)	USA	2,100 (100%)	N/A (under 18)	Prospective cohort	4 moderation	a) Race b) Socioeconomic status c) Low neighbourhood safety d) Community cohesion	a) Anxiety severity (SCARED)	a) Any alcohol use	High
(Schmidt et al., 2007)	USA	404 (61%)	19.3	Prospective cohort	4 moderation	a) Gender	a) Anxiety sensitivity total (Anxiety Sensitivity Index; ASI)	a) Alcohol use disorder (DSM-IV-TR)	High

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models [2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
							b) Anxiety sensitivity-physical concerns (ASI) c) Anxiety sensitivity-cognitive concerns (ASI) d) Anxiety sensitivity-social concerns (ASI)		
(Wolitzky-Taylor et al., 2021)	USA	232 (69.8%)	22.5	Prospective cohort	2 mediation 1 other (multiple mediation)	a) Worry (Penn State Worry Questionnaire) b) Rumination (Ruminative Responses Scale)	a) Anxiety disorder clinical severity rating (Structured Clinical Interview for the DSM-IV, non-patient; SCID-I/NP))	a) Alcohol use disorder symptom severity (SCID-I/NP)	High
(Zimmermann et al., 2003)	Germany	3,021 (N/A)	N/A (~14-24)	Prospective cohort	70 moderation	a) Gender	a) Panic disorder w or w/o agoraphobia b) Panic attack c) Agoraphobia w/o panic disorder d) Social phobia e) Specific phobia f) Phobia NOS g) GAD h) Any anxiety disorder	a) At least regular alcohol use b) Hazardous alcohol use c) Alcohol use disorder- abuse d) Alcohol use disorder- abuse e) Alcohol use disorder- dependence f) Alcohol use disorder- any	High
Alcohol → Anxiety models									
(Abrams et al., 2001)	USA	61 (60.66%)	32.3	Experimental	2 moderation	a) Time during experimental study	a) Beverage group (placebo, alcohol, control)	a) Performance anxiety (VAS) b) Performance anxiety: post speech (Audience Anxious Scale; AAS)	High
(Abrams, Matt, & and Reinertsen, 2002)	USA	61 (60.7%)	32.3	Experimental	2 mediation	a) Change in positive thoughts (bespoke measure) b) Change in negative thoughts (bespoke measure)	a) Beverage group (placebo, alcohol, control)	a) Subjective anxiety level (Visual analogue scale)	High

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models[2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
(Abrams et al., 2022)	USA	53 (56%)	21.9	Experimental	3 moderation	a) Tension reduction alcohol expectancies b) Anxiety sensitivity	a) Alcohol dose (placebo vs control)	a) State anxiety (STAI)	Some concerns
(Armeli, O'Hara, et al., 2014)	USA	1,421 (54%)	19.3	30- day daily diary	4 moderation	a) Social drinking (self-report) b) Non-social drinking (self-report)	a) Episode specific drinking to cope (adapted DMQ-R measure)	a) Anxiety symptoms (Positive and Negative Affect Schedule-Expanded)	High
(Carvalho et al., 2018)	Ireland	4,461 (51.7%)	63.3	Prospective cohort	4 moderation	a) Sex	a) Problem drinking (CAGE questionnaire) b) Alcohol consumption level	a) Incident anxiety (Hospital Anxiety and Depression Scale HADS-A) b) Persistent anxiety (HADS-A)	High
(Cook et al., 2024)	England	439,494 (42.75%)	N/A	Prospective cohort	1 moderation	a) History of past anxiety (hospital records)	a) Alcohol use disorder diagnosis (hospital records)	a) New episode of anxiety (hospital records)	High
(Ferariu et al., 2024)	USA	11,688 (48%)	N/A (9-10)	Prospective cohort	4 moderation	a) Study time (linear) b) Study time (quadratic)	a) Low vs high alcohol sipping class b) No vs high alcohol sipping class	a) Anxiety symptoms (Parent- CBCL)	Some concerns
(Sayette et al., 2001)	USA	169 (49.7)	N/A (21-28)	Experimental	1 moderation	a) Order of drink and stressor task	a) Beverage group (alcohol vs placebo)	a) State anxiety- brief (STAI-B)	High
(Sher et al., 2007)	USA	101 (0%)	N/A (~21-25)	Experimental	1 mediation 1 moderation	a) sustained attention via a continuous performance task	a) Alcohol beverage condition (alcohol vs placebo)	a) Change in anxiety (stress bar on computer)	High (mediation) High (moderation)
(Steele et al., 1986)	USA	62-71 (43.66% - 35.48%)	N/A (~21+)	Experimental	2 moderation	a) Activity group (distracted group vs no distraction group b) Time of measurement (post feedback vs post recovery)	a) Beverage group (alcohol vs placebo) b) Alcohol experimental condition alcohol + slides + expectancy vs. alcohol + slides + no expectancy vs. alcohol + no slides)	a) Anxiety symptoms (Multiple Affect Adjective Check list; MAACL. Anxiety subscale)	High
(Steele & Josephs, 1988)	USA	37 (45.95%)	N/A (~21+)	Experimental	4 other (three-way interaction)	a) Time b) Activity group (distracted group vs no distraction group)	a) Beverage group (placebo, alcohol)	a) State anxiety (STAI)	High

Author (year)	Country	Sample size (female %)	Sample mean age at baseline	Study design	Total models[2]	Mediator(s)/ Moderator(s) (measurement)	Predictor(s) (measurement)	Outcome(s) (measurement)	Study risk of bias
(Stevens et al., 2014)	Germany	95 (N/A)	N/A (~21-23)	Experimental	1 moderation 1 other (three-way interaction)	a) Time b) Social anxiety group (high vs normal)	a) Beverage group (placebo, alcohol, control)	a) Anxiety symptoms (VAS)	High
(Wojciechowski, 2024)	USA	1,001 (13.59%)	16.59	Prospective cohort	2 moderation	a) Major depressive disorder (CIDI)	a) Heavy episodic drinking frequency (four/five drinks on one occasion)	a) Anxiety symptoms in adolescence (BSI) b) Anxiety symptoms in emerging adulthood (BSI)	High
Both directions: Anxiety → Alcohol and Alcohol → Anxiety									
(Mackie et al., 2011)	England	393 (N/A)	13	Prospective cohort	10 moderation	a) Anxiety sensitivity (SURPS) b) Hopelessness (SURPS) c) Impulsivity (SURPS) d) Sensation seeking (SURPS) e) Gender	a) Anxiety symptoms (BSI)	a) Alcohol use (quantity x frequency)	Some concerns
(Parrish et al., 2016)	USA	620 (50%)	N/A (~14)	Prospective cohort	8 moderation	a) Gender b) Mexican Generational status	a) Frequency of alcohol use b) Anxiety symptoms (Mini-Mood and Anxiety Symptom Questionnaire; MASQ) c) Anxious arousal (MASQ)	a) Anxiety symptoms (MASQ) b) Anxious arousal (MASQ) c) Frequency of alcohol use	High
(Paulus et al., 2021)	USA	3,396 (53.4%)	14.1	Prospective cohort	4 mediation 1 other (moderated mediation)	a) Race/ethnicity b) Anxiety	a) Anxiety sensitivity (CASI) b) Alcohol problems (RAPI)	a) Alcohol problems (RAPI) b) Anxiety sensitivity (CASI)	High

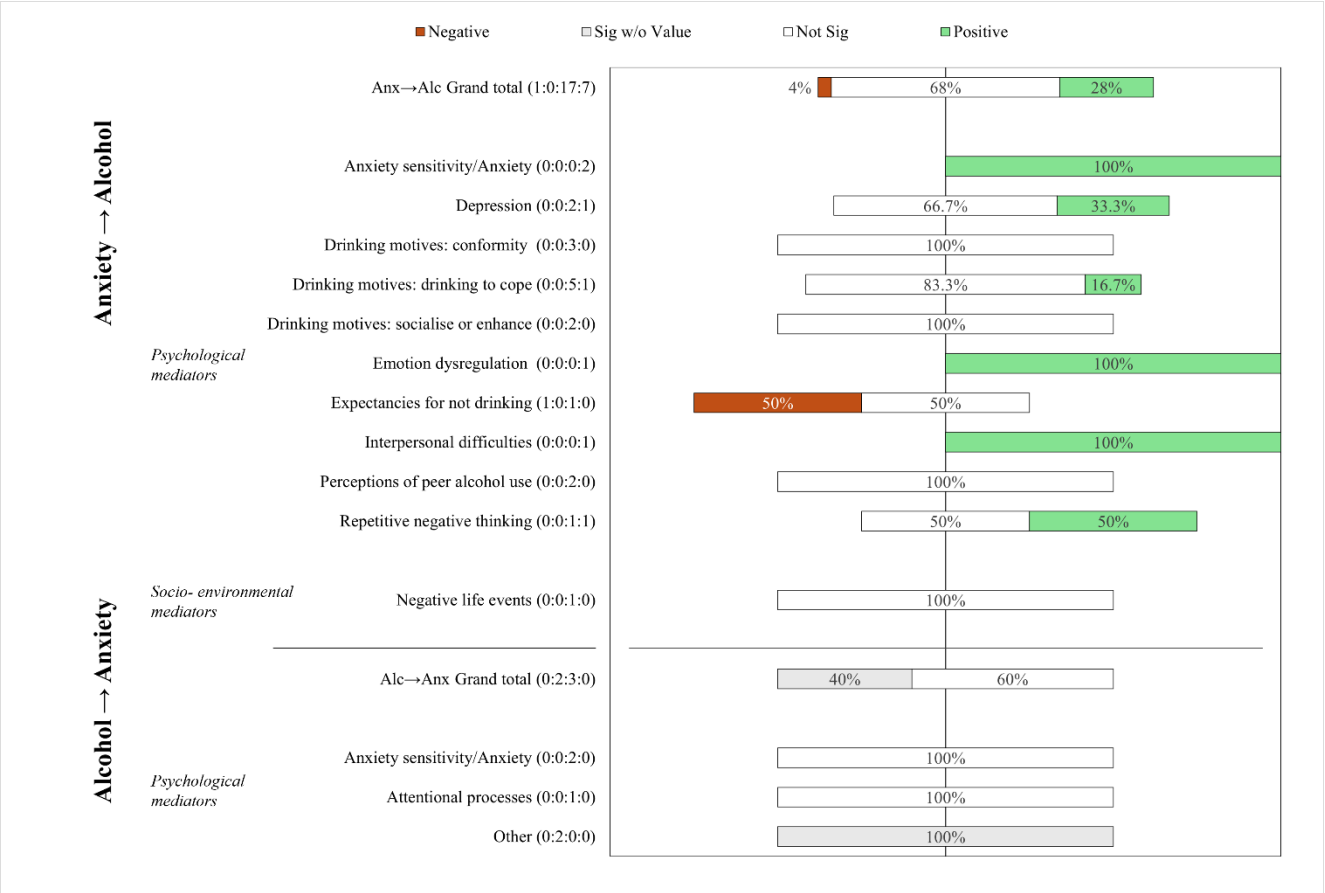
2.3.3 Results of the risk of bias assessment

The overall risk of bias for each study can be seen in Table 2.1 and the individual scores for the respective mediation and moderation domains in supplementary material (Appendix A: Table A20 and Table A21). Overall, the risk of bias of individual studies was high, with all mediation (10/10) and the majority of moderation (37/47) studies classified as having high risk of bias. No study had a low overall risk of bias. Across both mediation and moderation studies there were commonly identified biases pertaining to handling of missing data, reporting of null results, preregistration of analyses, and power to detect effects. Specifically, none of the mediation studies conducted a formal power analysis and only three of the 47 moderation studies discussed were adequately powered to detect small-medium interaction effects. For mediation studies specifically, there were also confounding biases and in some studies a violation of temporal precedence.

2.3.4 Results of mediation studies

Overall, there were 10 studies identified in the review which tested mediation models. Together there were 30 single mediation models which predominantly investigated mediators in the anxiety → alcohol pathway. Figure 2.4 provides an overarching summary of the mediation effects explored and study-reported statistical significance, grouped by subtheme and direction of relationship. These are expanded on in the narrative synthesis. Due to the limited number of studies and significant heterogeneity of mediating factors, mediation effects were not suitable for meta-analysis.

Figure 2.4: Summary of the identified mediation effects (n = 30).
Counts and proportions by statistical significance are reported for each mediator subtheme.



Note: The numbers in brackets for each subtheme correspond to the count of negative effects, significant effects without value reported, not significant effects, or positive effects identified.

2.3.4.1 Anxiety to alcohol pathway

Eight studies examined mediators in the anxiety → alcohol pathway, with 25 unique single mediation effects tested. All but one of these mediators was a psychological factor. No biological mediators were investigated in the included studies, and a single study looked at a socio-environmental factor, negative life events. Of the 25 effects identified only eight were significant. While no study reported a power analysis, sample sizes were modest ranging from 219 to 3,396. Table 2.2 presents each mediator effect pathway, their transformed effect size, and effects size classification. Supplementary Table A7 provides the original and transformed effects.

Table 2.2: Identified mediation effects in the anxiety → alcohol relationship

Mediator superordinate theme	Mediator subtheme	Effect label assigned ***Predictor → Outcome	Mediator***	Effect magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
Psychological	Anxiety sensitivity / Anxiety	Anxiety sensitivity → Alcohol problems | Anxiety (wave 2) (Paulus et al. 2021) [Sig]	0.040 (0.006 to 0.073)	Small Positive	3,396	Under 18	High
		Anxiety sensitivity → Alcohol problems | Anxiety (wave 3) (Paulus et al. 2021) [Sig]‡	0.025 (-0.009 to 0.058)	Small Positive	3,396	Under 18	High
	Depression	Anxiety sensitivity → Alcohol use frequency | Depressive symptoms (McCarty et al. 2023) [NS]	0.069 (-0.035 to 0.171)	NS	361	18-49	High
		Anxiety sensitivity → Alcohol use quantity | Depressive symptoms (McCarty et al. 2023) [NS]	0.091 (-0.012 to 0.193)	NS	361	18-49	High
		Anxiety sensitivity → Alcohol use problems | Depressive symptoms (McCarty et al. 2023) [Sig]	0.136 (0.034 to 0.236)	Small Positive	361	18-49	High
	Drinking motives: conformity	Social avoidance → Alcohol problems | Drinking motives: conformity (Collins et al. 2018) [NS]	0.066 (-0.067 to 0.197)	NS	219	18-49	High
		Anxiety sensitivity → Alcohol problems | Drinking motives: conformity (between-subject model) (Mackinnon et al. 2014) [NS]	0.095 (-0.018 to 0.206)	NS	302	18-49	High
		Anxiety sensitivity → Alcohol problems | Drinking motives: conformity (within-subject model) (Mackinnon et al. 2014) [NS]	0.068 (-0.046 to 0.179)	NS	302	18-49	High
	Drinking motives: drinking to cope	Social avoidance → Alcohol problems | Drinking motives: Drinking to cope with anxiety (Collins et al. 2018) [NS]	-0.141 (-0.269 to -0.009)	NS	219	18-49	High
		Anxiety sensitivity → Alcohol problems | Drinking motives: Drinking to cope with anxiety (between-subject model) (Mackinnon et al. 2014) [NS]	-0.014 (-0.127 to 0.099)	NS	302	18-49	High
		Anxiety sensitivity → Alcohol problems | Drinking motives: Drinking to cope with anxiety (within-subject model) (Mackinnon et al. 2014) [NS]	-0.048 (-0.160 to 0.065)	NS	302	18-49	High
		Social avoidance → Alcohol problems | Drinking motives: Drinking to cope with depression (Collins et al. 2018) [Sig] ‡	0.127 (-0.006 to 0.255)	Small Positive	219	18-49	High

‡Significance is reported as per the original study. Transformed effect sizes may not align with the reported significance.

Mediator superordinate theme	Mediator subtheme	Effect label assigned *Predictor → Outcome | Mediator*	Effect magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
Socio-environmental		Anxiety sensitivity → Alcohol problems | Drinking motives: Drinking to cope with depression (between-subject model) (Mackinnon et al. 2014) [NS] ‡	0.173 (0.062 to 0.281)	NS	302	18-49	High
		Anxiety sensitivity → Alcohol problems | Drinking motives: Drinking to cope with depression (within-subject model) (Mackinnon et al. 2014) [NS]	0.038 (-0.076 to 0.150)	NS	302	18-49	High
	Drinking motives: Socialise or enhance	Social avoidance → Alcohol problems | Drinking motives: enhancement (Collins et al. 2018) [NS]	0.075 (-0.058 to 0.206)	NS	219	18-49	High
		Social avoidance → Alcohol problems | Drinking motives: social (Collins et al. 2018) [NS]	0.088 (-0.045 to 0.218)	NS	219	18-49	High
	Emotion dysregulation	Anxious attachment → Alcohol problems | Emotion dysregulation (Goldstein et al. 2019) [Sig]	0.142 (0.004 to 0.274)	Small Positive	203	18-49	High
	Expectancies for not drinking	Social anxiety symptoms → Initiation of alcohol use | Expectancies for not drinking (Bekman et al. 2010) [Sig]	-0.107 (-0.180 to -0.031)	Small Negative	677	Under 18	High
		Social anxiety symptoms → Initiation of alcohol use | Expectancies for not drinking (Bekman et al. 2010) [NS]	-0.012 (-0.092 to 0.069)	NS	591	Under 18	High
	Interpersonal difficulties	Anxious attachment → Alcohol problems | Interpersonal difficulties (Goldstein et al. 2019) [Sig] ‡	0.129 (-0.009 to 0.262)	Small Positive	203	18-49	High
	Perceptions of peer alcohol use	Social anxiety symptoms → Initiation of alcohol use | Perceptions of peer alcohol use (Bekman et al. 2010) [NS]	-0.052 (-0.127 to 0.023)	NS	677	Under 18	High
		Social anxiety symptoms → Initiation of alcohol use | Perceptions of peer alcohol use (Bekman et al. 2010) [NS]	-0.042 (-0.122 to 0.039)	NS	591	Under 18	High
	Repetitive negative thinking	Anxiety disorder severity → Alcohol use disorder symptoms severity | Rumination (Wolitzky-Taylor et al. 2021) [Sig]	0.132 (0.003 to 0.256)	Small Positive	232	18-49	High
		Anxiety disorder severity → Alcohol use disorder symptoms severity | Worry (Wolitzky-Taylor et al. 2021) [NS]	0.051 (-0.078 to 0.179)	NS	232	18-49	High
	Negative life events	Social anxiety disorder → Alcohol use disorder | Negative life events (Buckner et al. 2009) [NS] ‡	-0.116 (-0.199 to -0.033)	NS	544	18-49	High

2.3.4.1.1 Psychological mediators

Psychological mediators spanning nine subthemes were identified across 24 models. **Drinking motives** were the most commonly investigated mediator, with 11 mediation models identified in the review**.**

Drinking to cope motives were evaluated in six of these models. Three models tested whether the anxiety → alcohol relationship was mediated by coping with *anxiety* motives and another three evaluated coping with *depression* motives (Collins et al., 2018; Mackinnon et al., 2014). Collins et al. (2018) found evidence that drinking to cope with *depression* mediated the relationship between social avoidance and alcohol problems among undergraduate students. The remaining five models did not find support for coping motives mediating the anxiety → alcohol relationship.

Two studies tested mediation by **conformity, social, and enhancement drinking motives**, but none found evidence that these motives mediated the relationship between social avoidance or anxiety sensitivity and alcohol problems (Collins et al., 2018; Mackinnon et al., 2014).

One study examined **expectancies for not drinking** and found evidence that they mediated the relationship between social anxiety and alcohol use initiation for boys but not girls (Bekman et al., 2010). For boys, higher social anxiety was associated with more positive expectancies for not drinking, which in turn predicted lower odds of initiating alcohol use. The same study also tested **perceptions of peer alcohol** use, with no evidence of mediation for either boys or girls (Bekman et al., 2010). Caution, however, should be placed on these findings as temporal precedence was not established between the predictor and mediating factors in this study.

One study among US veterans found **depression** mediated the relationship between anxiety sensitivity and alcohol use problems but not alcohol use quantity or frequency (McCarty et al., 2023).

One study tested whether transdiagnostic **anxiety** symptoms themselves were a mediator between anxiety sensitivity and alcohol problems (Paulus et al., 2021). Among a racially diverse sample of high school students' anxiety was a mediator across two different time frames (Paulus et al., 2021).

Additional psychological factors identified in a single study included **interpersonal difficulties** and **emotion dysregulation,** both of which mediated the association between anxious attachment and alcohol problems among 18-24-year-olds (Goldstein et al., 2019).

The final psychological mediator subtheme was related to **repetitive negative thinking**, examined in a single study. Wolitzky-Taylor et al. (2021) tested worry and repetitive negative thinking as two distinct mediating constructs. Among the young adult sample, rumination significantly mediated the relationship between anxiety disorder severity and AUD severity whilst worry did not.

2.3.4.1.2 Socio-environmental mediators

Only one socio-environmental factor, **negative life events**, was investigated in a longitudinal cohort of young adults. In this study, Buckner and Turner (2009) did not find support for negative life events mediating the pathway from SAD to an AUD. Whilst this study was longitudinal in design, both the SAD predictor and negative life events mediator were measured at time point one of the study, thereby violating temporal precedence requirements of mediation.

2.3.4.2 Alcohol to anxiety pathway

Only three singular mediator studies were identified which considered the relationship in the reverse direction, that is, alcohol use predicting anxiety outcomes. From these studies there were five effects, across three subthemes, all of which included psychological mediators. Table 2.3 provides each mediator effect pathway, their transformed effect size, and effects size classification. Supplementary Table A8 provides the original and transformed effects.

Table 2.3: Identified mediation effects in the alcohol → anxiety relationship.

Mediator super-ordinate theme	Mediator subtheme	Effect label assigned ***Predictor → Outcome	Mediator***	Effect magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
Psychological	Anxiety sensitivity/ Anxiety	Alcohol problems (wave 1) → Anxiety sensitivity (wave 3) | Anxiety (wave 2) (Paulus et al. 2021) [NS]	0.017 (-0.016 to 0.051)	NS	3396	Under 18	High
		Alcohol problems (wave 2) → Anxiety sensitivity (wave 4) | Anxiety (wave 3) (Paulus et al. 2021) [NS]	0.017 (-0.016 to 0.051)	NS	3396	Under 18	High
	Attentional processes	Alcohol dose (placebo vs control) → Anxiety symptoms | Sustained attention (Sher et al. 2007) [NS]	--	NS	101	18-49	High
	Other	Alcohol beverage group (alcohol expected, alcohol not expected, placebo) → Anxiety symptoms | Change in negative thoughts (Abrams et al. 2002) [Sig]	--	Sig w/o Z	61	18-49	High
		Alcohol beverage group (alcohol expected, alcohol not expected, placebo) → Anxiety symptoms | Change in positive thoughts (Abrams et al. 2002) [Sig]	--	Sig w/o Z	61	18-49	High

2.3.4.2.1 Psychological mediators

Paulus et al. (2021) examined **anxiety** as a mediator of the relationship between alcohol problems and anxiety sensitivity. Across two different longitudinal intervals (wave 1-3 and wave 2-4), there was no evidence that alcohol problems influenced anxiety sensitivity via anxiety in the high school sample. As outlined earlier, the reverse pathway, from anxiety sensitivity to alcohol problems, was mediated via anxiety. This suggests that despite prior evidence of a bidirectional relationship between anxiety and alcohol, the mediating factors may be unique to the direction of the relationship of interest.

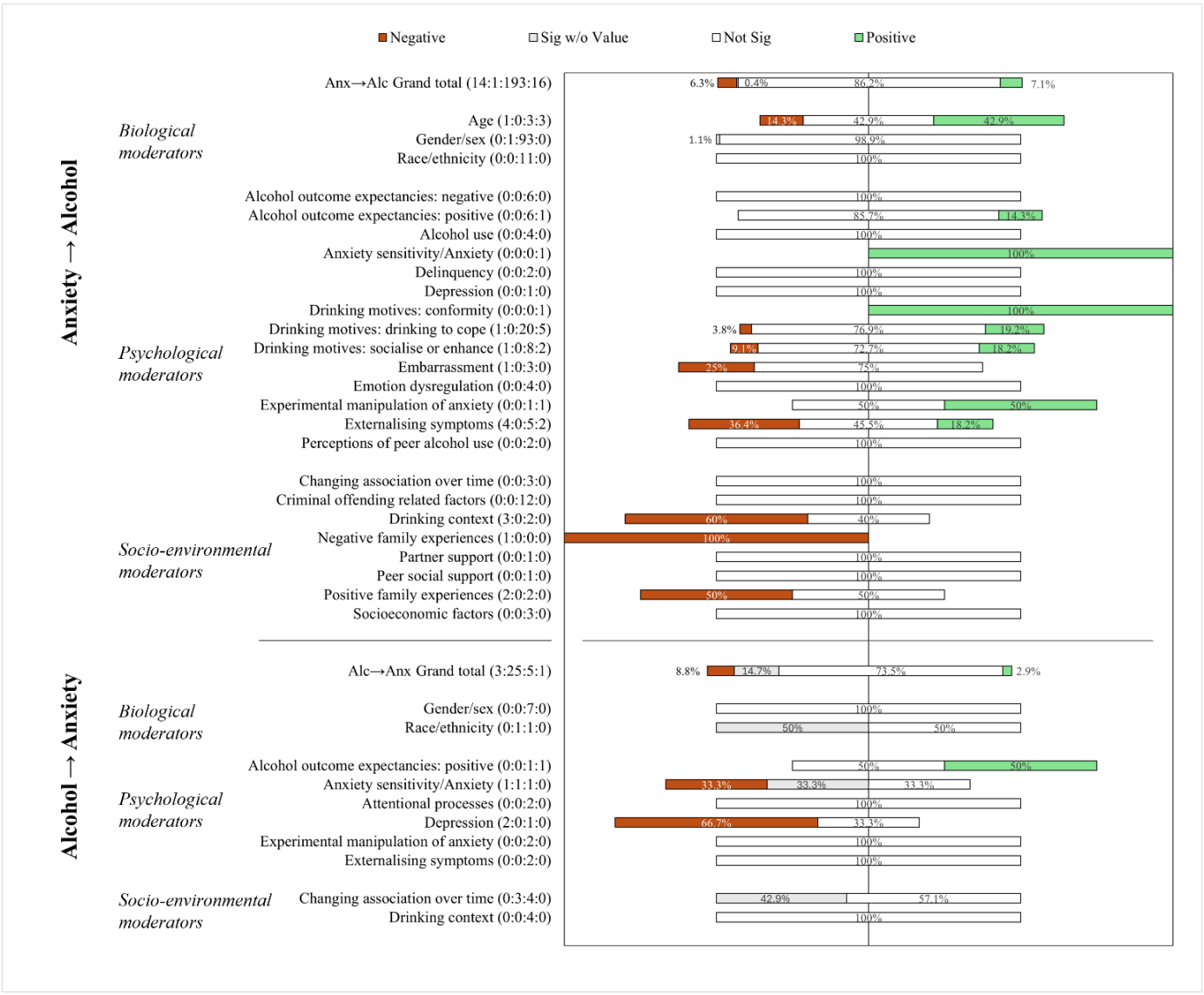
The remaining two studies were experimental in design and involved alcohol manipulation via administering placebo beverages. Sher et al. (2007) tested **attentional processes** (sustained attention) as a mediator of alcohol's effect on anxiety symptoms, in line with the stress response dampening model of alcohol use. In this sample of young adult men, sustained attention, in the form of a computerised continuous performance task, did not mediate the relationship between beverage condition (alcohol or placebo) and anxiety symptoms.

Among a small sample of adults with social phobia (n = 61), anxiety-relevant cognitions were tested mediators in a three-arm beverage manipulation design (alcoholic, placebo, or control beverage) (Abrams, Matt, & and Reinertsen, 2002). Both increases in **positive thought cognitions** and decreases in **negative thought cognitions** were found to mediate the relationship between beverage group and reductions in subjective anxiety during a public speaking task (Abrams, Matt, & and Reinertsen, 2002).

2.3.5 Results of moderation studies

Overall, there were 43 studies identified in the review which tested moderation models. Together, there were 258, single, moderation models tested. Again, the majority of these effects investigated moderators of the anxiety → alcohol relationship. Figure 2.5 provides an overarching summary of these 258 effects, group by subtheme and direction of relationship. As seen in the figure, there was a large count of effects which were non-significant. Few studies, however, reported if they were adequately powered to detect interaction effects. Each moderator subtheme is narratively synthesised below along with meta-analytic results if sufficient data was reported for meta-analysing the moderator subtheme. This meta-synthesis was possible for 13 of the subthemes identified in the anxiety → alcohol relationship and four subthemes identified in the alcohol → anxiety relationship.

Figure 2.5: Summary of identified moderation effects (n = 224)
Counts and proportions by statistical significance are reported for each moderator subtheme.



Note: The numbers in brackets for each subtheme correspond to the count of negative effects, significant effects without value reported, not significant effects, or positive effects identified.

2.3.5.1 Anxiety to alcohol pathway

Moderators of the anxiety → alcohol pathway represented the most frequently examined relationship in this review, with 224 effects identified. These effects spanned 25 subthemes. Owing to the significant number of effects, Table 2.4 provides a summary of the effects which provided sufficient reporting for effect transformation. A complete list of all effect pathways, their transformed effect size, and effects size classification, including those without numerical effect information can be found in Appendix A: Supplementary Table A9. All effects are narratively expanded on below. Results of the meta-synthesis are provided in Table 2.5. Counts

of all study effects versus the reduced study list with available data for meta-synthesis are also provide in this table. It is important to note that while this pathway has been most extensively studied, many moderation analyses were exploratory and often underpowered, meaning that null findings should be interpreted cautiously. This limitation is considered further in subsection 2.4.3.

Table 2.4: Identified moderation effects in the anxiety → alcohol relationship[4].

Moderator or super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome | Moderator*	Effect Magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
Biological	Age	Social anxiety symptoms → Alcohol problems | Age (Colder et al. 2017) [Sig]	-0.151 (-0.247 to -0.052)	Small Negative	387	Under 18	Some concerns
		Anxiety disorder → Alcohol use disorder | Age (Cheng et al. 2004) [NS]	0.061 (-0.028 to 0.148)	NS	491	18-49	High
		Anxiety disorder → Alcohol use disorder | Age (Cheng et al. 2004) [Sig]	0.171 (0.084 to 0.256)	Small Positive	491	18-49	High
	Gender/ sex	Anxiety symptoms → Initiation of alcohol use | Sex (Kaplow et al. 2001) [NS]	-0.030 (-0.094 to 0.034)	NS	936	Under 18	High
		Anxiety symptoms (general & separation) → Initiation of alcohol use | Sex (Kaplow et al. 2001) [NS]	-0.014 (-0.078 to 0.051)	NS	936	Under 18	High
		Anxiety sensitivity- Social concerns → Alcohol use disorder | Gender (Schimdt et al. 2007) [NS]	0.011 (-0.087 to 0.108)	NS	404	18-49	High
		Anxiety sensitivity- Physical concerns → Alcohol use disorder | Gender (Schimdt et al. 2007) [NS]	0.023 (-0.075 to 0.120)	NS	404	18-49	High
		Separation anxiety symptoms → Initiation of alcohol use | Sex (Kaplow et al. 2001) [NS]	0.041 (-0.024 to 0.104)	NS	936	Under 18	High
		Anxiety sensitivity- Cognitive concerns → Alcohol use disorder | Gender (Schimdt et al. 2007) [NS]	0.046 (-0.051 to 0.143)	NS	404	18-49	High
		Anxiety sensitivity → Alcohol use disorder | Gender (Schimdt et al. 2007) [NS]	0.061 (-0.037 to 0.157)	NS	404	18-49	High
		Anxiety symptoms → Alcohol use | Gender (Mackie et al. 2011) [NS]	0.071 (-0.028 to 0.168)	NS	393	Under 18	Some concerns
	Race/ ethnicity	Anxiety symptoms → Alcohol use initiation | Race/ethnicity (Black/other) (Cerda et al. 2013) [NS]‡	0.196 (0.107 to 0.282)	NS	460	Under 18	Some concerns
Psychological	Alcohol outcome expectancies: negative	Social anxiety symptoms → Drinks per drinking day | Impairment alcohol expectancies (Richton et al. 2017) [NS]	0.000 (-0.086 to 0.086)	NS	515	18-49	High
		Yearly social anxiety symptoms → Drinks per drinking day | Impairment alcohol expectancies (Richton et al. 2017) [NS]	0.000 (-0.086 to 0.086)	NS	515	18-49	High

[4] Only effects with sufficient data reported for effect estimate transformation are presented (n = 79). Full N =224 effects are in Supplementary Table A 9.

Moderator or super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome | Moderator*	Effect Magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
		Social anxiety symptoms → Any drinking | Impairment alcohol expectancies (Richton et al. 2017) [NS]	-0.043 (-0.127 to 0.042)	NS	537	18-49	High
		Yearly social anxiety symptoms → Any drinking | Impairment alcohol expectancies (Richton et al. 2017) [NS]	0.054 (-0.031 to 0.138)	NS	537	18-49	High
		Social anxiety symptoms → Drinks per drinking day | Impairment alcohol expectancies (yearly) (Richton et al. 2017) [NS]	-0.044 (-0.130 to 0.043)	NS	515	18-49	High
		Social anxiety symptoms → Any drinking | Impairment alcohol expectancies (yearly) (Richton et al. 2017) [NS]	0.054 (-0.031 to 0.138)	NS	537	18-49	High
	Alcohol outcome expectancies : positive	Anxiety sensitivity → Alcohol use (in past year) | Alcohol outcome expectancies: Positive (Borges et al. 2018) [Sig]‡	0.064 (-0.062 to 0.187)	Small Positive	246	Under 18	High
		Social anxiety symptoms → Drinks per drinking day | Tension-reduction (Richton et al. 2017) [NS]	-0.044 (-0.130 to 0.043)	NS	515	18-49	High
		Yearly social anxiety symptoms → Drinks per drinking day | Tension-reduction expectancies (Richton et al. 2017) [NS]	-0.066 (-0.151 to 0.021)	NS	515	18-49	High
		Social anxiety symptoms → Any drinking | Tension-reduction expectancies (Richton et al. 2017) [NS]	0.000 (-0.085 to 0.085)	NS	537	18-49	High
		Yearly social anxiety symptoms → Any drinking | Tension-reduction expectancies (Richton et al. 2017) [NS]	0.065 (-0.020 to 0.148)	NS	537	18-49	High
		Social anxiety symptoms → Drinks per drinking day | Tension-reduction expectancies (yearly) (Richton et al. 2017) [NS]	0.022 (-0.065 to 0.108)	NS	515	18-49	High
		Social anxiety symptoms → Any drinking | Tension-reduction expectancies (yearly) (Richton et al. 2017) [NS]	0.032 (-0.052 to 0.117)	NS	537	18-49	High
	Alcohol use	Anxiety symptoms → Any alcohol use at 32 weeks gestation | 1st trimester alcohol use (Leis et al. 2012) [NS]	0.000 (-0.017 to 0.017)	NS	12,824	18-49	Some concerns
		Anxiety symptoms → Binge drinking at 32 weeks gestation | 1st trimester alcohol use (Leis et al. 2012) [NS]	-0.007 (-0.024 to 0.010)	NS	12,824	18-49	Some concerns
		Anxiety symptoms → Drinking related problems | Means drinks (quantity x frequency) (Armeli et al. 2008) [NS]	0.033 (-0.035 to 0.100)	NS	844	18-49	High
		Anxiety symptoms (monthly) → Drinking related problems | Means drinks (quantity x frequency) (Armeli et al. 2008) [NS]	-0.002 (-0.069 to 0.066)	NS	844	18-49	High
	Anxiety sensitivity/ Anxiety	Anxiety symptoms → Alcohol use | Anxiety sensitivity (Mackie et al. 2011) [Sig]	0.131 (0.033 to 0.227)	Small Positive	393	Under 18	Some concerns

Moderator or super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome* | *Moderator*	Effect Magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
	Delinquency	--	--	--	--	--	--
	Depression	Anxiety symptoms → Alcohol use | Hopelessness (Mackie et al. 2011) [NS]	0.071 (-0.028 to 0.169)	NS	393	Under 18	Some concerns
	Drinking motives: conformity	Daily anxious mood → Daily alcohol use | Drinking motives: conformity (Grant et al. 2009) [Sig]	0.325 (0.169 to 0.465)	Moderate Positive	142	18-49	High
	Drinking motives: drinking to cope	Daily anxious mood → Daily alcohol use | drinking to cope (Grant et al. 2009) [NS]	-0.131 (-0.289 to 0.035)	NS	142	18-49	High
		Generalised anxiety disorder → Harmful drinking, AUDIT, age 21 | drinking to cope (le 1 et al. 2019) [NS]	-0.011 (-0.044 to 0.022)	NS	3,452	Under 18	Some concerns
		Generalised anxiety disorder → Hazardous drinking, AUDIT, age 21 | drinking to cope (Dyer et al. 2019) [NS]	-0.007 (-0.041 to 0.026)	NS	3,452	Under 18	Some concerns
		Anxiety symptoms (monthly) → Drinking related problems | drinking to cope (Armeli et al. 2008) [NS]	-0.004 (-0.072 to 0.063)	NS	844	18-49	High
		Generalised anxiety disorder → Harmful drinking, AUDIT, age 18 | drinking to cope (Dyer et al. 2019) [NS]	-0.004 (-0.037 to 0.030)	NS	3,452	Under 18	Some concerns
		Generalised anxiety disorder → Frequent bingeing, AUDIT, age 21 | drinking to cope (Dyer et al. 2019) [NS]	-0.002 (-0.036 to 0.031)	NS	3,452	Under 18	Some concerns
		Generalised anxiety disorder → Hazardous drinking, AUDIT, age 18 | drinking to cope (Dyer et al. 2019) [NS]	-0.002 (-0.035 to 0.031)	NS	3,452	Under 18	Some concerns
		Generalised anxiety disorder → Frequent drinking, AUDIT, age 21 | drinking to cope (Dyer et al. 2019) [NS]	0.000 (-0.033 to 0.033)	NS	3,452	Under 18	Some concerns
		Generalised anxiety disorder → Frequent bingeing, AUDIT, age 18 | drinking to cope (Dyer et al. 2019) [NS]	0.019 (-0.015 to 0.052)	NS	3,452	Under 18	Some concerns
		Generalised anxiety disorder → Frequent drinking, AUDIT, age 18 | drinking to cope (Dyer et al. 2019) [NS]	0.028 (-0.005 to 0.061)	NS	3,452	Under 18	Some concerns
		Anxiety symptoms → Drinking related problems | drinking to cope (Armeli et al. 2008) [Sig]	0.145 (0.078 to 0.210)	Small Positive	844	18-49	High
		Daily anxious mood → Daily alcohol use | drinking to cope (Grant et al. 2009) [Sig]	0.173 (0.008 to 0.328)	Small Positive	142	18-49	High
	Drinking motives: socialise or enhance	Daily anxious mood → Daily alcohol use | drinking to socialise (Grant et al. 2009) [Sig]	-0.230 (-0.380 to -0.068)	Small Negative	142	18-49	High
		Daily anxious mood → Daily alcohol use | drinking to enhance (Grant et al. 2009) [NS]	0.059 (-0.107 to 0.221)	NS	142	18-49	High

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome | Moderator*	Effect Magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
	Embarrassment	Social anxiety symptoms → Same day drinking | Embarrassing event (O'Grady et al. 2011) [NS]	0.023 (-0.067 to 0.113)	NS	476	18-49	High
		Social anxiety symptoms → Same evening drinking | Embarrassing event (O'Grady et al. 2011) [Sig]	-0.091 (-0.180 to -0.001)	Small Negative	476	18-49	High
		Social anxiety symptoms → Next day drinking | Embarrassing event (O'Grady et al. 2011) [NS]	-0.011 (-0.101 to 0.079)	NS	476	18-49	High
		Social anxiety symptoms → Next evening drinking | Embarrassing event (O'Grady et al. 2011) [NS]	-0.046 (-0.135 to 0.044)	NS	476	18-49	High
	Emotion dysregulation	Anxiety and withdrawal symptoms → Alcohol use disorder symptoms (binary) | Conduct disorder symptoms (Pardini et al. 2007) [NS]	-0.052 (-0.138 to 0.036)	NS	506	Under 18	Some concerns
		Anxiety and withdrawal symptoms → Alcohol use disorder symptoms | Conduct disorder symptoms (Pardini et al. 2007) [NS]	-0.020 (-0.107 to 0.067)	NS	506	Under 18	Some concerns
		Anxiety and withdrawal symptoms → Alcohol abuse disorder only | Conduct disorder symptoms (Pardini et al. 2007) [NS]	0.035 (-0.052 to 0.122)	NS	506	Under 18	Some concerns
		Anxiety and withdrawal symptoms → Alcohol dependence disorder only | Conduct disorder symptoms (Pardini et al. 2007) [NS]	0.015 (-0.072 to 0.102)	NS	506	Under 18	Some concerns
	Experimental manipulation of anxiety	Social anxiety symptoms → Alcohol use initiation onset | Anticipatory anxiety (Cloutier et al. 2019) [Sig]	0.282 (0.095 to 0.450)	Small Positive	104	Under 18	High
		Social anxiety symptoms → Alcohol use initiation onset | Post task anxiety (Cloutier et al. 2019) [NS]‡	0.192 (0.000 to 0.371)	NS	104	Under 18	High
	Externalising symptoms	Generalised anxiety symptoms → Drinks per year (binary) | Externalising symptoms (Colder et al. 2017) [Sig]	-0.159 (-0.255 to -0.060)	Small Negative	387	Under 18	Some concerns
		Generalised anxiety symptoms → Drinks per year | Externalising symptoms (Colder et al. 2017) [Sig]	-0.356 (-0.440 to -0.266)	Moderate Negative	387	Under 18	Some concerns
		Generalised anxiety symptoms → Alcohol problems | Externalising symptoms (Colder et al. 2017) [Sig]	-0.377 (-0.459 to -0.288)	Moderate Negative	387	Under 18	Some concerns
		Social anxiety symptoms → Drinks per year | Externalising symptoms (Colder et al. 2017) [Sig]	-0.631 (-0.687 to -0.567)	Large Negative	387	Under 18	Some concerns
		Social anxiety symptoms → Alcohol problems | Externalising symptoms (Colder et al. 2017) [Sig]	0.101 (0.001 to 0.199)	Small Positive	387	Under 18	Some concerns

Moderator or super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome | Moderator*	Effect Magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
Socio-environmental		Social anxiety symptoms → Weekly alcohol use | Impulsivity (Bilevicius et al. 2020) [NS]	-0.022 (-0.136 to 0.092)	NS	297	18-49	High
		Social anxiety symptoms → Alcohol related problems | Impulsivity (Bilevicius et al. 2020) [Sig]	0.190 (0.078 to 0.297)	Small Positive	297	18-49	High
		Anxiety symptoms → Alcohol use | Impulsivity (Mackie et al. 2011) [NS]‡	-0.103 (-0.200 to -0.004)	NS	393	Under 18	Some concerns
		Anxiety symptoms → Alcohol use | Sensation seeking (Mackie et al. 2011) [NS]	-0.058 (-0.156 to 0.041)	NS	393	Under 18	Some concerns
	Perceptions of peer alcohol use	Social anxiety disorder → Alcohol use disorder | Perceptions of peer alcohol use (Buckner et al. 2009) [NS]	-0.069 (-0.153 to 0.015)	NS	544	Under 18	High
		Anxiety symptoms → Alcohol related consequences | Perceptions of peer alcohol use (Pedersen et al. 2013) [NS]‡	-0.142 (-0.278 to -0.001)	NS	193	Under 18	High
	Changing association over time	Social phobia symptoms → Alcohol use | Time (follow-up) (Dahne et al. 2014) [NS]	0.102 (-0.016 to 0.217)	NS	277	Under 18	High
	Criminal offending related factors	--	--	--	--	--	--
	Drinking context	--	--	--	--	--	--
	Negative family experiences	Social anxiety disorder → Alcohol use disorder | Negative family interactions (Buckner et al. 2009) [Sig]‡	-0.083 (-0.166 to 0.001)	Small Negative	544	Under 18	High
	Partner support	Social anxiety disorder → Alcohol use disorder | Partner support (Buckner et al. 2009) [NS]	0.073 (-0.011 to 0.156)	NS	544	Under 18	High
	Peer social support	Social anxiety disorder → Alcohol use disorder | Peer social support (Buckner et al. 2009) [NS]	-0.051 (-0.135 to 0.033)	NS	544	Under 18	High
	Positive family experiences	Social anxiety disorder → Alcohol use disorder | Family cohesion (Buckner et al. 2009) [Sig]	-0.093 (-0.175 to -0.009)	Small Negative	544	Under 18	High
		Anxiety disorder → Alcohol use disorder (binary) | Maternal support (Gorka et al. 2014) [Sig]	-0.117 (-0.184 to -0.049)	Small Negative	817	Under 18	High
		Social anxiety disorder → Alcohol use disorder | Parent support (Buckner et al. 2009) [NS]	-0.059 (-0.142 to 0.025)	NS	544	Under 18	High

Moderator or super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome* | *Moderator*	Effect Magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
		Anxiety disorder → Alcohol use disorder (binary) | Paternal support (Gorka et al. 2014) [NS]	-0.054 (-0.122 to 0.014)	NS	817	Under 18	High
	Socioeconomic factors	--	--	--	--	--	--

Table 2.5: Meta-analytic results for moderators of the anxiety → alcohol relationship, grouped by moderator subtheme.

Moderator super-ordinate theme	**Moderator subtheme**	**Interaction meta-estimates with 95% confidence interval**	**Number of effects with sufficient data for meta-analysis** negative / not significant/ positive/ significant without numeric value reported	**Number of total effects identified** negative / not significant/ positive/ significant without numeric value reported
Biological	Age	**0.065 (0.017 to 0.113)**	3 (1 neg / 1 not sig / 1 pos / 0 sig w/o value)	7 (1 neg / 3 not sig / 3 pos / 0 sig w/o value)
	Gender/sex	0.003 (-0.016 to 0.021)	8 (0 neg / 8 not sig / 0 pos / 0 sig w/o value)	94 (0 neg / 93 not sig / 0 pos / 1 sig w/o value)
	Race/ethnicity	--	--	11 (0 neg / 11 not sig / 0 pos / 0 sig w/o value)
Psychological	Alcohol outcome expectancies: negative	0.004 (-0.034 to 0.041)	6 (0 neg / 6 not sig / 0 pos / 0 sig w/o value)	6 (0 neg / 6 not sig / 0 pos / 0 sig w/o value)
	Alcohol outcome expectancies: positive	0.007 (-0.029 to 0.043)	7 (0 neg / 6 not sig / 1 pos / 0 sig w/o value)	7 (0 neg / 6 not sig / 1 pos / 0 sig w/o value)
	Alcohol use	0.000 (-0.022 to 0.021)	4 (0 neg / 4 not sig / 0 pos / 0 sig w/o value)	4 (0 neg / 4 not sig / 0 pos / 0 sig w/o value)
	Anxiety sensitivity/ Anxiety	--	--	1 (0 neg / 0 not sig / 1 pos / 0 sig w/o value)
	Delinquency	--	--	2 (0 neg / 2 not sig / 0 pos / 0 sig w/o value)
	Depression	--	--	1 (0 neg / 1 not sig / 0 pos / 0 sig w/o value)
	Drinking motives: conformity	--	--	1 (0 neg / 0 not sig / 1 pos / 0 sig w/o value)
	Drinking motives: drinking to cope	0.007 (-0.006 to 0.019)	12 (0 neg / 10 not sig / 2 pos / 0 sig w/o value)	26 (1 neg / 20 not sig / 5 pos / 0 sig w/o value)
	Drinking motives: drinking to socialise or enhance	-0.088 (-0.208 to 0.032)	2 (1 neg / 1 not sig / 0 pos / 0 sig w/o value)	11 (1 neg / 8 not sig / 2 pos / 0 sig w/o value)
	Embarrassment	-0.031 (-0.079 to 0.017)	4 (1 neg / 3 not sig / 0 pos / 0 sig w/o value)	4 (1 neg / 3 not sig / 0 pos / 0 sig w/o value)
	Emotion dysregulation	-0.006 (-0.023 to 0.012)	4 (0 neg / 4 not sig / 0 pos / 0 sig w/o value)	4 (0 neg / 4 not sig / 0 pos / 0 sig w/o value)
	Experimental manipulation of anxiety	**0.242 (0.103 to 0.382)**	2 (0 neg / 1 not sig / 1 pos / 0 sig w/o value)	2 (0 neg / 1 not sig / 1 pos / 0 sig w/o value)
	Externalising symptoms	**-0.186 (-0.222 to -0.150)**	9 (4 neg / 3 not sig / 2 pos / 0 sig w/o value)	11 (4 neg / 5 not sig / 2 pos / 0 sig w/o value)
	Perceptions of peer alcohol use	**-0.076 (-0.119 to -0.033)**	2 (0 neg / 2 not sig / 0 pos / 0 sig w/o value)	2 (0 neg / 2 not sig / 0 pos / 0 sig w/o value)
Socio-environmental	Changing association over time	--	--	3 (0 neg / 3 not sig / 0 pos / 0 sig w/o value)
	Criminal offending related factors	--	--	12 (0 neg / 12 not sig / 0 pos / 0 sig w/o value)
	Drinking context	--	--	5 (3 neg / 2 not sig / 0 pos / 0 sig w/o value)
	Negative family experiences	--	--	1 (1 neg / 0 not sig / 0 pos / 0 sig w/o value)
	Partner support	--	--	1 (0 neg / 1 not sig / 0 pos / 0 sig w/o value)
	Peer social support	--	--	1 (0 neg / 1 not sig / 0 pos / 0 sig w/o value)
	Positive family experiences	**-0.081 (-0.098 to -0.064)**	4 (2 neg / 2 not sig / 0 pos / 0 sig w/o value)	4 (2 neg / 2 not sig / 0 pos / 0 sig w/o value)
	Socioeconomic factors	--	--	3 (0 neg / 3 not sig / 0 pos / 0 sig w/o value)
	Grand total		67 (9 neg / 51 not sig / 7 pos / 0 sig w/o value)	224 (14 neg / 193 not sig / 16 pos / 1 sig w/o value)

2.3.5.1.1 Biological moderators

Biological factors were the most commonly tested moderators, particularly gender/sex. As several studies did not report measurement details for the gender or sex variables used, these two factors were combined into a single subtheme. We acknowledge though they are distinct constructs which unfortunately could not be delineated in this review. Other biological moderator subthemes included age and race/ethnicity factors.

Gender/sex was examined as a moderator in 94 effects, but only one significant interaction was identified. In a large German longitudinal sample (n = 3,021; likely adequately powered), Zimmermann et al. (2003) found that sex moderated the association between phobia (not otherwise specified) and persistence of at least regular alcohol use. In this instance women (with phobia not otherwise specified), had significantly lower odds of persistent, regular alcohol use, compared to men. No other gender interactions were significant, including the remaining 69 effects tested in this single study across seven DSM-IV anxiety disorders and five alcohol-related outcomes (Zimmermann et al., 2003). Given the large number of effects examined in this study, the single significant gender effect may represent a spurious finding. Seven additional studies testing 24 potential moderator effects likewise found no evidence of sex/gender differences in anxiety-alcohol association (Colder et al., 2019; Dahne et al., 2014; Gohari et al., 2023; Kaplow et al., 2001; Mackie et al., 2011; Parrish et al., 2016; Schmidt et al., 2007).

Meta-analysis results: Only eight gender/sex effects of the 94 total effects from three studies provided sufficient data for meta-synthesis (Kaplow et al., 2001; Mackie et al., 2011; Schmidt et al., 2007). The meta-estimate suggests there was insufficient evidence of gender moderating the anxiety → alcohol relationship (Fisher's z: 0.003, 95% CI -0.016, 0.021). Heterogeneity between studies was very high for this moderation effect. Furthermore, certainty of evidence determined by GRADE was very low for this biological moderator.

Race/ethnicity was examined as a moderator in 11 effects across four studies with modest sample sizes, including analyses of Mexican Generational Status (Parrish et al., 2016), and race/ethnicity dichotomised as Black/other (Cerdá et al., 2013; Schleider et al., 2019), or African-American/other or Hispanic/other (Nichter & Chassin, 2015). None of these studies found evidence that race/ethnicity moderated the anxiety-alcohol relationship.

Age was the final biological moderator examined, with mixed evidence across the three studies. In one study, powered to detect small to moderate effects, Colder et al. (2017) found that age

moderated associations between social and generalised anxiety and both drinks per year and alcohol problems, with the link between social anxiety and alcohol problems weakening in later adolescence and young adulthood (β = -0.03, $p < .01$).

Meta-analysis results: Three effects from two studies provided sufficient information for meta-synthesis (Cheng et al., 2004; Colder et al., 2017). Whilst the meta-estimate suggests a significant, positive, effect of age moderating the anxiety → alcohol relationship (Fisher's *z*: 0.065, 95% CI: 0.017, 0.113) caution should be place on this finding owing to the very high heterogeneity between studies. As outlined in the narrative synthesis the populations within these studies were dissimilar which is also reflected in the very low GRADE rating.

2.3.5.1.2 Psychological moderators

Eighty two effects testing psychological moderators were identified across 19 studies. These moderators spanned 14 subthemes, expanded on below.

Similar to the mediation analyses, **drinking motives** were the psychological factor most commonly investigated, with 38 drinking motive moderation models identified. **Drinking to cope motives** made up 26 of these, and as seen in Table 2.4 moderating effects were mostly non-significant from six studies with reasonable sample sizes (*n* range = 142 - 3,452). Some small, mostly positive, moderation effects were, however, observed. In one daily diary study assessing to drinking cope with *depression* versus drinking to cope with *anxiety* a small positive moderating effect was seen for coping-anxiety but not coping-depression motives (V. V. Grant et al., 2009). In another daily diary study Armeli, Erik, et al. (2014) found drinking to cope motives moderated the relationship between average levels of anxiety and drinking related problems, but not monthly levels. A final daily diary study saw that, individuals with stronger drinking to cope motives initiated drinking earlier in the week during high-anxiety weeks, compared to low-anxiety weeks. Drinking to cope moderated the timing but not the likelihood of any drinking or heavy drinking (Armeli et al., 2008). Whilst the aforementioned studies focused on sub-clinical anxiety, Dyer, Heron, et al. (2019) examined whether GAD predicted harmful drinking in late adolescence and early adulthood (*n* = 3,452). GAD was associated with several harmful alcohol outcomes, but drinking to cope did not moderate these relationships at either age 18 or 21.

Conformity, enhancement and social drinking motives showed inconsistent moderating effects. One conformity effect had a moderate positive influence on the daily anxiety-drinking relationship in a small sample (n = 142; V. V. Grant et al., 2009). Social-enhancement motives

positively moderated the association between retrospective and daily anxiety and drinking frequency in daily diary study (Armeli et al., 2010), whereas V. V. Grant et al. (2009) found a negative effect of social motives In a smaller college sample Littlefield et al. (2012) found no evidence that social or enhancement motives moderated the anxiety-alcohol relationship.

Meta-analysis results: Twelve effects from three studies were included in the meta-analysis for drinking to cope motives. There was insufficient evidence of drinking to cope motives moderating the association between anxiety and alcohol use (Fisher's *z*: 0.007, 95% CI -0.006 to 0.019). Similarly, evidence from two effects derived from a single study found insufficient evidence of drinking to socialise or enhance moderating this relationship (Fisher's *z*: -0.088, 95% CI -0.208, 0.032). Heterogeneity for both drinking to cope motive studies and drinking to socialise or for mood enhancement was high. The certainty of evidence of both associations was very low.

Alcohol outcome expectancies, typically defined as the anticipated positive or negative effects of drinking, are another factor commonly associated with the anxiety-alcohol relationship. One study testing 12 models found no support for the moderating role of **positive expectancies** (i.e., tension reduction) nor **negative expectancies** (i.e., impairment) on the association between social anxiety and drinking outcomes in a multi-year micro-longitudinal study among college students (Richton et al., 2017). One other study tested the moderating effect of positive alcohol outcome expectancies on the relationship between anxiety sensitivity and alcohol use over time. In this adolescent sample, there was a significant effect, whereby anxiety sensitivity had a more positive relation to alcohol use for youth with high (relative to low) levels of positive drinking expectancies (Borges et al., 2018).

Meta-analysis results: For both positive and negative alcohol outcome expectances there was insufficient evidence of either factor moderating the anxiety-alcohol relationship, negative expectancies (Fisher's *z*: 0.004, 95% CI -0.034, 0.041) and positive expectancies (Fisher's *z*: 0.007, 95% CI -0.029, 0.043). Heterogeneity was low for both meta-estimates. For both positive and negative expectancies there was a very low certainty of evidence.

Consistent with the mediation studies, **perceptions of peer alcohol use** were also examined as a moderator. No evidence of moderation was found in a small adolescent sample (Pedersen et al., 2013) and a larger sample of young women (*n* = 544; Buckner & Turner, 2009).

Meta-analysis results: The two effects from the aforementioned studies contributed to the perceptions of peer alcohol use meta-estimate which identified a significant, small effect

(Fisher's *z*: -0.076, 95% -0.119, -0.033) (Buckner & Turner, 2009; Pedersen et al., 2013). Despite the individual studies not yielding significant results, the meta-synthesised results indicate a small, protective effect of perceptions of peer alcohol use in the association between anxiety and alcohol use. Heterogeneity between studies was low for the estimate and certainty of evidence determined by GRADE was very low.

Externalising symptoms (e.g., impulsivity or sensation seeking) were examined in four studies, with mixed evidence of their moderating role across 11 effects. In a well-powered study spanning adolescence into young adulthood, externalising symptoms were found to negatively moderate the relationship between generalised and social anxiety and alcohol use/problems (Colder et al., 2017). In general, anxiety symptoms were protective against alcohol consumption at high levels of externalising symptoms. For the alcohol problems outcome, however, the opposite was seen with externalising symptoms positively moderating the association between social anxiety and alcohol-related problems. Similarly, Bilevicius et al. (2020) found impulsivity amplified the link between social anxiety and alcohol problems but had no effect on alcohol use. Across four other effects there were non-significant moderating effects of impulsivity (Mackie et al., 2011), sensation seeking (Mackie et al., 2011) and urgency (Marmorstein, 2015).

Meta-analysis results: Nine effects from three studies provided sufficient data for externalising symptoms meta-estimation (Bilevicius et al., 2020; Colder et al., 2017; Mackie et al., 2011). This analysis yielded significant evidence of a small, negative moderating effect (Fisher's *z*: -0.186, 95% CI -0.222, -0.150). Together, this suggests impulsivity/sensation seeking has a small, protective effect on the relationship between anxiety and alcohol use. Study heterogeneity for this subtheme was high, with the certainty of evidence very low.

The moderating role of **embarrassment** was examined across three effects in one daily diary study of college students (O'Grady, Cullum, Armeli, & Tennen, 2011). There was only a significant, positive, interaction between embarrassing event and social anxiety for same evening drinking. This appeared to be driven by a reduction in drinking among those low in social anxiety, as individuals with high social anxiety drank in the evening regardless of embarrassing event occurrence.

Meta-analysis results: The subtheme of embarrassment had four effects from a single study (O'Grady, Cullum, Armeli, & Tennen, 2011) which did not yield evidence of this factor moderating the anxiety-alcohol relationship (Fisher's *z*: -0.031, 95% CI -0.079, 0.017). As this

meta-estimate was derived from effects in a single study, heterogeneity was low, however, the certainty of evidence was very low.

Alcohol use, as a moderating factor, was tested across four effects between anxiety and various alcohol outcomes. No significant moderating effects were found. Among college students, Armeli, Erik, et al. (2014) found no evidence that monthly alcohol use moderated the association between average or monthly anxiety symptoms and monthly drinking related problems (e.g., throwing up, missing work). Among a very large sample of pregnant women (*n* = 12,824*)*, Leis et al. (2012) found no evidence that 1st trimester alcohol use moderated the association between anxiety symptoms and alcohol use or binge drinking in the 3rd trimester.

Meta-analysis results: Four effects from two studies were eligible for synthesising the potential moderating effect of alcohol use (Armeli et al., 2008; Leis et al., 2012). Again, there was insufficient evidence of alcohol use itself being a moderator in the relationship between anxiety and alcohol (Fisher's *z*: 0.00, 95% CI -0.022, 0.021). This finding should, however, be considered in the context of the very high study heterogeneity and very low certainty of evidence.

Similar to alcohol being a hypothesised mediator, **anxiety** related factors were also examined as moderators in two studies. Mackie et al. (2011) evaluated the moderating effect of **anxiety sensitivity** on the association between anxiety symptoms and alcohol use in adolescents. Aligning with their hypothesis, a significant positive association was seen whereby adolescents with higher levels of anxiety and anxiety sensitivity demonstrated an increased rate of alcohol use. **Experimental manipulation of anxiety** was tested as a moderator in one longitudinal laboratory-based study among adolescent girls (Cloutier et al., 2019). Anticipatory anxiety, but not post task anxiety, was found to significantly and positively moderate social anxiety's association on alcohol use initiation onset at follow-up. These findings suggest that adolescent girls who are more susceptible to stress and anxiety are more likely to initiate alcohol use earlier than their less anxious peers.

Meta-analysis results: Two effects from a single study were meta-estimated for the moderating effect of experimental manipulation of anxiety (Cloutier et al., 2019). This yielded a significant, positive effect (Fisher's *z*: 0.242, 95% CI 0.103, 0.382). This suggests that within an experimental study context, manipulation of anxiety has a small, positive effect on the association between anxiety and alcohol use. Study heterogeneity was non-existent; however, as this meta-estimate was derived from a single study certainty of evidence was low.

Across the remaining psychological moderating factor subthemes, only singular studies were identified, each reporting non-significant findings. Among an adolescent boy sample, Pardini et al. (2007) found no support for **emotion dysregulation** moderating the relationship between anxiety/withdrawal symptoms and AUD symptoms. Similarly, among the same adolescent boy sample, Marmorstein et al. (2010) found no support for **delinquency** moderating the relationship between anxiety and onset of alcohol use. Lastly, **hopelessness** was not found to moderate anxiety and alcohol use among adolescents (Mackie et al., 2011).

Meta-analysis results: Meta-estimate results of four emotion dysregulation effects did not yield evidence of this being a significant moderator in the anxiety-alcohol relationship (Fisher's *z*: -0.006, 95% CI -0.023, 0.012) (Pardini et al., 2007). Study heterogeneity was low, and certainty of evidence was moderate for this effect.

2.3.5.1.3 Socio-environmental moderators

The role of socio-environmental moderating factors was investigated across 30 effects in seven studies, which spanned eight subthemes. As outlined in further detail below, the majority of these were non-significant or had contradicting evidence of their potential moderating effect.

Criminal offending related factors were the most commonly explored socio-environmental moderating factor, owing to one study testing 12 interactions (Nichter & Chassin, 2015). The two offending moderators, self-reported non-drug related offending and time spent in supervised facilities (i.e. juvenile detention) were not found to significantly moderate any anxiety-alcohol relationship in the male juvenile offender sample.

There was some evidence to support **drinking context**, conceptualised as social familiarity with individuals present when drinking, as a moderating factor. In a small sample of young, heavy social drinkers there were significant interactions between social anxiety and social familiarity in predicting drinking, whereby participants higher in social anxiety drank more in unfamiliar social environments. Interestingly when specific anxiety symptoms were broken into fear or avoidance symptom models, only the fear model was significantly moderated by social familiarity (Caumiant et al., 2023).

Positive and negative family experiences were another socio-environmental factor identified. Two studies looked at positive family experiences across four effects. Among 544 young women, Buckner and Turner (2009) found evidence of family cohesion, but not parent support, moderating the relationship between SAD and AUD. This same study also looked at negative family interactions as a moderator, which was found to be significant. As such, high family

cohesion could be considered a protective factor among women with SAD from developing an AUD. In another young adult sample, Gorka et al. (2014) evaluated the role of either maternal or paternal support in the association between anxiety disorders and AUD. Interestingly, maternal support but not paternal support was found to be a significant moderator. At low levels of maternal support, anxiety disorders were associated with an increased risk of developing an AUD.

Meta-analysis: The positive family experiences subtheme was eligible for meta-analysis. Four effects from two studies contributed to the significant, negative effect (Fisher's *z*: -0.081, 95% CI -0.098, -0.64). The small effect suggests a protective effect of positive family experiences in the association between anxiety and alcohol. Study heterogeneity for the subtheme was high, and the certainty of evidence determined by GRADE was very low.

Partner support and **peer social support** were additional factors considered by Buckner and Turner (2009). There was no evidence that they moderated the association between SAD and AUD among young women.

A single study found no evidence that three separate **socioeconomic factors** (community cohesion, low neighbourhood safety, socioeconomic status) moderated anxiety severity and alcohol use among adolescent girls (Schleider et al., 2019).

Lastly, two studies examined whether the anxiety-alcohol relationship varied over **time**, with no evidence to suggest time was a significant moderating factor. Dahne et al. (2014) found that youth with elevated social phobia symptoms at baseline had higher average odds of alcohol use at subsequent assessment points, but the strength of this association did not change as a function of time. Among an all boy sample, again no significant time moderation was seen between generalised or social anxiety and first use of alcohol (Marmorstein et al., 2010).

2.3.5.2 Alcohol to anxiety pathway

Like the mediation analyses, there were notably fewer studies which investigated moderators in the pathway from alcohol to anxiety. Overall, there were 34 effects identified which spanned 10 subthemes. Table 2.6 provides a summary of the effects which provided sufficient information for effect transformation. A complete list of all effect pathways, their transformed effect sizes, and effect size classification, including those without numerical effect information can be found in Appendix A: Supplementary Table A10. All effects are narratively expanded

on below. Results of the meta-synthesis are provided in Table 2.7. Counts of all study effects versus the reduced study list with available data for meta-synthesis are also provided in this table.

Table 2.6: Identified moderation effects in the anxiety → alcohol relationship[5].

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned ***Predictor → Outcome | Moderator***	Effect Magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
Biological	Gender/sex	Alcohol use → Anxiety symptoms | Gender (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	NS	393	Under 18	Some concerns
	Race/ethnicity	--	--	--	--	--	--
Psychological	Alcohol outcome expectancies: positive	Alcohol dose (placebo vs control) → Anxiety (state) | Alcohol outcome expectancies: tension reduction (Abrams et al. 2022) [NS]	0.263 (-0.008 to 0.498)	NS	53	18-49	Some concerns
		Alcohol dose (placebo vs control) → Anxiety (state) | Alcohol outcome expectancies: tension reduction (Abrams et al. 2022) [Sig]	0.305 (0.038 to 0.532)	Moderate Positive	53	18-49	Some concerns
	Anxiety sensitivity/ Anxiety	Alcohol dose (placebo vs control) → Anxiety (state) | Anxiety sensitivity (Abrams et al. 2022) [Sig]	-0.297 (-0.525 to -0.029)	Small Negative	53	18-49	Some concerns
		Alcohol use → Anxiety symptoms | Anxiety sensitivity (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	NS	393	Under 18	Some concerns
	Attentional processes	--	--	--	--	--	--
	Depression	Alcohol use → Anxiety symptoms | Hopelessness (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	NS	393	Under 18	Some concerns
		Heavy episodic drinking frequency → Anxiety symptoms in adolescence | Major depressive disorder (Wojciechowski et al. 2024) [Sig]	-0.068 (-0.130 to -0.006)	Small Negative	1,001	Under 18	High
		Heavy episodic drinking frequency → Anxiety symptoms in emerging adulthood | Major depressive disorder (Wojciechowski et al. 2024) [Sig]	-0.071 (-0.132 to -0.009)	Small Negative	1,001	Under 18	High
	Experimental manipulation of anxiety	--	--	--	--	--	--
	Externalising symptoms	Alcohol use → Anxiety symptoms | Impulsivity (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	NS	393	Under 18	Some concerns

[5] Only effects with sufficient data reported for effects estimates transformed are presented (n = 10). Full N =34 effects are in Supplementary Table A 10.

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome | Moderator*	Effect Magnitude (transformed to Fisher's *z*)	Effect interpretation	Sample size (N)	Sample age	Study risk of bias
		Alcohol use → Anxiety symptoms | Sensation seeking (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	NS	393	Under 18	Some concerns
Socio-environmental	Changing association over time	--	--	--	--	--	--
	Drinking context	--	--	--	--	--	--

Table 2.7: Meta-analytic results for moderators of the alcohol → anxiety relationship, grouped by moderator subtheme.

Moderator super-ordinate theme	**Moderator subtheme**	**Interaction meta-estimates with 95% confidence interval**	**Number of effects with sufficient data for meta-analysis** negative / not significant/ positive/ significant without numeric value reported	**Number of total effects identified** negative / not significant/ positive/ significant without numeric value reported
Biological	Gender/sex	--	--	7 (0 neg / 7 not sig / 0 pos / 0 sig w/o value)
	Race/ethnicity	--	--	2 (0 neg / 1 not sig / 0 pos / 1 sig w/o value)
Psychological	Alcohol outcome expectancies: positive	0.289 (-0.113 to 0.690)	2 (0 neg / 1 not sig / 1 pos / 0 sig w/o value)	2 (0 neg / 1 not sig / 1 pos / 0 sig w/o value)
	Anxiety sensitivity/ Anxiety	0.041 (-0.057 to 0.139)	2 (1 neg / 1 not sig / 0 pos / 0 sig w/o value)	3 (1 neg / 1 not sig / 0 pos / 1 sig w/o value)
	Attentional processes	--	--	2 (0 neg / 2 not sig / 0 pos / 0 sig w/o value)
	Depression	-0.070 (-0.166 to 0.027)	3 (2 neg / 1 not sig / 0 pos / 0 sig w/o value)	3 (2 neg / 1 not sig / 0 pos / 0 sig w/o value)
	Experimental manipulation of anxiety	--	--	2 (0 neg / 2 not sig / 0 pos / 0 sig w/o value)
	Externalising symptoms	0.050 (-0.019 to 0.120)	2 (0 neg / 2 not sig / 0 pos / 0 sig w/o value)	2 (0 neg / 2 not sig / 0 pos / 0 sig w/o value)
Socio-environmental	Changing association over time	--	--	7 (0 neg / 4 not sig / 0 pos / 3 sig w/o value)
	Drinking context	--	--	4 (0 neg / 4 not sig / 0 pos / 0 sig w/o value)
	Grand total		**9 (3 neg / 5 not sig / 1 pos / 0 sig w/o value)**	**34 (3 neg / 25 not sig / 1 pos / 5 sig w/o value)**

2.3.5.2.1 Biological moderators

Again, gender/sex, and race/ethnicity were biological moderators identified. Of the seven **gender/sex** effects investigated, none were significant. These effects came from three moderately sized studies which found no role of gender/sex in the association between alcohol use and anxiety (Mackie et al., 2011) or anxious arousal (Parrish et al., 2016), nor problem drinking and anxiety (Carvalho et al., 2018). One study looked at **race/ethnicity** across two effects. Mexican generational status (first generation versus second or more generation) moderated the association between frequency of alcohol use and anxiety arousal symptom but not general anxiety symptoms (Parrish et al., 2016).

2.3.5.2.2 Psychological moderators

Psychological moderators were tested across 14 alcohol → anxiety associations, five of which were found to be significant.

One experimental study examined whether tension-reduction **alcohol outcome expectancies** moderated the effect of alcohol on state anxiety (Abrams et al., 2022). Using an alcohol manipulation design in under 18-year-olds, two models tested this relationship: the first without covariates was not significant, while the second, adjusting for anxiety sensitivity and typical alcohol use, revealed a significant interaction. Specifically, higher tension reduction expectancies were associated with less reduction in state anxiety following alcohol consumption, however, caution should be exercised with this finding only evident in the adjusted model.

Meta-analysis: Two effects from a single study were included in the positive alcohol outcome expectancies estimate (Abrams et al., 2022). The meta-estimate did not provide evidence of positive alcohol expectancies moderating the association between alcohol use and anxiety (Fisher's *z*: 0.298, 95% CI -0.113, 0.690). As this estimate was derived from a single study heterogeneity was low, with the certainty of evidence as determined by GRADE low.

Anxiety related factors were considered as a moderator in three separate studies with mixed findings. In the same experimental study as above, which tested tension-reduction alcohol outcome expectancies, anxiety sensitivity was also found to significantly moderate the association between alcohol dose and state anxiety (Abrams et al., 2022). In contrast, a non-experimental investigation by Mackie et al. (2011) did not find support of anxiety sensitivity moderating alcohol use and anxiety symptoms in an under 18 sample. Lastly, among a sample

of individuals with type two diabetes, a history of past anxiety moderated the association between an AUD and a new episode of anxiety disorder (Cook et al., 2024).

Meta-analysis: Two anxiety/anxiety sensitivity effects derived from two studies were meta-analysed (Abrams et al., 2022; Mackie et al., 2011). The meta-estimate did not provide evidence of anxiety factors moderating the association between alcohol use and anxiety symptoms (Fisher's *z*: 0.041, 95% CI -0.057, 0.139). Study heterogeneity for this subtheme was high, and the certainty of evidence as determined by GRADE was very low.

Experimental manipulation of anxiety was evaluated in two studies. Among both a sample of young adult social drinkers (Sayette et al., 2001) and adult social drinkers (Steele et al., 1986) the order of an anxiety stress task did not moderate the association between beverage condition (alcohol versus placebo) and self-reported anxiety.

Depression-related factors were another psychological moderator investigated. Hopelessness was not found to moderate alcohol use and anxiety symptoms in one study comprised of an under 18 sample (Mackie et al., 2011). In contrast, major depressive disorder was identified as a significant, negative moderator among a sample of justice involved youth (Wojciechowski, 2024). Across both adolescence and emerging adulthood, the negative relationships suggested that individuals with major depressive disorder who engaged in heavy episodic drinking at higher frequencies experienced reduced anxiety symptoms.

Meta-analysis results: The three depression related effects were meta-analysed yielding inconclusive evidence of their moderating effect in the alcohol → anxiety relationship (Mackie et al., 2011). Heterogeneity, however, between studies was high and the certainty of evidence very low. This was particularly owing to indirectness due to the difference in depression constructs measured between the two studies.

Externalising symptoms (impulsivity and sensation seeking) were each tested in a single model. From these models there was no evidence of impulsivity or sensation seeking moderating the association between alcohol use and anxiety in a sample of 393 adolescents (Mackie et al., 2011).

Meta-analysis results: The two externalising symptoms from the single study were meta-analysed (Mackie et al., 2011). The meta-estimate did not provide evidence of this factor moderating the anxiety and alcohol relationship. Owing to the single study contribution study heterogeneity was low and the certainty of evidence determined by Grade was also low.

Attentional processes were the final psychological subtheme identified. In an experimental study among young adult men, Sher et al. (2007) found no significant evidence of sustained attention moderating the association between beverage group (alcohol or placebo) and self-reported anxiety change. Similarly, Steele et al. (1986) found no evidence that attentional engagement (via a neutral slide-rating task) moderated anxiety recovery following alcohol consumption, with no significant condition by time interaction observed despite anxiety increasing significantly after the stressor in all groups.

2.3.5.2.3 Socio-environmental moderators

Two socio-environmental moderator subthemes were identified, drinking context and changing association over time.

Armeli, O'Hara, et al. (2014) evaluated the role of **drinking context** (drinking alone or drinking with others) as potential moderators on the association between episodic specific drinking to cope and anxiety symptoms the day after drinking. Among this college student sample, there was no evidence that drinking context moderated the relationship, which was not consistent with the hypotheses of this study.

Two experimental studies and one prospective cohort study examined whether the alcohol → anxiety relationship varied over time. Evidence from the experimental studies points to a significant moderating effect of time of assessment, within an experimental/laboratory context, on alcohol's effects on anxiety. Stevens et al. (2014) reported a significant alcohol beverage condition by time interaction. Anxiety increased most over time in the control group, especially for high socially anxious participants, while both alcohol and placebo conditions reduced this rise, suggesting that alcohol's pharmacological and expectancy effects moderated anxiety over time. Abrams et al. (2001) found similar findings in their experimental study among adults with social phobia. A significant beverage by time interaction again was seen, whereby the alcohol group experienced a greater reduction in anxiety from the pre-beverage to the post-beverage speech challenge than did the control group. Among a large longitudinal adolescent sample there was no evidence of the relationship between latent alcohol sipping classes (e.g. low vs high sipping class) and anxiety symptoms changing over time (Ferariu et al., 2024).

2.3.6 Results of other complex mediation and moderation study designs

In addition to the single mediation and single moderation studies described, 27 other complex effects were identified comprising of multiple mediation, moderated mediation, or moderated

moderation (three-way interaction) analyses. Each of these 27 effects are summarised in Table 2.8 and are grouped by the analysis type.

Table 2.8: Identified complex effects, grouped by analysis type.

Effect Label Assigned ***Predictor → Outcome | Effect***	**Effect Magnitude (transformed to Fisher's *z*)**	**Effect interpretation**	**Sample size (N)**	**Sample age**	**Study risk of bias**
Multiple mediator effects					
Social anxiety symptoms → Drinking initiation (binary) | Expectancies for not drinking & Perceptions of peer alcohol use (male only model) (Bekman et al. 2010) [Sig]	-0.134 (-0.207 to -0.059)	Small Negative	677	Under 18	High
Social anxiety symptoms → Drinking initiation (binary) | Expectancies for not drinking & Perceptions of peer alcohol use (female only model) (Bekman et al. 2010) [Sig]	-0.121 (-0.199 to -0.040)	Small Negative	591	Under 18	High
Anxiety disorder severity → Alcohol use disorder symptoms severity (continuous) | Rumination & Worry (Wolitzky-Taylor et al. 2012) [NS]	--	NS	232	18-49	High
Moderated-mediation effects					
Anxiety sensitivity → Alcohol problems (continuous) | Anxiety symptoms (mediator) & Race/ethnicity (moderator) (Paulus et al. 2021) [NS]	--	NS	3,396	Under 18	High
Moderated moderation effects (3-way interactions)					
Anxiety symptoms- daily mean → Drinking frequency- monthly (diary) | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [Sig]	--	Sig w/o Z	530	18-49	High
Anxiety symptoms- daily mean → Drinking frequency- monthly (retrospective) | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	--	NS	530	18-49	High
Anxiety symptoms- daily mean → Drinking quantity- monthly (diary) | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	--	NS	530	18-49	High
Anxiety symptoms- daily mean → Drinking quantity- monthly (retrospective) | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	--	NS	530	18-49	High
Anxiety symptoms- daily → Any drinking (binary) | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	--	NS	530	18-49	High
Anxiety symptoms- daily → Drinks per drinking day | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	--	NS	530	18-49	High
Anxiety symptoms → Drinks per year (count) | Externalising symptoms & Age (Colder et al. 2017) [Sig]	--	Sig w/o Z	387	Under 18	Some concerns
Social anxiety symptoms → Drinks per year (count) | Externalising symptoms & Age (Colder et al. 2017) [Sig]	--	Sig w/o Z	387	Under 18	Some concerns

Effect Label Assigned ***Predictor → Outcome | Effect***	**Effect Magnitude (transformed to Fisher's *z*)**	**Effect interpretation**	**Sample size (N)**	**Sample age**	**Study risk of bias**
Social anxiety symptoms → Drinking problems (count) | Externalising symptoms & Age (Colder et al. 2017) [Sig]	-0.101 (-0.199 to -0.001)	Small Negative	387	Under 18	Some concerns
Daytime anxious mood → Drinking likelihood (binary) | Task switching & Age (Dvorak et al. 2014) [Sig]	--	Sig w/o Z	100	18-49	High
Daytime anxious mood → Level of intoxication (continuous) | Task switching & Age (Dvorak et al. 2014) [NS]	--	NS	100	18-49	High
Daytime anxious mood → Drinking likelihood (binary) | Sustained attention & Age (Dvorak et al. 2014) [Sig]	--	Sig w/o Z	100	18-49	High
Daytime anxious mood → Level of intoxication (continuous) | Sustained attention & Age (Dvorak et al. 2014) [Sig]	--	Sig w/o Z	100	18-49	High
Social anxiety symptoms → Drinking quantity | Perceptions of peer alcohol use & Year (O'Grady et al. 2011) [NS]	--	NS	574	18-49	High
Social anxiety symptoms → Any drinking (binary) | Tension reduction alcohol outcome expectancies & Sex (Richton et al. 2017) [Sig]	0.100 (0.016 to 0.183)	Small Positive	537	18-49	High
Anxiety symptoms → Drinking related problems (continuous) | Drinking to cope motives & past month drinking (Armeli et al. 2014) [Sig]	0.090 (0.023 to 0.157)	Small Positive	844	18-49	High
Anxiety symptoms monthly changes → Drinking related problems (continuous) | Drinking to cope motives & past month drinking (Armeli et al. 2014) [NS]	0.012 (-0.056 to 0.079)	NS	844	18-49	High
Alcohol beverage group (alcohol expected, alcohol not expected, placebo) → Trait anxiety | Social anxiety & Time (Stevens et al. 2014) [Sig]‡	0.167 (-0.036 to 0.357)	Small Positive	95	18-49	High
Anxiety activity session (anxiety vs reading challenge) → Alcoholic drink choice (weak, moderate or strong) | Drink-activity order & gender (Abrams et al. 2002) [Sig]	0.306 (0.010 to 0.552)	Small Positive	44	18-49	High
Alcohol beverage group (alcohol vs placebo) → State anxiety | Activity group (distracted or not distracted) (2) & Measurement time point of STAI (4) (Steele et al. 1986) [Sig]	0.467 (0.182 to 0.679)	Moderate Positive	40	18-49	High
Alcohol beverage group (alcohol vs placebo) → State anxiety | Activity group (distracted or not distracted) (2) & Measurement time point of STAI (2) (Steele et al. 1986) [Sig]	0.630 (0.397 to 0.787)	Large Positive	40	18-49	High
Alcohol beverage group (alcohol vs placebo) → State anxiety | Activity group (distracted or not distracted) (2) & Measurement time point of STAI (4) (Steele et al. 1986) [Sig]‡	0.309 (-0.017 to 0.576)	Moderate Positive	37	18-49	High
Alcohol beverage group (alcohol vs placebo) → State anxiety | Activity group (distracted or not distracted) (2) & Measurement time point of STAI (2) (Steele et al. 1986) [Sig]	0.401 (0.088 to 0.642)	Moderate Positive	37	18-49	High

2.3.6.1 Multiple mediator studies

Two studies tested multiple mediation models for the anxiety-alcohol relationship, building on their single mediation models described earlier.

Bekman et al. (2010) combined their two mediators of interest, **expectancies for *not* drinking** and **perceptions of peer alcohol use**, in a multiple mediation model for social anxiety predicting alcohol initiation. In separate models for boys and girls, the combined mediators had a small negative effect on the odds of initiation. For girls, where single mediators were non-significant, the joint model suggests a protective effect arises from their combined influence.

Similarly, Wolitzky-Taylor et al. (2021) combined their two mediators of interest, **worry** and **rumination**, in a multiple mediation model. Results of this model revealed that it was the unique variance explained by rumination which accounted for the association between anxiety disorder symptoms severity and AUD symptom severity, rather than the shared variance between worry and rumination, or by worry alone.

2.3.6.2 Moderated-mediation studies

A single study tested a moderated-mediation model which covered both psychological and biological domains. Among a racially diverse high school sample, Paulus et al. (2021) assessed whether race/ethnicity moderated anxiety sensitivity via anxiety on alcohol problems. The model was not significant suggesting that indirect effects, via anxiety symptoms, were not different across Latinx, Asian, White, or other students.

2.3.6.3 Three-way interaction moderation studies

Nine studies tested multiple moderators in three-way interaction (moderated moderation) models. Across the 9 studies there were 23 effects tested which included combinations of two psychological factors, psychological and biological factors, and psychological and socio-environmental factors.

2.3.6.3.1 Anxiety to alcohol pathway

Drinking motives were a focus in two studies which tested three-way interaction models. Further to the single drinking motive models tested, Armeli et al. (2010) also tested combined moderation models which included both drinking to cope and drinking to socialise/enhance motives. They examined six models with different alcohol-related outcomes, but only found a significant three-way interaction between anxiety symptoms and drinking frequency based on daily diary reports. In another study, Armeli, Erik, et al. (2014) examined the combined

moderating effects of drinking to cope motives and past-month alcohol use. They found that these factors significantly strengthened the association between anxiety and drinking-related problems at the between-person level, but not when looking at monthly within-person changes.

Colder et al. (2017) found that age and externalising symptoms moderated the effects of social and generalised anxiety on alcohol use. Both were protective at high externalising levels but became risk factors at low externalising levels with age. Only social anxiety showed this pattern for alcohol-related problems.

Another significant three-way interaction was seen between positive alcohol outcome expectancies (tension reduction) and sex on the association between social anxiety and likelihood of any drinking (Richton et al., 2017). Probing the interaction demonstrated that yearly changes in social anxiety and daily tension reduction expectancies significantly predicted alcohol use for females but not males.

A non-significant three-way interaction between social anxiety, year, and event-specific drinking norms on drinking quantity indicated there aren't changes over time in college related to these factors (O'Grady, Cullum, Tennen, & Armeli, 2011).

Using a combined laboratory and ecological momentary design Dvorak and Simons (2014) evaluated the role of attentional processes (set shifting and sustained attention) and gender on the association between daytime anxiety and alcohol use. Four, three-way interaction models were tested with all but one found to be significant suggesting possible gender-specific drinking responses to daily negative affect and attentional processes.

One experimental study tested a three-way interaction between anxiety activity type, drinking-activity order, and gender, which was significant (Abrams, Kushner, et al., 2002). Results showed that participants consumed more alcohol after the social anxiety task (speaking) than the control task (reading), with men generally selecting stronger drinks across both conditions and showing a greater tendency to drink before the control task compared to women.

2.3.6.3.2 Alcohol to anxiety pathway

Two experimental studies tested three-way interactions to understand the alcohol-anxiety pathway. Steele and Josephs (1988) evaluated 4 models regarding beverage content, anxiety inducing activity, and measurement time period, with all models finding significant effects. Results demonstrate that news of an upcoming speech task increased anxiety, and drinking alcohol prior to the task reduced anxiety. Stevens et al. (2014) tested one model with a 3-way

interaction which showed that high socially anxious individuals reported more anxiety than low socially anxious participants during anticipation and speech in a control beverage condition, but these group differences were not present in the alcohol and placebo conditions. This suggests that both alcohol and the expectation of alcohol attenuated the heightened anxiety response in anxious individuals, albeit the samples were small for these experimental studies (range n = 37-95).

2.4 Discussion

This is the first systematic review of mediators and moderators in the bidirectional relationship between anxiety and alcohol use and related harms. We synthesised 315 effects, spanning biological, psychological and socio-environmental factors, derived from 55 studies. Across both mediation and moderation studies, commonly explored subthemes included sex/gender, drinking motives, alcohol outcome expectancies, and externalising factors. Our broad inclusion criteria aimed to provide comprehensive coverage on the current evidence regarding potential factors driving the bidirectional anxiety-alcohol relationship. Unfortunately, despite the broad inclusion criteria of this review, few longitudinal mediational studies were identified, thus prohibiting meta-analyses to be carried out. Few studies investigated comparable subthemes, with the majority being psychological factors, of which none consistently showed a significant mediation effect. Whilst there was considerably more moderation studies included, meta-analyses were limited to a small number of subthemes. We found limited evidence of any biological moderating factors in the anxiety-alcohol relationship with some evidence for the psychological subthemes of perceptions of peer alcohol use, impulsivity/sensation seeking, experimental manipulation of anxiety, and the socio-environmental subtheme of positive family experiences. These findings and their limitations are expanded on below.

2.4.1 Evidence from mediation analyses

Synthesis of mediation analyses was intended to identify potential factors of the anxiety → alcohol or alcohol → anxiety pathway which could be targeted in prevention and treatment approaches. Overall, of the 10 studies identified, there were no mediators which can conclusively be said to contribute to the bidirectional relationships. Unsurprisingly, drinking motives were the most common subtheme of psychological factors identified. Numerous

previous studies have looked at the association between anxiety, alcohol, and drinking motives e.g., DeMartini and Carey (2011); however, this review demonstrated that there are considerably fewer studies which investigate this relationship in *longitudinal* study designs. Of the two studies which tested drinking motives as potential mediators, all alcohol outcomes in the tested models were alcohol related problems (Collins et al., 2018; Mackinnon et al., 2014). Results did not suggest any of the five drinking motives; enhancement, social, conformity, coping-anxiety, or coping-depression, mediate the relationship between anxiety and alcohol problems (e.g., neglecting responsibilities or tolerance to alcohol). However, it's unclear what mechanistic role they may play in alcohol use itself, rather than alcohol-related problems.

Results of other psychological mediator subthemes were mixed, with individual studies providing evidence of significant singular mediating effects for interpersonal difficulties (Goldstein et al., 2019), emotion dysregulation (Goldstein et al., 2019), and rumination (Wolitzky-Taylor et al., 2021) as drivers of the anxiety → alcohol relationship. It should be noted, however, that true temporal precedence was not established by Goldstein et al. (2019) in their longitudinal mediation study. This limited evidence aligns with prior work linking anxiety, rumination, and emotion dysregulation to alcohol use and misuse in cross-sectional studies (Harwell et al., 2011; Paulus et al., 2017; Sorid et al., 2021). In contrast, other psychological subthemes identified in this review, including depression and perceptions of peer alcohol use, were not supported as mediating factors. Whilst depression has independently been associated with both anxiety (D. M. Grant et al., 2007; Melton et al., 2016) and alcohol use (Li et al., 2020), and in cross-sectional work has been found to mediate the relationship between anxiety sensitivity and alcohol dependence (Lechner et al., 2014), the single longitudinal study we identified in the review did not provide support for depression as a mediator (McCarty et al., 2023). Similarly, perceptions of peer alcohol use were not found to mediate social anxiety and initiation of alcohol use among adolescents (Bekman et al., 2010), despite being associated, cross-sectionally, with anxiety and alcohol use (Osberg & and Boyer, 2018; Villarosa et al., 2016). Caution, however, should be placed on these findings given the conclusions can only be drawn from the singular studies which contributed to each psychological subtheme.

This review identified one study testing a single socio-environmental mediating factor, negative life events, which did not mediate the relationship between SAD and AUD (Buckner & Turner, 2009). Relatedly, despite considerable theoretical evidence that several biological factors, namely neurotransmitters such as GABA and Gamma, affect the anxiety-alcohol relationship, no biological mediators were identified in this review. Such studies would have

provided a test of the "kindling"/stress hypothesis (Breese et al., 2005) which suggests repeated withdrawal from chronic alcohol use can contribute to the development of withdrawal-induced anxiety. The dearth of socio-environmental and biological factors identified leaves considerable questions regarding the potential role neurobiological, genetic, or neighbourhood factors, for example, may play as mechanistic drivers in the maintenance of co-occurring anxiety and alcohol use concerns.

2.4.2 Evidence from moderation analyses

Similar to the mediation analyses, drinking motives were the most frequent psychological subtheme examined across the included studies. Although drinking motives have received considerable attention in the literature as factors in the anxiety → alcohol relationship, findings from this review do not support a moderating effect of any specific drinking motive. Despite considerable heterogeneity among studies examining the drinking motives subthemes, results generally indicated no moderating effect of drinking motives on the relationship between generalised anxiety symptoms and harmful drinking among relatively well sized samples (Armeli et al., 2008; Dyer, Heron, et al., 2019; Littlefield et al., 2012). However, daily diary studies suggest that drinking to cope and drinking to socialise/enhance may play a role in the relationship between daily anxious mood states and drinking initiation or frequency (Armeli et al., 2010; Armeli et al., 2008; V. V. Grant et al., 2009).

Gender/sex emerged as a recurring moderator subtheme across numerous analyses. Although prior epidemiological research has identified gender differences in both alcohol use and related harms (White, 2020) and in the prevalence of anxiety disorders (McLean et al., 2011), this review suggests that in the context of co-occurring anxiety and alcohol use the relationship is consistent across sex/gender. This finding contrasts with previous cross-sectional studies suggesting that women with higher anxiety drink more (Buckner et al., 2023; Johannessen et al., 2017). However, in the current review, focused on longitudinal studies, there was no consistent evidence to support evidence of gender as a moderating factor. Of the 94 effects tested across seven studies, only one significant effect was identified which was likely to be a spurious finding. Overall, the breadth of other moderating subthemes identified highlights factors which could be targeted in prevention and treatment approaches. However, the conflicting findings and limited number of studies contributing to each subtheme synthesis restrict the ability to draw meaningful conclusions. Meta-analysis of moderator subthemes,

with sufficiently reported data, attempted to synthesise the available evidence. These analyses identified three psychological, one biological, and one socio-environmental subtheme as significant moderators of the anxiety → alcohol pathway. Findings suggest that positive family experiences exert a protective effect, weakening the association between anxiety and alcohol use at higher levels of family support. This aligns with broader theoretical frameworks linking mental health to adverse childhood experiences and familial influences (Samji et al., 2024; Scully et al., 2020). Additionally, meta-synthesis of perceived peer alcohol use from two effects and externalising symptoms from nine effects significantly moderated the anxiety → alcohol relationship. Contrary to predictions, both appeared to buffer the association, such that higher levels of these factors were linked to a weaker relationship between anxiety and alcohol use. Finally, evidence from one experimental study (Cloutier et al., 2019) yielded a positive meta-estimate, showing that experimentally induced anxiety moderated the effect of social anxiety on alcohol use initiation among females. While this finding supports self-medication and tension reduction models of anxiety-alcohol comorbidity, further research is needed to confirm this effect.

2.4.3 Methodological limitations of included studies

The strengths of this review's conclusions are inherently limited by the quality of the included studies. Risk of bias and GRADE assessments indicated that caution is warranted when interpreting findings from several studies. Across both mediation and moderation analyses, a common limitation was poor reporting, particularly of non-significant or null results. This likely reflects the nature of the included studies, many of which examined the relevant mediation or moderation analyses as secondary or exploratory aims, rather than primary hypotheses, leading to incomplete or inconsistent reporting. Notably, none of the studies pre-registered their mediation or moderation analyses, no mediation studies and only three moderation studies conducted a formal power calculation. Many moderation analyses were likely underpowered, meaning non-significant effects may reflect insufficient sample sizes rather than a true absence of moderation. While some studies had relatively large samples that may have provided adequate power, the lack of formal power analyses limits confidence in the findings. Consequently, null results should not be interpreted as evidence of no effect. A priori planning, particularly for mediation studies, would enhance the validity of findings and help address key methodological limitations outlined below. Another frequent source of bias was

related to participant sample selection. While some studies included large and diverse samples (Colder et al., 2019; Zimmermann et al., 2003) the majority relied on convenience or non-representative samples, often composed of college student samples in the United States. This significantly limits the generalisability of findings, particularly for more diverse populations.

Despite significant statistical advancements in mediation analysis since the traditional approach first proposed by Baron and Kenny (1986), this method still dominated the mediation studies identified in our review. The limitations of the Baron and Kenny approach have been well documented (Schuler et al., 2025), with alternative causal inference methods, such as those based on the potential outcomes framework, widely regarded as superior for decomposing causal mediation effects. However, no studies in our review employed such methods. This lack of uptake is not unique to our research area, as the broader field continues to face challenges in adopting causal inference approaches (Rijnhart et al., 2021; Schuler et al., 2025). Mediation analyses also carry specific risks of bias, including those related to temporal ordering and confounding. By limiting inclusion to longitudinal studies, we excluded many that would have violated the assumption of temporal precedence. Nonetheless, three included studies failed to establish clear temporal order between the exposure, mediator, and outcome. These three studies contributed the entirety of effects for several psychological mediation subthemes including expectancies for not drinking (2/2 effects), perceptions of peer alcohol use (2/2 effects), emotion dysregulation (1/1 effect), interpersonal difficulties (1/1 effect), and the single socio-environmental subtheme, negative life events (1/1 effect). Further longitudinal research, with appropriate temporal sequencing is required to determine potential mediation effects across these psychological and socio-environmental domains. Additionally, the identification and control of confounding variables were suboptimal across studies, reducing confidence that observed effects were not due to unmeasured confounding (Vo et al., 2022). Beyond these methodological concerns, there were also limitations in model design. Most studies relied on single mediator models, with only four testing more complex effects: three using multiple mediation and one using moderated mediation. The reliance on single mediator models likely oversimplifies the relationship between anxiety and alcohol use, reducing it to a unidimensional pathway and neglecting the multiple, potentially interacting mechanisms that may be at play. Additionally, three studies investigated the anxiety-alcohol relationship in both directions; and two of these formally tested longitudinal, bidirectional relationships with cross-lagged model designs (Parrish et al., 2016; Paulus et al., 2021). The limited evidence provided from bidirectional, longitudinal designs specifically prohibits conclusions to be drawn regarding

mediating or moderating factors which potentially drive the anxiety-alcohol association in *both* directions.

2.4.4 Strengths and limitations

The major strength of this review is its comprehensive synthesis of mediators and moderators of the anxiety and alcohol relationship, mapped onto biological, psychological, and socio-environmental themes, and subsequent subthemes. By not placing limitations on the type of mediating or moderating factors eligible, this review captures the current body of evidence about how and for whom anxiety and alcohol concerns co-occur. Our focus on longitudinal study designs also provided additional clarity above and beyond what has previously been captured in cross-sectional research, whilst also reducing risk of bias arising from weaker methodological designs. Lastly, we developed two risk of bias tools to assess biases specific to studies of etiology (association) which conduct mediation or moderation analyses. Previous work has highlighted this as a gap and the importance of capturing biases specific to mediation analyses (Vo et al., 2022). The tools we developed build on previous tools and checklists whilst aiming to overcome their limitations, such as inability to translate across review questions or aims (Hoppen & Chalder, 2018). As such, these risk of bias assessment tools, which are provided in full in Appendix B and Appendix C, can be utilised by future reviews of mediation or moderation studies.

Limitations of the review process used should also be considered. Firstly, although a quantitative synthesis of mediating factors was pre-planned, we were unable to do so owing to the limited number of studies reporting mediation analyses. Despite eight studies with 25 effects in the anxiety → alcohol pathway, the heterogeneity of the mediators, as well as predictor and outcome measures, in the identified models prohibited quantitative synthesis. Although we were able to provide meta-analytic coverage of moderation subthemes with sufficient data, the heterogeneity of constructs and outcomes necessitated the aggregation of related variables, introducing a degree of conceptual simplification. This approach also required retaining multiple effect sizes from some individual studies to preserve coverage across conceptually diverse moderation pathways, resulting in potential non-independence among estimates. Due to the small number of studies and sparse data within several subthemes, formal modelling of effect dependency (e.g., three-level meta-analysis or robust variance estimation) was not feasible. Consequently, studies contributing multiple effect sizes may have

exerted disproportionate influence on pooled estimates, and findings should therefore be interpreted with appropriate caution. We further acknowledge the uncertainty of conclusions drawn from these estimates due to the risk of bias ranging from 'some concerns' up to 'high concerns' for the majority of included studies. This limitation is representative of mediation and moderation literature more broadly though, with greater guidance needed for researchers to correctly conduct these types of analyses which have seen advancements in recent years. Thus, our review highlights the need for more rigorous studies and analytic approaches to address the evidence gaps in this topic area. Another limitation is the process used to classify superordinate and subthemes of mediating and moderating factors. Such categorisation was necessary to delineate the broad range of factors identified; however, the grouping of factors into subthemes may have suppressed specific effects which were only significant at the raw variable level, rather than the subtheme level. Lastly, the restriction to only include longitudinal moderation studies may have excluded potentially important moderating factors that have been examined solely in cross-sectional research. This limits the breadth of moderators captured in the current review. However, prioritising longitudinal designs also represents a methodological strength, as it allows for the examination of moderation effects within a temporal framework. Establishing time order is essential for understanding how anxiety and alcohol use influence one another across development, and how specific factors shape these prospective pathways. By focusing on longitudinal evidence, the review is better positioned to identify moderators that operate over time, reduce ambiguity regarding directionality, and provide clearer insights into developmental processes underlying anxiety-alcohol comorbidity.

2.4.5 Implications for practice and future research

Investigating the mechanisms underlying the bidirectional relationship between anxiety and alcohol is complex, yet essential to advancing clinical and theoretical understanding of this common comorbidity. Our review identified limited factors that consistently moderated the anxiety-to-alcohol pathway, with even fewer studies examining the reverse direction (alcohol-to-anxiety). The available evidence suggests that age, impulsivity/sensation seeking, perceived peer alcohol use, and positive family experiences were the most consistent moderators of the anxiety-alcohol association, and may be promising targets for prevention and intervention. Additionally, experimental findings that induced anxiety increases the likelihood of alcohol initiation warrant further exploration in naturalistic settings. This raises the possibility that the

opposite effect may also be possible, whereby reducing real-world anxiety symptoms may offer a protective effect against early alcohol use. One other factor of particular theoretical importance is gender/sex, and this was reflected in the large number of studies which investigated it as a potential moderator. Results, however, indicated that sex and/or gender does not moderate the association between anxiety and alcohol, and future research should, instead, investigate other putative moderators. With regard to mediating mechanisms, the evidence base was sparse and inconclusive. Nonetheless, factors such as anxiety symptoms following anxiety sensitivity, rumination, and emotion regulation emerged as potential intervention targets. While these findings are preliminary, they highlight the need for future research to employ causal mediation analyses to enable stronger inferences, an approach not used in any of the included studies. In addition to advanced methods is the need to make headway in identifying and testing new potential candidates which may mediate or moderate the anxiety and alcohol relationship. Overall, this review advances our understanding of the interplay between anxiety and alcohol use but underscores key gaps in knowledge about when and how these concerns co-occur. Addressing these gaps will be critical to informing effective prevention and treatment efforts and ultimately improve the outcomes for individuals impacted by these concerns.

Chapter 3

Developmental shifts in the anxiety and hazardous alcohol use relationship: moderating factors from adolescence to young adulthood

Preface

Understanding the developmental onset and nature of co-occurring anxiety and alcohol use concerns is paramount for designing support options that can effectively prevent or disrupt the trajectory toward more severe problems. As outlined in **Chapter 1**, evidence has been mixed regarding whether anxiety serves as a risk or protective factor for alcohol use during adolescence. This chapter aims to clarify these inconsistent findings and extend the literature by examining how the association between anxiety and alcohol use varies across developmental periods and under what conditions it strengthens or weakens.

Using a school-based cohort of Australian adolescents, this chapter investigates the cross-sectional and longitudinal relationship between anxiety symptoms and hazardous alcohol use, across seven timepoints spanning early adolescence to young adulthood (mean ages 13.4 to 20.5). Building on the potential moderating factors identified in **Chapter 2**, it evaluates whether this association is moderated by key individual factors across these developmental periods. Moderators examined include sex, depressive symptoms, externalising symptoms (i.e., impulsivity and sensation seeking), and drinking motives. By assessing both the developmental timing and the contextual conditions under which anxiety and alcohol use co-occur, this chapter provides nuanced insight into when, how, and for whom anxiety increases risk for hazardous drinking. These findings offer important implications for the tailoring of developmental-stage-specific prevention and early intervention strategies.

This chapter addresses the second objective of this thesis, which is to:

Examine developmental associations between, and moderators of, anxiety and hazardous alcohol use across multiple timepoints from early adolescence through to young adulthood.

This study is currently under review in *Behaviour Research and Therapy* as:

Gückel, T., Newton, N.C., Prior, K. & Stapinski, L. A. Developmental shifts in the anxiety and hazardous alcohol use relationship: moderating factors from adolescence to young adulthood. *Behaviours Research and Therapy*.

Supplementary materials for **Chapter 3** are provided in Appendix E.

Abstract

Findings on the relationship between anxiety symptoms and hazardous alcohol use across adolescence and young adulthood has been mixed. Evidence suggests that anxiety may function as either a risk or protective factor, depending on the age examined. Moderating biological and psychological factors may help explain these age-related differences. To clarify the developmental nature of the anxiety-alcohol relationship, this study examined both cross-sectional and longitudinal associations across seven timepoints, spanning mean ages 13.4 to 20.5 years. Potential biological (sex) and psychological (depression, externalising symptoms, and drinking motives) moderators of the anxiety-alcohol relationship were also explored. Data were drawn from the Australian *Climate and Preventure* study (n = 418). Cross-sectional analyses revealed a consistent positive association between anxiety and hazardous drinking across the first five waves (ages 13.4 to 16.4), which did not persist into young adulthood. Evidence to support longitudinal associations from one timepoint to the next was weak, although middle adolescence (ages 14.5-15.4) emerged as a potentially critical developmental window. The cross-sectional effect between anxiety and hazardous alcohol use during early adolescence was weaker for girls than boys. Depression, impulsivity, sensation seeking, and drinking motives (coping-anxiety, conformity, enhancement, and social motives) significantly moderated the cross-sectional anxiety-alcohol relationship up to middle adolescence. These findings highlight early to middle adolescence as a key period for interventions aimed at preventing the escalation and persistence of alcohol-related harms. Tailored approaches may be particularly important for youth experiencing elevated negative affect and externalising symptoms.

3.1 Introduction

3.1.1 Co-occurring anxiety and alcohol use

Anxiety disorders and AUD frequently co-occur, with symptoms often emerging in adolescence, and disorder onset typically following in young adulthood (Dawson et al., 2008; Li et al., 2004; Lijster et al., 2017; Robson et al., 2025). Generally, the onset of anxiety disorders precedes that of an AUD (Stapinski et al., 2024), with 26% of individuals with social phobia and 21% with GAD also meeting criteria for AUD (Glantz et al., 2020). Despite consistent evidence of this comorbidity in adult samples, findings on the nature of the relationship during adolescence and young adulthood are mixed (Dyer, Easey, et al., 2019; Pardee et al., 2014). Hazardous alcohol use, defined as a score ≥ 8 on the Alcohol Use Disorders Identification Test (AUDIT) (Babor et al., 2001), is particularly salient during youth as it is linked to both short and long term consequences which often persist into adulthood (Marshall, 2014). Anxiety has been shown to be either positively or negatively associated with alcohol use across these developmental periods (Pardee et al., 2014; Peeters et al., 2024). Clarifying the nature of the anxiety and hazardous alcohol use relationship across youth is critical for advancing theoretical understanding of comorbidity and for identifying key developmental targets for prevention and treatment.

3.1.2 Adolescence and young adulthood being critical timepoints

Given the complex and sometimes contradictory findings on the comorbidity between anxiety and alcohol use, it is essential to consider the developmental context in which these associations unfold. Adolescence and young adulthood represent critical periods of psychological, social, and biological change (Bonnie et al., 2019), which may influence the direction and strength of the anxiety-alcohol relationship. Understanding how this relationship evolves across these life stages can help clarify inconsistencies in the literature and inform more developmentally sensitive approaches to intervention. From early adolescence (ages 10-12) (Sawyer et al., 2018) through to young adulthood (beginning around age 18), individuals undergo continual developmental shifts (Patton et al., 2016; Sawyer et al., 2018). Notably the anxiety-alcohol relationship has been shown to differ across these developmental stages, which may be reflective of the significant changes during these life phases. Initially, during early adolescence, there is evidence of anxiety functioning as either a protective factor (Kaplow et al., 2001;

Malmberg et al., 2010; Peeters et al., 2024; Sawyer et al., 2018) or as a risk factor (Birrell et al., 2020; Black et al., 2015; Kaplow et al., 2001; Wu et al., 2010) for alcohol use initiation and later hazardous drinking. The possible protective effect in early years is suggested to be due to social withdrawal, reducing exposure to alcohol in social settings, and fear of potential negative consequences associated with drinking (Kaplow et al., 2001; Wills et al., 1999; Wu et al., 2010). As individuals transition into late adolescence, favourable peer norms around alcohol use intensify which often coincides with drinking initiation (Brooks-Russell et al., 2014; Eisenberg et al., 2014). Earlier initiation of alcohol use is associated with subsequent hazardous alcohol use, alcohol related harms, and AUD, therefore delaying this onset for as long as possible is ideal (DeWit et al., 2000; Gardner et al., 2024). Recent studies, however, suggest that any protective effects of anxiety appear to diminish in the transition from late adolescence to young adulthood (Pardee et al., 2014; Peeters et al., 2024). Young adulthood is a period marked by greater independence and emphasis on peer relationships, as well as seminal life changes such as finishing school, and in places such as Australia and Europe, legal availability of alcohol. By early adulthood, evidence for the anxiety-alcohol relationship is more consistent, with anxiety symptoms and disorders associated with greater alcohol use, harms, and AUD (Conway et al., 2016; Dyer, Easey, et al., 2019; Robinson et al., 2011). Although research has begun to explore the dynamic nature of the anxiety-alcohol relationship, longitudinally and across developmental periods, the factors that moderate its strength and direction remain under explored. Individual, moderating factors may provide insight into the developmental inconsistencies observed whereby specific biological or psychological differences could be moderating the anxiety and alcohol relationship during youth. Determining whether such individual differences exist will highlight developmental hotspots for targeted interventions to prevent the exacerbation and entrenchment of anxiety and alcohol comorbidity into adulthood.

3.1.3 Considering individual differences in this relationship i.e., moderating factors

Moderating factors capture the specific conditions under which two variables are related, offering insight into who is affected and under what circumstances the relationship holds (MacKinnon & Luecken, 2008). In the context of the anxiety-alcohol relationship, several factors have been proposed as moderators, the most common being gender and biological sex. Epidemiological research has demonstrated greater prevalence of anxiety disorders among

females compared to males (Asher et al., 2017; McLean et al., 2011), whereas males typically exhibit greater hazardous alcohol use and a higher prevalence of AUD (Agabio et al., 2017; Slade et al., 2025; White, 2020). Despite these differences, longitudinal studies examining biological sex as a moderator of the anxiety-alcohol relationship have frequently reported null findings, included those presented in **Chapter 2** (Gückel, Prior, et al., 2025). In contrast, among young adults, sex differences have been more consistently observed in cross-sectional research, with several studies reporting stronger associations between anxiety or psychological stress and alcohol use among women than men (Keough et al., 2015; Papachristou et al., 2018; Schry et al., 2014). Women appear more likely to use alcohol as a coping mechanism for anxiety, especially in social contexts, while men may show different patterns depending on the type of anxiety and situation (Gückel, Prior, et al., 2025; Smith & Randall, 2012). Despite considerable attention to date, the moderating influence of sex across developmental stages remains insufficiently explored. These potential sex differences further support the inclusion of sex as an a priori covariate in other moderation models.

Alongside anxiety, depression is the other mental health concern most commonly associated with alcohol use. Independent studies have found evidence of an association between both depressive symptoms and major depressive disorder with hazardous alcohol use and AUD (Åhlin et al., 2015; Brière et al., 2014; McHugh & Weiss, 2019) as well as with anxiety (Kessler & Wang, 2008; Kircanski et al., 2017; Strauss et al., 1988). Despite the potential moderating effect of depression in the anxiety-alcohol relationship, no longitudinal studies have tested this. Only a single study has tested the related construct of hopelessness as a moderator (Mackie et al., 2011). In this adolescent sample, hopelessness was not found to moderate the association between anxiety symptoms and alcohol use. In another longitudinal study, however, drinking to cope with depression was found to mediate the relationship between social avoidance and alcohol problems (Collins et al., 2018), signalling the potential moderating role of depression related constructs. As such, the current study will determine whether depression moderates the relationship between anxiety and hazardous alcohol use across adolescence and young adulthood.

Externalising factors are other potential psychological moderators, with impulsivity (Bilevicius et al., 2020; Hardee & Duval, 2025) and sensation seeking (Hardee & Duval, 2025; Mackie et al., 2011) previously shown to positively moderate the anxiety-alcohol relationship over time. Research has also established consistent links between internalising and externalising traits (Kessler et al., 2011), externalising traits and hazardous alcohol use (Krueger et al., 2009;

Savage & Dick, 2023), and associations among all three constructs (Colder et al., 2017; Meque, Dachew, et al., 2019; Savage & Dick, 2023). However, the meta-analysis presented in **Chapter 2** found an overall *negative* moderating effect of externalising factors on the anxiety-alcohol relationship (Gückel, Prior, et al., 2025). This conflicting finding may reflect the aggregation of studies across different ages and developmental stages, with two studies contributing multiple significant positive effects and one study contributing four significant negative effects. Given these mixed results, further research is needed to clarify the role of impulsivity and sensation seeking in the relationship between anxiety and hazardous alcohol use across adolescence and young adulthood.

Finally, the role of drinking motives (i.e., drinking for coping, social, enhancement, or conformity reasons) in the anxiety-alcohol relationship have garnered considerable attention in the literature, yet evidence of their role in moderating the anxiety-alcohol relationship is inconsistent and often focused on a single developmental period (Gückel, Prior, et al., 2025). For example, one longitudinal study looked at the association between anxiety at age 18 and various alcohol outcomes at age 21, and whether drinking to cope motives moderated this association (Dyer, Heron, et al., 2019). During this young adulthood period, no evidence was found that drinking to cope motives moderate the association between GAD and alcohol use. Another study among college students investigated the role of five drinking motive constructs, with anxiety coping motives and conformity motives found to positively moderate the association between daily anxious mood and daily alcohol consumption (V. V. Grant et al., 2009). Social motives were seen to have the opposite effect, negatively moderating the association between daily anxious mood and daily alcohol consumption (V. V. Grant et al., 2009). This work provides some insight into the moderating role of drinking motives; however, the potential effect these motives have across developmental periods is unknown. Specifically, given the importance of peer approval and its relation to alcohol use during adolescence, determining if there are key windows to target drinking motives, like drinking for conformity, are needed.

More broadly, sociocultural background (i.e., country of birth) may influence both mental health experiences and drinking norms through differences in acculturation, family expectations, and substance use attitudes (Dandy et al., 2025; Rowe et al., 2020). Academic performance has also been linked to both internalising symptoms and alcohol involvement, with poorer school functioning associated with elevated psychological distress and greater engagement in health risk behaviours (Balsa et al., 2011; Holtes et al., 2015). Accordingly,

these variables were considered important potential covariates alongside the potential moderators of interest.

3.1.4 Current study objectives

The overall objective of the current study is to examine age-related differences in the relationship between anxiety and hazardous alcohol use across youth, given the rapid developmental and social changes that occur from early adolescence into young adulthood. Due to inconsistencies in findings across both cross-sectional and longitudinal research, this study aims to clarify at what developmental stages, and under what conditions, the anxiety → alcohol relationship is most pronounced. In particular, longitudinal analyses aim to clarify the temporal ordering of the association, with a focus on anxiety as a predictor of subsequent hazardous alcohol use., thereby providing insight into potential causal pathways relevant for prevention and early intervention efforts. Collectively, this study bridges two areas of research: those that focus on developmental associations and those that examine moderating factors, which are often studied in isolation.

Across seven waves of data and a 7-year period from early adolescence to young adulthood, the study has three aims:

- Aim 1: Examine the cross-sectional associations between anxiety and hazardous alcohol use from early adolescence into young adulthood.
- Aim 2: Examine the longitudinal, unidirectional, associations between anxiety and hazardous alcohol use from early adolescence into young adulthood, utilising data from consecutive waves i.e. Wave 1 → Wave 2, Wave 2 → Wave 3 etc.
- Aim 3: Examine whether biological (sex) and psychological factors (depression, impulsivity, sensation seeking, coping-anxiety motives, conformity motives, enhancement motives, social motives) moderate the cross-sectional and longitudinal associations between anxiety and hazardous alcohol use.

3.2 Methods

3.2.1 Participants and data

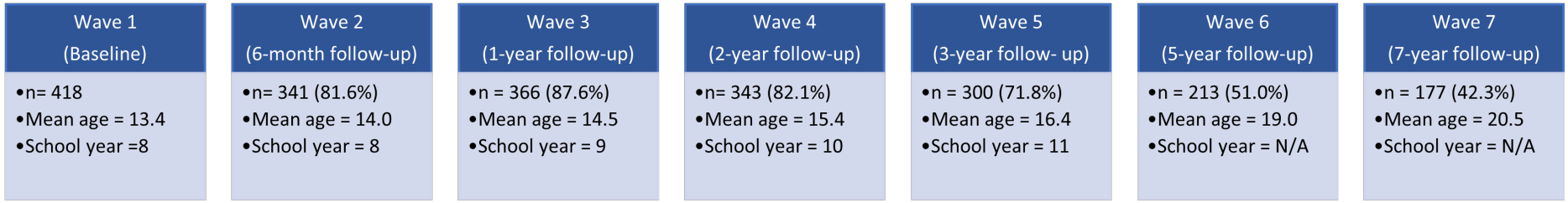
This paper utilises a subset of data collected as part of the Climate and Preventure (CAP) four-arm cluster randomised controlled trial. This trial investigated the effectiveness of integrated,

universal, and selective alcohol prevention education in Australian secondary schools. A total of 26 schools from two Australian states, New South Wales and Victoria, participated in the trial. Participants in the trial were followed up across seven waves from 2012 to 2018. Figure 3.1 summarises key information across the seven study waves, which followed up participants from early adolescence (M age = 13.4) to young adulthood (M age = 20.5).

The subset of eligible participants for the current study were adolescents attending five independent schools that were both randomised to the control condition. The restriction to control schools was intended to prevent contamination from the intervention condition on the study's measures of interest. The restriction to independent schools was necessary due to ethical requirements in government schools (n = 2 control government schools), which prohibited the assessment of mental health measures. At baseline, 418 participants from these five independent control schools were included in the current analysis. Data were analysed across all seven available timepoints: baseline (wave 1), 6 months (wave 2), 1 year (wave 3), 2 years (wave 4), 3 years (wave 5), 5 years (wave 6), and 7 years (wave 7) post-baseline.

Full protocol details for the original trial and subsequent long-term follow-up study are reported elsewhere (Newton et al., 2018; Newton et al., 2012). Ethics approval for the studies was granted by the University of New South Wales Human Research Ethics Committee (HC1274 and HC16881), the University of Sydney Human Research Ethics Committee (2018/845), the Sydney Catholic Education Office (772), and the New South Wales Department of Education and Training (SERAP 2011201). Participation in the study was voluntary, with independent schools requiring written, informed consent from parents (passive) and students (active) for students to participate.

Figure 3.1: Overview of the trial waves and current sub-sample characteristics at each follow-up point.



3.2.1.1 Measures

All measures were collected via self-report surveys which were predominately completed during school for earlier study waves (e.g., waves 1-5), and outside of the school setting for later waves (e.g., waves 6 and 7). Students were financially compensated with vouchers for their time completing the surveys.

Predictor: anxiety symptoms

Anxiety symptoms were assessed as the independent (predictor) variable using the anxiety subscale of the Brief Symptom Inventory (BSI) (Derogatis, 1993). The full BSI consists of 53-items, six of which make up the anxiety symptom measure. Participants responded on a 5-point Likert scale ranging from 0 'not at all' through to 4 'extremely' regarding intensity of distress in the past 7 days. Due to a survey error in the early waves of the study, two anxiety subscale items, "feeling so restless you can't sit still" and "feeling fearful", were not usable for scoring. Therefore, for the current study, we used an abridged 4-item version for all waves to enable consistency across survey instances. The included items were "nervousness or shakiness inside", "suddenly scared for no reason", "feeling tense or keyed up", and "spells of terror or panic". The maximum possible score from the four items was 16. At baseline, internal consistency for this 4-item measure was good ($\alpha = 0.8$). At later waves, internal consistency was high for both the 4- and 6-item versions (Time 6: 4-item $\alpha = 0.9$, 6-item $\alpha = 0.9$; Time 7: 4-item $\alpha = 0.9$, 6-item $\alpha = 0.9$). Correlations between the 4- and 6-item versions were also very high (Time 6 = 0.98; Time 7 = 0.98), supporting the use of the 4-item measure across all waves.

Outcome: hazardous alcohol use

Hazardous alcohol use as the outcome variable was measured using three items adapted for youth which map onto the 3-item Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) (Bush et al., 1998). The items measured the following consumption behaviours in the past 6-months: *alcohol use quantity* (standard drinks), coded as 0 (none), 1 (1-2), 2 (3-4), 3 (5-6) and 4 (7+), *alcohol use frequency* coded as 0 (never), 1 (less than monthly), 2 (2-4 times a month), 3 (2-4 times a week) and 4 (4 or more times a week), and *binge drinking frequency* coded as 0 (never), 1 (less than monthly), 2 (monthly), 3 (weekly) and 4 (daily or almost daily). The total maximum score for the three questions is 12, with higher scores reflecting greater hazardous drinking. There was good internal consistency ($\alpha = 0.8$) for this measure within the present sample.

Moderators

Sex: At baseline (Wave 1), participants were asked a binary question: "Are you male or female?". This baseline measure of biological sex was used in models across all timepoints.

Depressive symptoms: Depressive symptoms were assessed using the depression subscale of the BSI (Derogatis, 1993). This subscale consists of six items (e.g., "feeling no interest in things"), rated on a 5-point Likert scale from 0 (not at all) to 4 (extremely), reflecting the intensity of symptoms experienced in the past seven days. Item scores were summed to yield a total score ranging from 0 to 28, with higher scores indicating greater depressive symptoms. In the present sample, the subscale demonstrated very good internal consistency ($\alpha = 0.9$).

Externalising (impulsivity and sensation seeking): Impulsivity and sensation seeking were measured with the Substance Use Risk Profile Scale (SURPS) (Woicik et al., 2009). This 23-item scale assesses personality profiles which increase risk of substance use, including externalising domains of impulsivity and sensation seeking. Participants indicated the extent to which they agreed with the 5 impulsivity and 5 sensation seeking items, respectively on a 4-point Likert scale (1= strongly disagree to 4= strongly agree). Total scores were calculated for each subscale, with higher scores reflective of greater endorsement of that personality profile. The SURPS has demonstrated good reliability and validity, including among Australian adolescents (Newton, Barrett, et al., 2016). Within the present sample there was good internal consistency for both subscales (impulsivity: $\alpha = 0.8$, sensation seeking: $\alpha = 0.7$).

Drinking motives: Drinking motives were assessed using the five-factor Modified Drinking Motives Questionnaire-Revised (Modified DMQ-R) (V. V. Grant et al., 2007). Twenty-eight items are used to assess five subscales, of which conformity, coping-anxiety, enhancement, and social motives were of interest in the current study. Participants respond to each item on a 5-point Likert scale ranging from 1 (almost never/never) to 5 (almost always/always). Subscale total scores range from 1 to 20 for coping-anxiety motives and 1 to 25 for conformity, enhancement, and social motives. Higher scores indicate a greater endorsement of that drinking motive. Internal consistency within the current sample was very good across the conformity ($\alpha = 0.96$), coping-anxiety ($\alpha = 0.9$), enhancement ($\alpha = 0.9$), and social ($\alpha = 0.9$) subscales. Drinking motives were not included in the study battery at wave 1, therefore were only included in models from wave 2 onwards.

Potential confounders

The following variables were included as potential confounders in all adjusted models. They were selected based on previous literature demonstrating their a priori association with both anxiety and alcohol use amongst youth (Bie et al., 2024; Holtes et al., 2015; Rowe et al., 2020; White, 2020). Correlations between confounders and BSI anxiety symptoms and hazardous alcohol use at baseline are provided in Appendix E (Table E1).

Country of birth: Participants' country of birth, as reported at baseline, was included in models as a covariate. The free-text response was recoded into three categories as 'Australia', 'another English-speaking country', and 'non-English speaking-country'.

School grades: School grades were derived from a single question which asked, "What grades do you usually get in school?", with response options including: '90-100%', '80-89%', '70-79%', '60-69%', '50-59%', or '49% and below'. Participant's response at baseline was included as a covariate.

Sex: Baseline biological sex (male/female) was included as a covariate in all models.

3.2.2 Statistical analyses

All analyses were conducted in R version 4.5.1 (R Core Team, 2025). To address aims 1 and 2 of the study, we used linear regression models to examine both cross-sectional and longitudinal associations between anxiety symptoms and hazardous alcohol use from adolescence into young adulthood.

For the cross-sectional analyses, seven separate models were run, each testing the association between anxiety symptoms and hazardous alcohol use at the same wave e.g., Wave 1 anxiety symptoms with Wave 1 hazardous alcohol use, Wave 2 with Wave 2 etc. For the longitudinal, lagged analyses, six models were run to test whether anxiety symptoms at one wave predicted hazardous alcohol use at the subsequent wave e.g., Wave 1 anxiety symptoms with Wave 2 hazardous alcohol use, Wave 2 with Wave 3 etc.

To address aim 3 of the study, each regression model described above was extended to include anxiety symptoms, a potential moderator, and their interaction term. Eight moderators were examined: sex, depression symptoms, externalising symptoms (impulsivity and sensation seeking), and drinking motives (coping-anxiety, conformity, enhancement, and social).

Separate models were run for each moderator, and interaction effects were tested regardless of whether the simple linear regression showed a significant anxiety-alcohol association in the cross-sectional or longitudinal models. Each model included main effects (anxiety and the moderator) their interaction, and sex, country of birth, and baseline average school grades as covariates.

3.2.2.1 Missing data

Figure 3.1 presents a breakdown of follow-up rates across each study wave. Data was provided for at least four timepoints by 83.5% of participants. Patterns of missingness for key study variables are detailed in supplementary material (Appendix E: Table E2). To address and maintain a comparable cohort across timepoints, the baseline sample (n = 418) was included in all analyses, with multiple imputation used to estimate missing data. Complete case analyses can be biased if data are not missing completely at random (MCAR), thus we imputed 73 datasets, each for 5 iterations using multivariate imputation by chained equations with the MICE package in R (van Buuren & Groothuis-Oudshoorn, 2011). The number of imputed datasets were based on the percentage of missing data across study waves. Imputation was conducted using fully conditional specification, incorporating all variables from the analysis models along with additional auxiliary predictors of missingness and/or the missing variable. To enhance the estimation of missing values and strengthen the assumption that data were Missing at Random (MAR), baseline measures of anxiety sensitivity (using the SURPS), binge drinking (binary; defined as five or more drinks on one occasion), and alcohol quantity were included as auxiliary variables. As missingness was confined to continuous variables, predictive mean matching was used as the imputation method. Although the data had a multilevel structure due to school clustering, intraclass correlations between school class and key variables were below .10, supporting the use of a single-level imputation model (Buuren, 2012). Analysis models using imputed data are presented as the primary analyses, to provide a more robust and comparable cohort across timepoints.

3.2.2.2 Sensitivity Analyses

Sensitivity analyses replicating all models using complete case data are available in supplementary material (Appendix E: Table E3 to Table E6). Additional sensitivity analyses applied the Benjamini–Hochberg procedure to control for multiple comparisons (Benjamini & Hochberg, 1995). Corrections were conducted within four analytic "sets": cross-sectional models, longitudinal models, cross-sectional moderation models, and longitudinal moderation

models. Raw and adjusted *p*-values are available in supplementary material (Appendix E: Table E7 to Table E10)

3.3 Results

3.3.1 Sample characteristics

At baseline, approximately one-third of the sample was male (28.22%) with a mean age of 13.38 years (SD = 0.44). Most participants were born in Australia (89.71%), while the remainder were born in another English-speaking country (5.02%) or non-English-speaking country (5.26%). Sample demographics and raw descriptive data across the seven study waves are presented in Table 3.1. Both anxiety symptoms and hazardous alcohol use increased with age, although trajectories across waves were not formally tested as this was outside the aims of the study. There was a more pronounced rise observed for hazardous alcohol use (range: 0.25 at Wave 1 to the peak of 6.13 at Wave 6), compared to anxiety. Depressive symptoms also increased across waves, peaking at Wave 6 (M = 6.03). Impulsivity and sensation seeking were relatively stable across waves. Drinking motives were consistent from Waves 1 to 5, however, showed a noticeable increase at Waves 6 and 7. Appendix E Table E11presents the differences between available data and imputed data for key study variable means.

Table 3.1: Characteristics of the available sample across study waves

Variable, *M (SD)*	**Wave 1 Baseline**	**Wave 2 6-month follow-up**	**Wave 3 1-year follow-up**	**Wave 4 2-year follow-up**	**Wave 5 3-year follow-up**	**Wave 6 5-year follow-up**	**Wave 7 7-year follow-up**
	418	341	366	343	300	213	177
Age (years)	13.38 (0.44)	13.97 (0.42)	14.47 (0.37)	15.42 (0.36)	16.41 (0.35)	19.03 (0.41)	20.45 (0.4)
Anxiety symptoms (BSI)	1.94 (2.57)	2.15 (3.26)	1.99 (2.98)	2.58 (3.5)	2.68 (3.51)	3.11 (3.47)	3.22 (3.24)
Hazardous alcohol use (AUDIT-C)	0.25 (0.82)	0.4 (1.41)	0.43 (1.28)	1.32 (2.21)	2.51 (2.86)	6.13 (2.67)	5.92 (2.69)
Depressive symptoms (BSI)	3.55 (4.34)	3.73 (4.7)	3.89 (5.01)	4.62 (5.47)	4.4 (5.2)	6.03 (5.18)	5.68 (4.89)
Impulsivity (SURPS)	10.96 (2.56)	11.06 (2.83)	10.93 (2.67)	11.07 (2.84)	10.9 (3.4)	10.08 (2.72)	9.50 (2.51)
Sensation seeking (SURPS)	15.66 (3.21)	15.64 (3.42)	15.7 (3.41)	15.85 (3.6)	16.24 (3.8)	15.94 (3.52)	15.75 (3.72)
Coping-anxiety drinking motives (Modified DMQ-R)	N/A	4.38 (1.84)	4.37 (1.77)	5.10 (2.66)	5.88 (3.39)	7 (3.48)	7.36 (3.25)
Conformity drinking motives (Modified DMQ-R)	N/A	5.50 (2.34)	5.38 (2.07)	5.71 (2.4)	6.56 (3.98)	6.44 (3.09)	6.50 (2.96)
Enhancement drinking motives (Modified DMQ-R)	N/A	5.74 (2.84)	5.76 (2.6)	7.22 (4.4)	9.18 (5.65)	12.04 (5.6)	11.90 (5.2)
Social drinking motives (Modified DMQ-R)	N/A	5.91 (2.89)	5.98 (2.66)	7.69 (4.61)	9.91 (5.46)	15.00 (4.94)	15.78 (4.6)

3.3.2 Association between anxiety and hazardous alcohol use

3.3.2.1 Cross-sectional relationship

Cross-sectional associations between anxiety and hazardous alcohol use, derived from linear regression models, are presented in Table 3.2. Across the first five study Waves (ages 13.4 to 16.4), there was strong evidence of a positive association between anxiety and hazardous alcohol use. During this adolescent period, anxiety symptoms appeared to have a small to moderate positive association with hazardous alcohol use. In young adulthood, at age 19, the association was weaker (B = 0.109, p =.059), and no significant association was observed (B = 0.028, p = .645) by age 20.5. These findings were robust to adjustment of sex, country of birth, and average school grades as confounders.

Table 3.2: Linear regression examining the cross-sectional associations between anxiety symptoms (predictor) and hazardous alcohol use (outcome) at each study wave

Wave, mean age	**Unadjusted model**				**Adjusted model†**			
	B	95% Confidence Interval		*p*	B	95% Confidence Interval		*p*
		LL	UL			LL	UL	
Wave 1, 13.4 years	0.046	0.016	0.077	**.003**	0.041	0.011	0.070	**.007**
Wave 2, 14.0 years	0.155	0.113	0.198	**<.001**	0.158	0.115	0.202	**<.001**
Wave 3, 14.5 years	0.101	0.057	0.145	**<.001**	0.1	0.056	0.144	**<.001**
Wave 4, 15.4 years	0.074	0.011	0.138	**.021**	0.085	0.021	0.149	**.01**
Wave 5, 16.4 years	0.123	0.032	0.214	**.008**	0.141	0.051	0.232	**.002**
Wave 6, 19.0 years	0.076	-0.035	0.187	.178	0.109	-0.004	0.221	.059
Wave 7, 20.5 years	0.017	-0.113	0.147	.797	0.028	-0.093	0.149	.645

†Adjusted models include sex, country of birth, and average school grades at Wave 1.
p values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

3.3.2.2 Longitudinal, lagged, relationship

Results of the longitudinal, lagged associations between anxiety symptoms at one Wave and hazardous alcohol use at the subsequent Wave are presented in Table 3.3. In contrast to the cross-sectional findings, these longitudinal associations were generally weaker. Only one model, spanning mean ages of 14.5 to 15.4, showed evidence of a small, significant relationship, with anxiety symptoms predicting later hazardous alcohol use (B = 0.091, *p* =.016). This effect remained robust after adjusting for confounders. Across other age transitions, the results were weaker, particularly in adjusted models compared to unadjusted ones.

Table 3.3: Linear regression of the longitudinal, lagged associations between anxiety symptoms (predictor) and hazardous alcohol use (outcome)

Wave, mean age	**Unadjusted model**				**Adjusted model†**			
	B	95% Confidence Interval		*p*	B	95% Confidence Interval		*p*
		LL	UL			LL	UL	
Anxiety Wave 1, 13.4 years to Alcohol Wave 2, 14 years	0.035	-0.021	0.092	.220	0.034	-0.023	0.091	.244
Anxiety Wave 2, 14 years to Alcohol Wave 3, 14.5 years	0.047	-0.001	0.095	.054	0.043	-0.006	0.091	.086
Anxiety Wave 3, 14.5 years to Alcohol Wave 4, 15.4 years	0.09	0.017	0.163	**.016**	0.091	0.017	0.165	**.016**
Anxiety Wave 4, 15.4 years to Alcohol Wave 5, 16.4 years	0.039	-0.050	0.127	.392	0.049	-0.039	0.137	.271
Anxiety Wave 5, 16.4 years to Alcohol Wave 6, 19 years	-0.013	-0.118	0.091	.799	0.024	-0.077	0.126	.634
Anxiety Wave 6, 19 years to Alcohol Wave 7, 20.5 years	0.045	-0.072	0.162	.451	0.067	-0.052	0.185	.266

†Adjusted models include sex, country of birth, and average school grades at Wave 1.
p values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

3.3.3 Moderating effects between anxiety and hazardous alcohol use

3.3.3.1 Cross-sectional moderation

Table 3.4 presents the results of the adjusted linear regression models testing interaction effects between anxiety symptoms and potential moderators on hazardous alcohol use. Significant moderating effects were observed across the first five study waves (ages 13.4 to 16.4), indicating that the relationship between anxiety and hazardous alcohol use may vary depending on individual characteristics during adolescence. However, no significant moderation effects were found in young adulthood (ages 19 and 20.5). Results of specific moderating factors are expanded on below.

Sex moderation

While sex did not consistently moderate the relationship between anxiety symptoms and hazardous alcohol use across adolescence, significant interaction effects were observed at ages 14 (B = −0.163, p = .02) and 14.5 (B = −0.211, p < .001). These findings suggest that the association between anxiety and hazardous alcohol use was weaker for females compared to males during early adolescence, specifically around school years 8 to 9. It should be noted, however, that in complete case analyses, a small positive interaction between sex and anxiety was observed at age 15 (Wave 4), which was not supported in the imputed model. This discrepancy may reflect differences in sample composition or statistical power between the complete case and imputed datasets.

Depressive symptom moderation

Depressive symptoms moderated the relationship between anxiety symptoms and hazardous alcohol use in early to middle adolescence, with significant interaction effects observed across three study waves (Waves 2 to 4). Small, positive interactions were found at mean ages 14.0 (B = 0.014, p = <.001), 14.5 (B = 0.009, p = .001), and 15.4 (B = 0.01, p = .032) suggesting that the association between anxiety and hazardous alcohol use was slightly stronger among adolescents reporting higher levels of depressive symptoms at these times. However, these interaction effects did not persist into later adolescence or young adulthood.

Externalising moderation

The relationship between anxiety symptoms and hazardous alcohol use was moderated by both impulsivity and sensation seeking, predominately during early adolescence. Small, positive interactions were seen for both externalising factors in the first three study waves at mean ages

13.4, 14.0, and 14.5 years. Interaction estimates for impulsivity and sensation seeking were similar for the same study wave i.e. at age 13.4 impulsivity (B = 0.18, p = <.001) and sensation seeking (B = 0.17, p = <.001). Similar to depressive symptoms, these interaction effects did not persist into later adolescence or young adulthood.

Drinking motive moderation

Like other factors tested, drinking motives moderated the relationship between anxiety symptoms and hazardous alcohol use during early adolescence. All four drinking motives, conformity, coping-anxiety, enhancement, and social motives, showed small, positive interaction effects at mean ages 14.0 and 14.5, indicating that higher endorsement of these motives slightly strengthened the association between anxiety and hazardous drinking during this period. A persistent moderating effect was observed for social drinking motives into later adolescence with small but significant interactions at ages 15.4 (B = -0.012, p = .002) and 16.4 (B = 0.01, p = .044). The negative interaction at age 15.4 suggests a reversal in the pattern. At this age, in contrast to the earlier timepoints, the association between anxiety symptoms and hazardous alcohol use was weaker among adolescents who more strongly endorsed social drinking motives.

Table 3.4: Linear regressions examining the potential moderating effect of factors on the association between anxiety and hazardous alcohol use cross-sectionally across seven separate ages†

Wave, mean age	**Moderator[#]**	**Unstandardised Beta for interaction term**	**95% Confidence Interval**		***p***
			LL	UL	
Wave 1, 13.4 years					
	Sex (reference male)	0.063	-0.014	0.140	.107
	Depression	0.001	-0.003	0.005	.600
	Impulsivity	0.018	0.010	0.026	**<.001**
	Sensation seeking	0.017	0.008	0.026	**<.001**
Wave 2, 14.0 years					
	Sex (reference male)	-0.163	-0.300	-0.027	**.020**
	Depression	0.014	0.008	0.019	**<.001**
	Impulsivity	0.049	0.036	0.062	**<.001**
	Sensation seeking	0.049	0.027	0.046	**<.001**
	Conformity drinking motives	0.043	0.034	0.053	**<.001**
	Coping-anxiety drinking motives	0.043	0.034	0.052	**<.001**
	Enhancement drinking motives	0.027	0.021	0.033	**<.001**
	Social drinking motives	0.027	0.021	0.033	**<.001**
Wave 3, 14.5 years					

Sex (reference male)	-0.211	-0.335	-0.088	**<.001**
Depression	0.009	0.003	0.014	**.001**
Impulsivity	0.033	0.017	0.048	**<.001**
Sensation seeking	0.027	0.016	0.038	**<.001**
Conformity drinking motives	0.016	0.008	0.025	**<.001**
Coping-anxiety drinking motives	0.013	0.002	0.024	**.019**
Enhancement drinking motives	0.008	0.0004	0.015	**.040**
Social drinking motives	0.012	0.005	0.020	**.001**
Wave 4, 15.4 years				
Sex (reference male)	0.019	-0.136	0.173	.814
Depression	0.01	0.001	0.019	**.032**
Impulsivity	0.008	-0.011	0.027	.408
Sensation seeking	0.006	-0.010	0.021	.478
Conformity drinking motives	-0.0003	-0.015	0.015	.967
Coping-anxiety drinking motives	0.007	-0.006	0.020	.300
Enhancement drinking motives	-0.001	-0.009	0.007	.771
Social drinking motives	-0.012	-0.020	-0.004	**.002**
Wave 5, 16.4 years				
Sex (reference male)	0.188	-0.046	0.422	.115
Depression	0.004	-0.009	0.017	.501
Impulsivity	0.005	-0.018	0.029	.650
Sensation seeking	-0.009	-0.028	0.009	.326
Conformity drinking motives	0.006	-0.010	0.021	.460
Coping-anxiety drinking motives	0.006	-0.010	0.022	.473
Enhancement drinking motives	0.005	-0.005	0.015	.321
Social drinking motives	0.01	0.000	0.020	**.044**
Wave 6, 19.0 years				
Sex (reference male)	0.012	-0.183	0.208	.900
Depression	0.0003	-0.014	0.015	.970
Impulsivity	0.006	-0.020	0.032	.652
Sensation seeking	-0.006	-0.029	0.017	.596
Conformity drinking motives	-0.004	-0.023	0.016	.696
Coping-anxiety drinking motives	0.0002	-0.019	0.019	.984
Enhancement drinking motives	-0.002	-0.016	0.013	.829
Social drinking motives	-0.002	-0.019	0.014	.786
Wave 7, 20.5 years				
Sex (reference male)	0.038	-0.189	0.264	.744
Depression	0.002	-0.015	0.018	.854
Impulsivity	0.005	-0.026	0.035	.749
Sensation seeking	-0.004	-0.026	0.018	725
Conformity drinking motives	0.006	-0.019	0.030	.648
Coping-anxiety drinking motives	-0.006	-0.032	0.021	.663
Enhancement drinking motives	-0.006	-0.022	0.010	.467
Social drinking motives	-0.006	-0.024	0.012	.512

†Adjusted models include sex, country of birth, and average school grades at wave 1. Main effects were also included in models but are not reported for brevity.
#Each moderator was tested in a separate model; interaction terms reflect results from individual analyses.
p values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

3.3.3.2 Longitudinal, lagged moderation

In contrast to the cross-sectional moderation results, there was little evidence that biological or psychological factors consistently moderated the association between anxiety at one wave and hazardous alcohol use at the subsequent wave. These moderating effects are presented in Table 3.5. This is not unexpected, given that the primary longitudinal, lagged models were largely non-significant. One time-specific moderation effect was identified in middle adolescence. Depressive symptoms significantly moderated the association between anxiety at a mean age of 14.5 and hazardous alcohol use at a mean age of 15.4 (B = 0.01, p = .03). At this timepoint, anxiety was also significantly associated with later hazardous alcohol use, suggesting that co-occurring depressive symptoms may amplify the impact of anxiety during this developmental period. Nonetheless, interaction effects can emerge even in the absence of a significant main effect, particularly when a moderating variable meaningfully alters the strength or direction of an association. This, however, was not identified for any of the moderating factors longitudinally.

Table 3.5: Linear regressions examining the potential moderating effect of factors on the association between anxiety and hazardous alcohol use longitudinally across adolescence and young adulthood†

Wave, age	Moderator[#]	Unstandardised Beta for interaction term	95% Confidence Interval		*p*
			LL	UL	
Anxiety Wave 1, 13.4 years to Alcohol Wave 2, 14 years					
	Sex (reference male)	0.121	-0.034	0.276	.126
	Depression	0.007	-0.002	0.015	.137
	Impulsivity	0.014	-0.006	0.033	.170
	Sensation seeking	0.011	-0.006	0.033	.262
Anxiety Wave 2, 14 years to Alcohol Wave 3, 14.5 years					
	Sex (reference male)	-0.052	-0.178	0.074	.414
	Depression	0.004	-0.001	0.010	.14
	Impulsivity	0.003	-0.009	0.015	.587
	Sensation seeking	0.007	-0.003	0.016	.174
	Conformity drinking motives	0.006	-0.004	0.016	.215
	Coping-anxiety drinking motives	0.002	-0.010	0.014	.693
	Enhancement drinking motives	-0.05	-0.013	0.003	.187
	Social drinking motives	-0.004	-0.012	0.004	.367
Anxiety Wave 3, 14.5 years to Alcohol Wave 4, 15.4 years					
	Sex (reference male)	-0.101	-0.310	0.107	.341
	Depression	0.01	0.001	0.020	.030
	Impulsivity	0.021	-0.005	0.046	.113
	Sensation seeking	0.016	-0.002	0.034	.077
	Conformity drinking motives	0.006	-0.009	0.021	.431

Coping-anxiety drinking motives	0.003	-0.016	0.022	.749
Enhancement drinking motives	-0.0009	-0.015	0.014	.906
Social drinking motives	0.006	-0.008	0.021	.406
Anxiety Wave 4, 15.4 years to Alcohol Wave 5, 16.4 years				
Sex (reference male)	0.169	-0.041	0.379	.114
Depression	0.01	-0.002	0.023	.100
Impulsivity	0.003	-0.022	0.028	.815
Sensation seeking	-0.009	-0.030	0.012	.420
Conformity drinking motives	0.003	-0.016	0.023	.737
Coping-anxiety drinking motives	0.01	-0.010	0.031	.324
Enhancement drinking motives	-0.001	-0.015	0.012	.851
Social drinking motives	-0.006	-0.018	0.005	.287
Anxiety Wave 5, 16.4 years to Alcohol Wave 6, 19 years				
Sex (reference male)	0.077	-0.137	0.291	.481
Depression	-0.003	-0.016	0.010	.66
Impulsivity	-0.01	-0.034	0.014	.419
Sensation seeking	-0.008	-0.026	0.010	.364
Conformity drinking motives	-0.005	-0.020	0.010	.495
Coping-anxiety drinking motives	-0.0003	-0.018	0.018	.97
Enhancement drinking motives	-0.001	-0.014	0.011	.848
Social drinking motives	-0.002	-0.015	0.012	.804
Anxiety Wave 6, 19 years to Alcohol Wave 7, 20.5 years				
Sex (reference male)	-0.01	-0.218	0.200	.932
Depression	-0.005	-0.021	0.011	.561
Impulsivity	-0.002	-0.033	0.028	.874
Sensation seeking	-0.008	-0.035	0.018	.531
Conformity drinking motives	-0.007	-0.028	0.015	.544
Coping-anxiety drinking motives	-0.005	-0.026	0.015	.621
Enhancement drinking motives	-0.008	-0.024	0.008	.317
Social drinking motives	-0.005	-0.023	0.012	.546

†Adjusted models include sex, country of birth, and average school grades at wave 1. Main effects were also included in models but are not reported for brevity.
#Each moderator was tested in a separate model; interaction terms reflect results from individual analyses.
p values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

3.3.4 Sensitivity analyses

Complete case and imputed models produced comparable results, except for the cross-sectional sex moderation models noted above. Primary findings were largely replicated following application of the Benjamini–Hochberg false discovery rate correction. However, there was no longer strong evidence of a longitudinal lagged association between anxiety and hazardous alcohol use during middle adolescence (mean ages 14.5–15.4 years). Similarly, coping-anxiety and enhancement drinking motives were no longer supported as moderators of the anxiety–alcohol association among 14.5-year-olds, whereas conformity and social motives remained statistically significant moderators. The Benjamini–Hochberg correction also attenuated

evidence for a sex moderation effect among 14-year-olds, suggesting reduced certainty around these findings and highlighting the need for replication.

3.4 Discussion

The current study examined both cross-sectional and longitudinal relationships between anxiety → hazardous alcohol use, as well as their associations with biological and psychological moderators from early adolescence to young adulthood. Across early to middle adolescence, there was clear evidence of a positive, cross-sectional relationship between anxiety symptoms and hazardous alcohol use. Although some prior research has suggested that anxiety may exert a protective effect against alcohol use during early adolescence, this was not observed in the current sample. Instead, higher anxiety was positively associated with hazardous alcohol use across the first five study waves, spanning ages 13.4 to 16.4. Interestingly, cross-sectional, positive, associations did not persist into young adulthood, with no evidence of a relationship at ages 19 or 20.5. Given the increased legal and social availability of alcohol at these ages, and the high prevalence of risky drinking (41.7%) (AIHW, 2025a), the normative nature of alcohol use in young adulthood may mean that hazardous drinking is more pervasively experienced beyond individuals with heightened anxiety. A small number of cross-sectional studies have likewise found no association between anxiety and hazardous alcohol use among women in their early 20s (Caldwell et al., 2002) or treatment seeking young adults (Hermens et al., 2013), although this remains a minority perspective in the literature. The dominant evidence for an anxiety-alcohol relationship among young adults typically stems from studies of individuals meeting clinical thresholds or treatment-seeking samples, which may further explain why this relationship was not observed in our non-clinical sample. Overall, adolescence appears to be a key developmental window for the co-occurrence of anxiety-alcohol comorbidity, with prevention efforts to minimise harm during this period needed. Moreover, the apparent “ageing out” of the cross-sectional associations observed in our study may suggest that specific dimensions of anxiety symptomology become more influential in young adulthood, dimensions that may not have been adequately captured with the largely somatic BSI anxiety measure used in this study. In particular panic disorder and social anxiety/phobia have been shown to exhibit the strongest comorbidity with hazardous alcohol use and disorders (Buckner, Schmidt, et al., 2008; Morris et al., 2005; Smith & Randall, 2012), especially among young adults (Lewis & O'Neill, 2000).

While there was a consistent cross-sectional anxiety-alcohol association from early-adolescence through to middle-adolescence, the longitudinal lagged results did not show this same pattern across study waves. A single positive association between anxiety symptoms at age 14.5 and hazardous drinking at age 15.4 was identified. After adjusting for multiple comparisons, this result was no longer significant suggesting a potentially spurious finding. The significant, cross-sectional, within-wave associations observed suggest that anxiety and alcohol use are concurrently related, but the effects may not persist over shorter inter-wave intervals (~6 months to 2.5 years) outside of middle adolescence, or at all during youth. The absence of consistent longitudinal, wave-to-wave associations across shorter developmental intervals aligns with previous research on the association between child and adolescent anxiety and later alcohol use. A systematic review found insufficient evidence to support a clear association between childhood/adolescent anxiety and later alcohol use, although the evidence was slightly stronger for later AUD compared to drinking frequency or quantity (Dyer, Easey, et al., 2019). Among adult samples there is evidence that, across a two-year longitudinal period, there are small reciprocal relationships between heavier alcohol use and greater anxiety (D'Aquino et al., 2025). Evidently, further work is needed to unpack the nature of the anxiety-alcohol relationship during adolescence and young adulthood to determine the nature of onset and potential causal drivers of this comorbidity. Nonetheless, cross-sectional evidence highlights middle adolescence as a potentially vulnerable developmental period for experiencing negative affect and engaging in self-medication with alcohol (Turner et al., 2018), emphasising the importance of prevention and intervention efforts prior and during this stage. Previous work has established the need for adolescent prevention programs to promote adaptive coping strategies, such as increasing positive reappraisal and reducing overt emotional expression, given their mediation role in the causal pathway between negative affect and hazardous alcohol use (Antuña-Camblor et al., 2025).

The role of moderating factors highlights anxious youth who could benefit from additional targeted approaches. Biological (sex) and psychological factors (depression, externalising symptoms, and drinking motives) in the current study were found to moderate the cross-sectional anxiety-alcohol associations, predominantly in early- to middle-adolescence but not in young adulthood. The absence of moderation effects in the later waves is not unexpected, given the weak main effects between anxiety and hazardous alcohol use at those timepoints. Biological sex was not a consistent moderator across developmental periods; however, our results show age 14 as a particularly salient time for sex differences. At this age, it may be that

females with anxiety are more anxious about the negative effects of alcohol use, thus are less likely than their male counterparts to engage in hazardous drinking. Our findings align with the notion that girls with social anxiety and distress in new or unfamiliar situations are less likely than boys to have started drinking in adolescence (Tomlinson et al., 2013). The converse has been observed in young adulthood, whereby females with social anxiety are more likely than males to have an AUD or experience alcohol related problems (Black et al., 2015; Norberg et al., 2009).

Across the psychological factors tested in the current study, depressive symptoms most consistently moderated the cross-sectional anxiety-alcohol relationship. The positive moderating role of depressive symptoms was observed in middle adolescence across three study waves, from ages 14 to 15.4. Aligning with prior work on the interplay between anxiety, depression, and alcohol (Johannessen et al., 2017; Kaplow et al., 2001), early- to middle-adolescence should be considered a key developmental stage to target with alcohol prevention efforts, particularly with approaches for individuals to manage negative affect i.e. symptoms of anxiety and/or depression. During this developmental period of rapid change, the combined load of experiencing both anxiety and depressive symptoms may increase vulnerability to self-medication with alcohol. Conformity, enhancement, and social drinking motives also appear to be important intervention targets during middle adolescence, consistent with previous findings (DeMartini & Carey, 2011). Interestingly, social drinking motives were a risk factor for alcohol use in early adolescence, appeared briefly protective at age 15.4, and then became a risk factor again by age 16. The protective role of social motives at age 15 could be indicative of a protective effect of peers more broadly at this age, whereby adolescents who are motivated to drink for social reasons have stronger peer networks that provide social support to mitigate negative affect and subsequent maladaptive coping behaviour like self-medication. Externalising symptoms, including impulsivity and sensation seeking, were also clear moderating factors across early- to middle- adolescence, strengthening the cross-sectional association between anxiety and alcohol use. The positive moderating effect of externalising symptoms in our study, contrasts with the protective interaction reported by Colder et al. (2017) and may reflect differences in developmental timing, measurement of impulsivity and sensation seeking, or sample characteristics. Notably, both studies indicate that the moderating effects of externalising symptoms are less pronounced by young adulthood. Overall, the moderating role of both biological and psychological factors appears greatest in earlier years, driving home the importance of prevention and early intervention approaches during

adolescence, particularly for youth with greater negative affect or maladaptive coping behaviours. Indeed, substance use prevention programs delivered in early adolescence targeting personality vulnerabilities such as impulsivity and anxiety sensitivity, have exhibited positive long-term effects in reducing alcohol use and related harms (Edalati & Conrod, 2018; Newton, Conrod, et al., 2016; Newton, Stapinski, et al., 2022). Overall, these moderating cross-sectional effects should be considered in the broader context of the current study, which did not find evidence that biological or psychological factors moderated the longitudinal pathways from anxiety to alcohol use. This lack of moderation is likely attributable to the absence of significant main effects within these unidirectional, longitudinal models. Continuing to prioritise the identification of potential moderating factors in the anxiety-alcohol relationship will ensure prevention and early-intervention efforts can be appropriately tailored and disrupt longer-term harms.

3.4.1 Strengths and limitations

A strength of our study is the prospective, multi-wave design spanning early adolescence through to young adulthood. Additionally, the combination of both cross-sectional and longitudinal analyses, which also incorporated probable moderating factors, bridges the potential gaps between these separate research domains. Several limitations of the study should be noted. First, the transdiagnostic anxiety measure (BSI) used may have masked disorder-specific relationships. Specifically, the included BSI anxiety items are largely somatic in focus, limiting broader conclusions to be drawn about the association between social or generalised anxiety disorder and hazardous alcohol use during these developmental stages. Nonetheless, this measure captures an appropriate construct for the non-clinical population of interest. Similarly, the alcohol outcome used in the current study was a measure of hazardous alcohol use (AUDIT-C), limiting the conclusions that can be drawn about other patterns or types of alcohol use behaviours. Given conflicting evidence in studies assessing the anxiety-alcohol relationship across different alcohol use measures (e.g., frequent drinking versus hazardous drinking) (Dyer, Heron, et al., 2019; Eggleston et al., 2004), future research incorporating additional alcohol measures would be advantageous. As only one-third of the sample was male, caution should be exercised when generalising the current findings. Furthermore, although the majority of findings were robust to the Benjamini–Hochberg correction, several effects were attenuated after adjustment for multiple comparisons, introducing uncertainty and raising the

possibility of Type I error. Replication in larger samples is therefore needed. However, given the modest sample size, correction procedures may also increase the risk of Type II error, potentially obscuring true but small effects. Accordingly, findings that were attenuated following correction should be interpreted cautiously. Lastly, while the multiple timepoints are a key strength of the study, one timepoint was not measured that may have provided valuable insights. In Australia, the legal drinking age is 18, however, the original study from which this sample was derived did not collect data at this age. Future longitudinal studies on the anxiety-alcohol relationship should endeavour to capture multiple developmental periods, including the age of legal alcohol availability. Given this study focused on the unidirectional relationship between anxiety and alcohol future work is also needed to examine potential bidirectional or reciprocal associations over time. Such analyses would yield insight into changes over time, across developmental periods, above and beyond the prospective associations observed in the current study.

3.4.2 Conclusions

Understanding individual differences in the nature of co-occurring anxiety and alcohol use across youth is essential for disentangling the developmental timing of this common comorbidity. The current study highlights early-to-middle adolescence as a critical developmental window, with more anxious youth aged 13 to 16 years showing greater likelihood of hazardous drinking. Contrary to some prior work suggesting a potential protective effect of anxiety in early adolescence (Pardee et al., 2014; Peeters et al., 2024), this pattern was not observed. Furthermore, the moderating roles of depression, externalising symptoms, and drinking motives, particularly anxiety-coping motives, indicate that youth experiencing greater negative affect and relying on maladaptive coping strategies are at heightened risk for hazardous alcohol use. Together, these findings emphasise the need for early, targeted interventions that address both emotion dysregulation such as impulsivity and coping drinking motives to reduce the emergence of harmful drinking behaviours during adolescence.

Chapter 4

Psychological Mechanisms of Change in Reducing Co-occurring Social Anxiety and Alcohol Use: A Causal Mediation Analysis of the Online Inroads Intervention

Preface

Chapters 2 and **3** focused on disentangling the anxiety-alcohol use association and identifying the factors that drive their co-occurrence. These findings help clarify the theoretical underpinnings of intervention approaches, which aim to target the mechanisms that maintain or exacerbate these concerns. Building on this foundation, the present chapter empirically examines the theory-driven psychological mechanisms of change within an integrated early intervention program that concurrently targets anxiety symptoms and hazardous alcohol use. To achieve this, multiple-mediation models were tested in a sample of Australian young adults recruited to a RCT of the online, evidence-based *Inroads* program. *Inroads* is the first online early intervention designed to simultaneously address both anxiety and hazardous drinking, yet no prior research has examined the mechanisms of intervention effects in this comorbid context.

Guided by theory and preliminary evidence of mediators in **Chapter 2**, improvements in social anxiety were hypothesised to occur through reductions in maladaptive emotion regulation and alcohol use. Reductions in hazardous drinking were hypothesised to occur through reductions in maladaptive emotion regulation, positive drinking motives, and alcohol outcome expectancies. **Chapter 4** addresses these hypotheses by applying causal multiple-mediation analyses to delineate the processes driving observed reductions in social anxiety and hazardous alcohol use among participants who received the *Inroads* intervention compared to control. Findings from mediation analyses of RCTs can provide meaningful insights to inform clinical refinements, enhance intervention precision, and guide policy decisions.

This chapter addresses the third objective of this thesis, which is to:

Investigate the causal mechanisms responsible for reducing social anxiety and hazardous drinking within an efficacious online early intervention program for young adults.

This study has been published as part of a special issue entitled 'Online Therapy Mechanisms' as:

Gückel, T., Prior, K., Newton, N. C., Baillie, A. J., Teesson, M., & Stapinski, L. A. (2025). Psychological mechanisms of change in reducing co-occurring social anxiety and alcohol use: A causal mediation analysis of the online Inroads intervention. *Behaviour Research and Therapy*, *191*, 104766. https://doi.org/10.1016/j.brat.2025.104766

The published manuscript of this study is provided in Appendix F. Supplementary materials for **Chapter 4** are provided online and in Appendix G.

Abstract

Research has documented the prevalence and treatment of co-occurring anxiety and alcohol use, but the mechanisms underlying treatment efficacy, especially in online interventions, remain unclear. This study investigated the potential behavioural, cognitive, and motivational mechanisms mediating the effectiveness of '*Inroads*,' the first online early intervention for co-occurring anxiety and hazardous alcohol use in young adults. Data from an Australian RCT with 123 participants aged 17-24 (M= 21.6) was used. Causal multiple mediation analysis tested whether improvements in social anxiety symptoms could jointly be attributable to reductions in maladaptive emotion regulation and alcohol use, and whether reductions in alcohol use (mean drinks per day) could jointly be attributable to reductions in maladaptive emotion regulation, alcohol motives (drinking to cope with anxiety and for enhancement), and alcohol outcome expectancies (tension reduction and social lubrication). The results did not support a joint mediated effect for the hypothesised mechanisms in the social anxiety or alcohol use model. Additional research is required to further understand the specific mechanisms, driving reductions in social anxiety and alcohol use within integrated treatments. This is especially true for social anxiety, where there was no evidence to suggest that the hypothesised mediators contributed to change in social anxiety symptoms.

4.1 Introduction

4.1.1 Background and rationale

The expansion of online interventions and treatments for psychological disorders provides great promise for improving accessibility and equitability to mental health care. Online treatments have the potential to circumvent barriers to traditional face-to-face care which can include, but are not limited to, stigma, cost, privacy concerns, and difficulty accessing evidence-based treatment at a convenient time or location (Lattie et al., 2022). Several reviews have established the efficacy of online treatments for a number of psychological disorders including depression (Ahern et al., 2018; Linardon et al., 2019), anxiety and emotional disorders (Linardon et al., 2019; Taylor et al., 2021), eating disorders (Taylor et al., 2021), and substance use disorders (Taylor et al., 2021). Furthermore, evidence has also emerged which shows comparable clinical effects between face-to-face and online CBT for depression and anxiety disorders (Esfandiari et al., 2021; Kambeitz-Ilankovic et al., 2022). Despite the indicated advantages of online treatments, they are not without limitations. Low adherence persists as a significant challenge for the field; with studies often reporting poor engagement and completion of online mental health interventions or tools (Leung et al., 2022). Supported or guided online treatments, however, have been found to improve adherence and outcomes for individuals (Andersson & Titov, 2014; Leung et al., 2022). Another limitation of online interventions is the limited research on their suitability for individuals with comorbid mental health and substance use conditions (Andersson & Titov, 2014; Boumparis et al., 2019). While studies and trials of online interventions have predominately focused on disorder-specific treatments, few have explored intervention effectiveness in individuals with multiple conditions. Given the frequent overlap of mental health and substance use concerns, further research is necessary to understand how online interventions may benefit those with co-occurring conditions (Kingston et al., 2017; Lai et al., 2015).

Two prevalent psychological disorders which frequently co-occur are anxiety disorder and AUD (Glantz et al., 2020; Lai et al., 2015). Research suggests that one in four individuals (25.9%) with SAD also experience an AUD, a rate significantly higher than that observed in the general population (Glantz et al., 2020). Treatment-seeking populations exhibit even higher rates of co-occurrence, with as many as one in three individuals receiving treatment, for either AUD or SAD, experiencing both conditions concurrently (Bakken et al., 2005). The co-occurrence of these two disorders can be complex, as each disorder can reinforce and intensify

the other in a feed-forward or mutual maintenance pattern (Smith & Randall, 2012). Unsurprisingly, single-disorder treatments targeting anxiety or AUD in isolation are less effective for people with these co-occurring concerns (Kelly & Daley, 2013; Smith & Randall, 2012; Stapinski et al., 2024; Wolitzky-Taylor, 2023). Instead, integrated treatments, which target the mechanisms driving the interrelation between the two concerns, are advantageous in improving treatment outcomes (Stapinski et al., 2024). Differing from single-disorder or dual-focused treatments, integrated treatments harness effective components from both anxiety and AUD treatments, offering explicit guidance on managing behaviours that reinforce the inter-relationship between these two disorders (Stapinski et al., 2015). To date, few integrated treatments simultaneously addressing both anxiety disorders and AUD have been developed, and these treatments have primarily been tested among adults in traditional face-to-face settings (Kushner et al., 2013; Morley et al., 2016; Stapinski, Sannibale, et al., 2021; Wolitzky-Taylor et al., 2022). The efficacy of these face-to-face treatments has been established in reducing social anxiety symptoms (Stapinski, Sannibale, et al., 2021; Wolitzky-Taylor et al., 2022) and improving alcohol-related outcomes (Kushner et al., 2013; Morley et al., 2016), although the benefits for transdiagnostic anxiety-related outcomes have been less pronounced. Given that 75% of mental health disorders emerge before age 24, and young adulthood is also the time when alcohol use and anxiety disorders typically peak and symptoms escalate (de Lijster et al., 2017; McEvoy et al., 2011; Teesson et al., 2010), early interventions are needed during this critical period. Building upon the efficacy of integrated anxiety-alcohol treatments among adults, interventions addressing these concerns among young adults offer the potential to prevent the progression and escalation to chronic, life-long anxiety and alcohol use disorders. Furthermore, online interventions have the potential for significant benefit among this age group, with two-thirds of young people reporting they would access online interventions for their mental health (Sweeney et al., 2019). Previous research has also shown the efficacy of online CBT for depression and anxiety in this population (Kessler et al., 2005). Therefore, the online integrated *Inroads* program for anxiety and alcohol was developed specifically for young adults.

The *Inroads* program is the first online, integrated, intervention for young adults that targets anxiety symptoms, hazardous alcohol use, and the interconnections between both concerns (Stapinski et al., 2019). Early interventions which target hazardous or risky drinking (defined as a score ≥ 8 on the AUDIT (Babor et al., 2001)) are advantageous among young adults as consumption at hazardous levels is common and predicts progression to AUD (Harrison et al.,

2008; Kranzler & Soyka, 2018). Comprising of five online modules delivered over five weeks, combined with psychologist support via email or phone, the *Inroads* program's content is underpinned by CBT and motivational enhancement therapy to, in an integrated delivery, target symptoms of generalised and/or social anxiety and hazardous alcohol use concurrently. The program was co-developed with the target population, drawing on components of effective face-to-face anxiety-alcohol treatments (Stapinski et al., 2015), with input from clinicians who work with youth.

In a RCT of the program among Australians aged 17-24, the integrated *Inroads* intervention group (n = 62) saw significant improvement across anxiety and alcohol outcomes compared to an alcohol assessment plus alcohol information control group (n = 61). While the control condition provided psychoeducation for alcohol use only, it was chosen to establish a baseline from which to measure the incremental benefits of the integrated treatment for both anxiety and alcohol use. This approach demonstrated the added value of addressing both conditions simultaneously, setting the stage for future comparisons with more comprehensive, disorder-specific treatments.

During the trial, both groups reduced their drinking across primary and secondary alcohol use outcomes. At the post-intervention 2-month follow-up participants in both groups had reduced on the primary outcome of mean standard drinks per day in the past month and secondary outcomes of hazardous alcohol use (AUDIT total score) and binge drinking (≥5 standard drinks on a single occasion). However, by the 6-month follow-up, significant group differences emerged for mean daily alcohol use and hazardous alcohol use, suggesting a rebound effect in the control group's drinking, whilst the *Inroads* group saw sustained effects (Stapinski, Prior, et al., 2021). In regard to anxiety outcomes, social anxiety symptoms significantly improved in the *Inroads* group, with between group differences sustained at the 6-month follow-up. Participants in the control group did not significantly improve their social anxiety. Superior reductions in generalised anxiety, in the *Inroads* group, were only observed post-intervention. By the 6-month follow-up the control group achieved comparable reductions in generalised anxiety symptoms to the intervention group. The current study is a secondary analysis of this RCT to explore potential mediators of these alcohol and social anxiety outcomes. The anxiety outcomes observed align with findings from face-to-face treatments, where superior benefits are often found for social anxiety treatments over generalised or transdiagnostic anxiety treatments which are integrated with alcohol treatments (Kushner et al., 2013; Morley et al., 2016; Stapinski et al., 2024; Stapinski, Sannibale, et al., 2021; Wolitzky-Taylor et al., 2022).

This may be due to the greater chronicity and natural fluctuations in the course of generalised anxiety compared to social anxiety. Unlike social anxiety, which tends to show more stable treatment gains, generalised anxiety is often influenced by external life stressors and has a more variable long-term course, with periods of remission and relapse even after treatment (Keller, 2002; Rowa et al., 2017).

4.1.2 Mechanisms of change in co-occurring anxiety and alcohol use treatment

Integrated treatment for anxiety and alcohol use is underpinned by a CBT framework, with the aim of treatment to address the motivational, cognitive, and behavioural processes that drive and maintain each condition and the interactions between them (Stapinski et al., 2015; Wolitzky-Taylor et al., 2022). For effective treatment of co-occurring anxiety and alcohol use problems, it is important to promote the ability to adaptively regulate emotional responses to internal and external stressors. Furthermore, in view of the mutually reinforcing relationship between anxiety and alcohol use, it is also important to address this interconnection and challenge inaccurate and unhelpful cognitions or expectations regarding the positive effects of alcohol on anxiety (e.g., improved social performance) (Kushner et al., 2013; Stapinski et al., 2015). Despite a strong theoretical basis for the co-occurrence and treatment of these two conditions, to date, specific mechanisms driving treatment efficacy have not been tested. Given the efficacy of the online *Inroads* anxiety-alcohol intervention on reducing social anxiety symptoms and mean daily alcohol use (Stapinski, Prior, et al., 2021), understanding *how* the program is able to reduce these outcomes is important. This will be done by testing hypothesised mechanisms of change, i.e. mediating factors. Knowing explicitly *how* interventions work is vital for advancing the effectiveness of co-occurring anxiety and alcohol interventions, particularly in the context of online intervention delivery given their potential for low-cost, widespread dissemination. Given the limited trials on integrated treatments for co-occurring social anxiety and alcohol use, the underlying mechanisms thought to drive treatment efficacy are yet to be tested. As such the hypothesised mediators for this study are guided by the clinical, theoretical, and cross-sectional research on co-occurring anxiety and alcohol use.

4.1.2.1 Mediators for social anxiety treatment in the context of comorbid alcohol use

For social anxiety, the key mechanisms theorised to underlie integrated interventions are reductions in both maladaptive emotion regulation behaviours and alcohol use, which are hypothesised mechanisms to drive improvements in social anxiety symptoms (Stapinski et al.,

2015). Underlying cognitions in social anxiety tend to be dominated by fear of negative evaluation and an inflated likelihood of negative consequences (Hofmann, 2007; Rapee & Heimberg, 1997). Within the *Inroads* program, CBT aims to target these cognitions and behaviours by helping individuals identify and reappraise threat cognitions to determine their realistic probability and potential outcomes. Two maladaptive emotion regulation processes are targeted; cognitive reappraisal and expressive suppression (Stapinski et al., 2015). Cognitive reappraisal is defined as the attempt to reinterpret emotion-eliciting situations in a way which alters its meaning and emotional impact (Lazarus & Alfert, 1964), while expressive suppression is a form of response modulation which attempts to reduce or conceal outward emotional expressions (Gross, 1998). Targeting maladaptive or negative cognitions is not unique to integrated treatment however, with increases in reappraisal and decreases in negative cognitions also found to mediate treatment outcomes for SAD in single-disorder CBT treatments (Goldin et al., 2012; Kivity et al., 2021). A hypothesised mechanism unique to integrated treatment, however, is the reduction of alcohol use. Due to alcohol's demonstrated rebound effects, both pharmacologically and physiologically, on anxiety symptoms, reducing alcohol consumption is thought to mediate reductions in social anxiety symptoms (Kushner et al., 2000; Stapinski et al., 2015). Whilst individuals may see short-term benefits to anxiety symptoms from drinking, over the long-term intoxication or withdrawal from alcohol may exacerbate anxiety symptoms via directly inducing symptoms of trait, generalised, or panic anxiety, generating additional psychosocial stressors (Kushner et al., 2000). Furthermore, a reliance on alcohol within social settings prevents disconfirmation of threat expectancies and reduces confidence to manage these situations without alcohol (Stapinski et al., 2015).

4.1.2.2 Mediators for alcohol use treatment in the context of comorbid social anxiety

Notably, the mechanisms hypothesised to change and reduce alcohol use in the context of co-occurring anxiety-alcohol use extend beyond simply reducing anxiety symptoms. Instead, they involve challenging positive drinking motives and positive alcohol expectancies. Drinking motives are conceptualised as an individual's reasons for choosing to drink (Cooper, 1994), while alcohol expectancies refer to the beliefs an individual holds about the physical or social outcomes that will occur from drinking (Jones et al., 2001). While both motives and expectancies are associated with alcohol use, an individual's expectation about a particular effect of alcohol, does not necessarily mean they will drink for that related motive (Cox & Klinger, 1988). Within the current context, the *motivation* for individuals to drink typically stems from a belief that alcohol will have potential anxiety-reducing effects (Anker & Kushner,

2019; Stapinski et al., 2015). Within the four-factor drinking motive framework, both enhancement and coping motives have consistently been related to heavier drinking and alcohol-related problems (Cooper, 1994). Enhancement motives are characterised as an internally generated, positive motive to drink to enhance positive mood or wellbeing (Cooper, 1994). Prior research has found enhancement motives mediate the relationship between social anxiety and alcohol-related problems (Buckner et al., 2006). Whilst some studies have found evidence for other drinking motives, such as social and conformity motives, influencing drinking behaviours (Boyle et al., 2022; Sheehan et al., 2013) this evidence has been inconsistent, particularly among younger age groups (Rowicka, 2021; Sheehan et al., 2013; Sjodin et al., 2021). A newer five-factor model for measuring drinking motive constructs has been developed, however, which separates motives for coping with anxiety versus coping with depression drinking (V. V. Grant et al., 2007). Despite a significant body of work on the role of drinking motives in the context of anxiety concerns, much of this work has been in cross-sectional or non-treatment contexts. This empirical evidence points to coping-anxiety drinking motives and enhancement drinking motives as theoretically hypothesised mediators in anxiety-alcohol treatment. Alcohol outcome *expectancies* also contribute to the motivations and maintenance of alcohol use. Individuals with anxiety hold optimistic and positive expectancies about alcohol's effects including its potential to aid social situations, i.e. tension reduction expectancies and social lubricant expectancies (Moss & Albery, 2009; Stapinski et al., 2015). Thus, hypothesised mechanisms underlying co-occurring anxiety-alcohol problems are the expectancy that alcohol will act as a relaxant (tension-reduction) and the motive to use alcohol to cope with their anxiety. Within integrated interventions, like *Inroads,* motives for drinking and the tension reduction and social lubricant alcohol expectancies are explicitly identified and targeted through motivational, cognitive, and behavioural strategies (V. V. Grant et al., 2007; Kushner et al., 1994). This includes experimental designs which help individuals identify and challenge alcohol-related motivation and expectancy cognitions, i.e. "drinking thinking". Doing so helps individuals evaluate the realistic evidence about what happens when they drink, i.e. expectation versus reality, with the aim of eliciting corrective evidence of the true cost of drinking. Interventions challenging alcohol expectancies, outside the co-occurring anxiety and alcohol context, have been found to significantly reduce alcohol use and related outcomes (Scott-Sheldon et al., 2012). In addition to challenging the positive beliefs about alcohol, reducing maladaptive emotion regulation is also a hypothesised mechanism of change for alcohol use reduction (Stapinski et al., 2015). Similar to social anxiety, CBT strategies for alcohol use reduction aim to help individuals more adaptively regulate their emotional

responses, by increasing cognitive reappraisal and decreasing expressive suppression (Kushner, Donahue, et al., 2009; Stapinski et al., 2015). Previous research, in the context of interventions for alcohol use alone, have also shown these cognitive processes to be influential factors in improving alcohol related treatment outcomes (Petit et al., 2015; Rodriguez et al., 2019). Whilst factors such as self-efficacy, social support, and craving have been identified as mediators in alcohol and other drug treatment, research has not established these as core to integrated treatments and as such were not included in the current models (Maisto et al., 2024).

4.1.3 The current study objectives

This is the first study to investigate joint mediators of an efficacious, online, integrated intervention aimed at reducing anxiety and hazardous alcohol use among young adults. The study's objectives are to assess the hypothesised causal pathways that underpin the effectiveness of an online anxiety-alcohol intervention among young adults, using a causal inference framework. To establish temporal precedence among exposure, mediators, and outcomes (Kazdin, 2007), the study analyses mediating variables at time 2 (post-treatment, 2 months post-baseline, follow-up 1) and significant outcome variables at time 3 (6 months post-baseline, follow-up 2). In the RCT of the primary study the anxiety-alcohol intervention group exhibited superior improvements in social anxiety but not general anxiety symptoms at time 3 (6 months post-baseline), thus this study focuses on identifying mediators related to social anxiety treatment efficacy. As outlined earlier, significant improvements were observed across various alcohol-related outcomes including reductions in mean drinks per day, hazardous alcohol use (per the AUDIT), and frequency of binge drinking. Thus, to align with the primary alcohol outcome of the original trial we focused on mean drinks per day in this study. Building upon theoretical foundations in anxiety, alcohol use, and their co-occurrence, it is hypothesised that:

- Decreases in maladaptive emotion regulation (cognitive reappraisal and expressive suppression) and alcohol use at 2-months post baseline will jointly mediate the effects of the *Inroads* program on reducing **social anxiety symptoms** at 6-months, with the combined influence of these mediators resulting in significant mediation.
- Decreases in maladaptive emotion regulation (cognitive reappraisal and expressive suppression), alcohol motives (drinking to cope with anxiety and enhancement), and alcohol outcome expectancies (tension reduction and social lubricant) 2-months post baseline will jointly mediate the effects of the *Inroads* program on reducing **mean**

drinks per day at 6-months, with the combined influence of these mediators resulting in significant mediation.

4.2 Methods

4.2.1 Study design and source of data

This study was designed and written in accordance with the guidelines for reporting mediation analyses (AGReMA) (Lee et al., 2021). Data for the current study were derived from a parallel RCT conducted online, nationally, across Australia. The design and protocol for the original study can be found in (Stapinski et al., 2019). The current study was not registered alongside the original RCT protocol and thus should be considered exploratory. Eligible participants were randomised to either the *Inroads* intervention condition or an alcohol information and safe drinking guidelines control condition.

4.2.2 Participants

Recruitment to the original study ran from December 2017 to September 2018. The target population were 17-24-year-olds in Australia reporting hazardous alcohol use and at least mild generalised or social anxiety symptoms. These thresholds were aligned with the nature of the treatment which is an early intervention designed to provide an intervention to individuals experiencing sub-threshold symptoms, to prevent the exacerbation to a more chronic disorder. Hazardous alcohol use was determined by scores ≥8 on the AUDIT (Babor et al., 2001). Scores ≥20 on the AUDIT were used to determine probable alcohol dependence in this population (Babor et al., 2001; O'Brien et al., 2020). Mild anxiety was determined by a score of ≥5 on the Generalised Anxiety Disorder-7 (GAD-7) Questionnaire (Spitzer et al., 2006) or a score ≥6 on the Mini-Social Phobia Inventory (Mini-SPIN) (Seeley-Wait et al., 2009). Although the Mini-SPIN focusses on anxiety symptoms consistent with SAD, the GAD-7 has been found to index symptoms across multiple disorders and is sensitive to GAD, panic, and SAD, facilitating screening of young people with a range of anxiety presentations. Total scores on the GAD-7 range from 0 to 21, with scores of ≥5, ≥10, and ≥15 representing cut points for mild, moderate, and severe anxiety, respectively (Kroenke et al., 2007). Individuals currently receiving ongoing psychological treatment or requiring more intensive or specialised support (e.g., with current active suicidal ideation) were excluded from the study. No further eligibility requirements were dictated for participants to be included in the mediation analysis. From 547 participants

screened for eligibility, a total of 123 were eligible and randomised to either *Inroads* (n = 62) or control (n = 61). The 123 eligible participants had a mean age of 21.6 years (SD = 2.2) and comprised of 32% male, 67% female, and 1% transgender or non-binary individuals. The majority of participants were born in Australia (82%), resided in a major city (89%), were heterosexual (73%), and were employed full time (40%) or part time/casually (27%). Full exclusion criteria, participant flow through the trial, and demographic data are reported in the main outcomes paper (Stapinski, Prior, et al., 2021).

4.2.3 Effects of interest

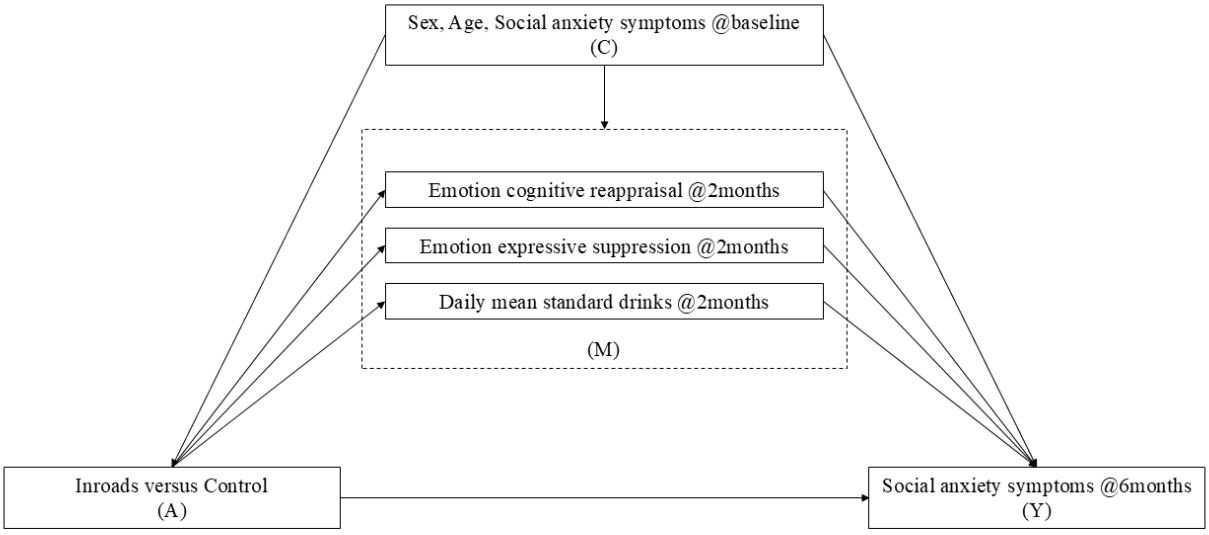
In the current study, the pure natural direct effect (PNDE), total natural indirect effect (TNIE), and total effect (TE) were estimated for each causal mediation model (Robins & Greenland, 1992). These estimates are part of the 'counterfactual causal framework or 'potential outcomes framework' which is unique to causal mediation (Rubin, 1978). Causal mediation analysis defines the difference between two potential outcomes and is advantageous over traditional mediation analysis because it allows for a more precise understanding of the causal pathways by isolating the direct effects of an intervention from its indirect effects through mediators (Pearl, 2001; VanderWeele, 2015). This method provides clearer insights into how and why an intervention works, offering a more detailed breakdown of the mechanisms at play. In the current study, the PNDE represents the direct effect of the exposure variable (*Inroads* versus control) on the outcome of interest (either anxiety or alcohol), whilst hypothetically holding the mediator's constant at typical or average values that would be observed in the control group. This helps assess the independent contribution of the intervention (exposure) on outcomes, separate from any mediated effects through the mediators. The TNIE represents the indirect intervention effect on the outcome of interest through the multiple mediators. Within the potential outcomes framework, this TNIE represents a hypothetical scenario in which the *Inroads* intervention is implemented, causing the mediators to take on the values they would have had if participants moved from the control group to the intervention group. Lastly, the TE is calculated as the intervention's effects on the outcomes that come from both the direct (PNDE) and indirect (TNIE) effects of the mediators, i.e., TE= PNDE + TNIE.

4.2.4 Assumed causal models

In line with the study objectives and the effects of interest, Figure 4.1 and Figure 4.2 depict the assumed causal models we tested. Across both models the exposure (A) is the intervention

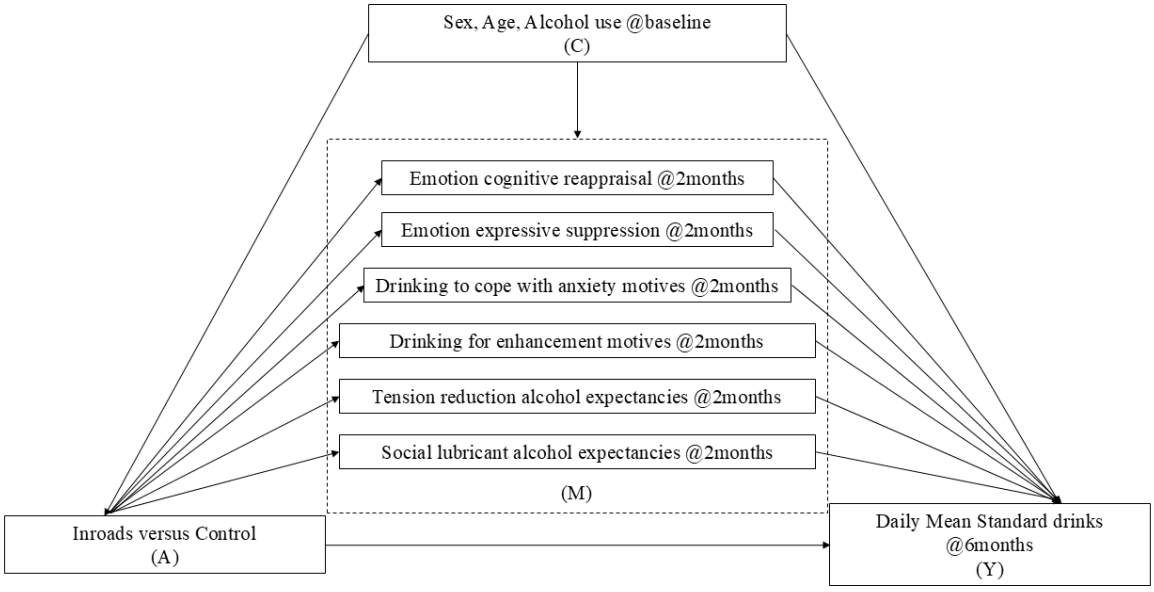
group (*Inroads* versus control), and the outcome (Y) is either social anxiety symptoms as seen in Figure 4.1 or daily mean standard drinks as seen in Figure 4.2.

Figure 4.1: Directed Acyclic Graph illustrating the causal model of interest for social anxiety symptom outcome



A (exposure): Inroads versus control.
M (mediators): Emotion cognitive reappraisal, emotion expressive suppression, daily mean standard drinks.
Y (outcome): social anxiety symptoms.
C (confounders not affected by the exposure): Sex, age, and social anxiety symptoms at baseline.

Figure 4.2: Directed Acyclic Graph illustrating the causal model of interest for daily mean standard drinks outcome



A (exposure): Inroads versus control.
M (mediators): Emotion cognitive reappraisal, emotion expressive suppression, drinking to cope with anxiety motives, drinking for enhancement motives, tension reduction alcohol expectancies, social lubricant alcohol expectancies.
Y (outcome): Daily mean standard drinks.
C (confounders not affected by the exposure): Sex, age, daily mean standard drinks at baseline.

Note: hypothesised mechanisms of change for reducing alcohol use are the psychological factors thought to underlie the link between social anxiety and alcohol use: anxiety motives for drinking, and tension-reduction expectancies about alcohol.

4.2.5 Causal assumptions

To draw causal inference several assumptions must be met to estimate direct and indirect effects (VanderWeele & Vansteelandt, 2014), these include:

1. No unmeasured confounding on the intervention-outcome relationship.
2. No unmeasured confounding on the intervention-mediator relationship.
3. No unmeasured confounding on the mediator-outcome relationship.
4. No mediator-outcome confounder influenced by the intervention.
5. No mediator-mediator interactions that influence the outcome.

It can be expected that treatment randomisation to either the intervention or control will hold assumptions 1 and 2 true (VanderWeele & Vansteelandt, 2014). To increase the plausibility of no unmeasured confounding, multiple baseline covariates were accounted for in the models

and sensitivity analyses for unmeasured confounding were conducted. The covariates included age, sex, and either anxiety symptoms or daily alcohol use at baseline.

4.2.6 Measurement

All measures were collected via self-report surveys, administered via the study website. The data used for mediation analyses were all individual-level data collected within the eligibility and baseline (time 1), 2-months post baseline follow-up (time 2), and 6-months post baseline follow-up (time 3) surveys.

4.2.6.1 Exposure

Intervention: The exposure of interest was assignment to either the online *Inroads* anxiety-alcohol intervention group or control group (time 1). Following consent and completion of the online eligibility and baseline surveys, participants were randomised via the trial website using a computer-generated sequence which the research team were blinded to. Individuals randomised to the anxiety-alcohol intervention were given access to the five, online self-guided *Inroads* program modules. The modules are designed to be completed sequentially and consist of the following content: 1) Understanding alcohol use motives and inter-relationship with anxiety; 2) Cognitive therapy for anxious thoughts; 3) Strategies for sticking to drinking limits and addressing positive alcohol beliefs; 4) Facing fears through behavioural experiments; 5) Social support, goal-setting, and relapse prevention (Stapinski et al., 2019). Within the modules, there is a combination of static information, videos, case vignettes, quizzes, and open-ended questions for participants to use as reflection points. In addition to the online content, participants received support from a clinical psychologist via personalised weekly feedback emails and a 30-minute telephone or text chat session following modules 1 and 4. Although the intervention was designed to be completed over 5 weeks, participants were given flexibility and allowed to finish the modules up until the first study follow-up (time 2), which occurred 2 months after the baseline assessment. Further details of the intervention and its theoretical underpinnings are provided elsewhere (Stapinski et al., 2019).

Control: Individuals randomised to the control group received a pamphlet containing information about the effects and harms of alcohol use, national Australian safe drinking guidelines, and links to national telephone helplines and information websites. This information was provided on screen immediately following randomisation and was also emailed to participants.

4.2.6.2 Mediators

Maladaptive Emotion Regulation behaviours

The Emotion Regulation Questionnaire for Children and Adolescents (ERQ-CA) was used to assess expressive suppression (i.e., the forced attempt to not express discomfort) and cognitive reappraisal (i.e., the attempt to acknowledge and reinterpret emotions) at 2-months post-baseline (time 2, follow-up 1) (Gullone & Taffe, 2012). The child and adolescent version of the ERQ was developed in an Australian sample and was based on the original model of emotion regulation developed by Gross et al. which has demonstrated construct validity for measuring expressive suppression and cognitive reappraisal (Gross & John, 2003). Four questions were used to assess expressive suppression such as "I control my feelings by not showing them". Scores on this scale ranged from 4-20, with higher scores corresponding to greater expressive suppression. Six questions were used to assess cognitive reappraisal such as "I control my feelings about things by changing the way I think about them". Scores on this scale ranged from 6-30, with higher scores reflecting more positive emotion regulation via cognitive reappraisal (Robins & Greenland, 1992). Within the study's sample, the scores from these scales had acceptable internal consistency at baseline with a Cronbach's Alpha of $\alpha = 0.69$ for the expressive suppression scale and $\alpha = 0.85$ for the cognitive reappraisal scale.

Drinking Motives

The five-factor Modified Drinking Motives Questionnaire Revised (DMQ-R) was used to measure drinking motives 2-months post-baseline (time 2, follow-up 1) (V. V. Grant et al., 2007). Across twenty-eight questions, participants indicated their motivation for alcohol consumption based on specific reasons using a 5-point Likert scale, ranging from 1 ('almost never'/ 'never') to 5 ('almost always'/ 'always'). Higher scores on each scale indicated a greater inclination to drink alcohol for those reasons. Of the five-factors measured, coping-anxiety motives and enhancement motives were considered potential mediators in the current study. Within the current study's sample good internal consistency at baseline was seen for both subscale scores, with $\alpha = 0.73$ for coping-anxiety motives and $\alpha = 0.8$ for enhancement motive measures.

Alcohol Outcome Expectancies

Tension reduction and social lubricant alcohol outcome expectancies 2-months post-baseline (time 2, follow-up 1) were measured with the Alcohol Outcome Expectancies questionnaire developed by Kushner et al. (1994). Nine questions such as "drinking helps me to forget my

worries" were used to assess tension reduction alcohol expectancies and eight questions such as "drinking makes me feel less shy" were used for social lubricant alcohol expectancies. Within the current study, there was good internal consistency of these measures at baseline, with $\alpha = 0.85$ for tension reduction alcohol expectancies and $\alpha = 0.88$ for social lubricant alcohol expectancies. Questions were answered on a 5-point Likert scale ranging from 0 (not at all) to 4 (a lot) with higher scores indicating a greater expectancy for the respective alcohol outcome.

Alcohol use- mean drinks per day

For the anxiety outcome model, alcohol use 2-months post-baseline (time 2, follow-up 1) was considered a mediator. This was assessed by mean standard drinks consumed per day over the past month, collected via an online version of the Timeline Follow Back (TLFB) procedure (Hareskov Jensen et al., 2023). A standard drink was defined as 10g (12.5ml) of pure alcohol.

4.2.6.3 Outcomes

Anxiety outcome

Social anxiety symptoms at 6-months post-baseline (time 3, follow-up 2) were assessed with the shortened forms of the Social Interaction Anxiety Scale (SIAS-6) and Social Phobia Scale (SPS-6) developed by (Peters et al., 2012). The SIAS-6/SPS-6 includes 12-items which are scored on a 5-point Likert scale from 0 "Not at all characteristic or true of me" to 4 "Extremely characteristic or true of me". Total possible scores can range from 0-48, with higher scores indicative of greater social anxiety, and a score ≥ 7 on the SIAS-6 indicative of a probable social anxiety diagnosis (Peters et al., 2012). Excellent internal consistency was seen at baseline within this samples' SIAS-6/SPS-6 scores ($\alpha = 0.88$) and previous research has demonstrated its utility in clinical and undergraduate samples (Carleton et al., 2014; Peters et al., 2012).

Alcohol mean drinks per day outcome

Alcohol use 6-months post-baseline (time 3, follow-up 2) was assessed by mean standard drinks consumed per day over the past month, collected via an online version of the TLFB procedure (Hareskov Jensen et al., 2023). A standard drink was defined as 10g (12.5ml) of pure alcohol.

All mediators and outcome measures were kept as continuous variables to draw meaningful clinical conclusions to treatment outcomes that would otherwise be lost with dichotomising the covariates of interest (Altman & Royston, 2006).

4.2.6.4 Confounders

The following baseline (time 1) measures were included as confounders in both models: age in years, sex, and either the anxiety or alcohol outcome of interest at time 1.

4.2.7 Statistical methods

4.2.7.1 Causal multiple mediation analysis

Causal multiple mediation analysis under the counterfactual framework using the potential outcomes approach was conducted to infer causal inference. Two separate models investigated the effects associated with the anxiety and alcohol outcomes of interest. Models used the linear regression-based approach as outlined in VanderWeele and Vansteelandt (2014) to estimate direct and indirect effects of interest. See Supplementary material F1 or VanderWeele and Vansteelandt 2014, page 108 for the equations for the PNDE, TNIE, and TE. This approach is suitable for models with a continuous outcome and multiple continuous mediators. All analyses were done with R studio version 4.3.2, with the "cmest" function in the CMAverse R package (Shi et al., 2021) used to estimate causal effects, with results reported on the mean difference scale. Bias-corrected and accelerated bootstrapping with 500 samples were used to calculate standard errors and 95% confidence intervals for estimated effects. Primary analyses were two separate multiple mediation models developed for the two outcomes of interest as seen in Figure 4.1 and Figure 4.2. Both models accounted for baseline confounders unaffected by the exposure, including sex, age, and baseline levels of the outcome measure.

4.2.7.2 Data imputation

Missing data were handled using multivariate imputation by chained equations (MICE) (Azur et al., 2011). Of the 123 participants, 80 (65%) provided complete data for *both* the 2- and 6-month follow-up variables of interest, and 96 (78%) provided data for *at least one* of the 2- or 6-month follow-up assessments. Individuals with incomplete data or loss to follow-up at 2 and/or 6 months did not differ significantly at baseline in sociodemographic or outcome variables from those who completed assessments. All 123 participants had complete baseline data and participants who did not have follow-up data for both 2- and 6-month follow-up variables (43, 35%) were included in analysis with their follow-up data handled with MICE, under the assumption of Missing at Random (MAR). To ensure the MAR assumption (i.e. missingness is assumed to be independent of unobserved variables) was reasonable, our imputation models included key study variables and covariates (i.e. baseline measures of

outcome variables, sex, age) predictive of attrition or missing responses. Imputation of missing values was done by predictive mean matching informed by variables included within the respective models (i.e., exposure, mediators, outcome, and confounders). This was done with the "args_mice" argument of the cmest function within the CMAverse R package. Eighty imputed datasets run for twenty cycles were utilised for each model, to improve the stability of estimates and reduce power falloff (Graham et al., 2007). Imputed models are reported for all analyses with complete case models reported in supplementary material (Appendix F: Table F1).

4.2.7.3 Sensitivity analyses

To test robustness of the mediation analyses, extrapolation of unmeasured mediator-outcome confounding was calculated. E-values were calculated using the "cmsens" function from the CMAverse package (Shi et al., 2021) and are reported for the PNDE and TNIE for the two causal models of interest. As the causal estimates were for continuous outcomes on the difference scale, E-values were transformed into risk ratios using the transformation as described by VanderWeele and Ding (2017). E-values closer to 1 indicate the results may be more sensitive to potential unmeasured confounding.

Furthermore, in addition to the two primary multiple mediation models, two additional sensitivity analyses were conducted to examine i) whether treatment effects immediately post-treatment (2-months) were mediated by changes in mediators at the same time point and ii) potential confounding in the mediator-outcome relationship. Both imputed and complete case analyses were conducted for these models.

The first set of models assessed whether post-treatment (2-month) mediators explained short-term (2-month) treatment effects on outcomes (i.e. cross-sectional multiple mediation analyses), rather than longer-term (6-month) effects. This analysis aimed to determine whether changes in mediators observed at 2 months played a direct role in shaping outcomes at the same timepoint. This informs questions about whether a short time-lag between the mediator and the outcome might be more sensitive to mediated effects than the 4-month time-lag within the primary models. One model included 2-month social anxiety mediators predicting 2-month social anxiety outcomes, and another model included 2-month alcohol mediators predicting 2-month alcohol outcomes. Otherwise, the same mediators and covariates as the primary analyses were included (see Figure 4.1 and Figure 4.2) and a linear regression-based approach was used. The second set of models explored potential confounding in the mediator-outcome relationship

by including 2-month outcome measures as an additional covariate. This analysis aimed to account for the possibility that changes in the outcome variable (e.g. social anxiety or alcohol use) occurred alongside changes in the mediators, rather than being temporally separated and caused by them. One model included 2-month social anxiety mediators predicting 6-month social anxiety outcomes, adjusting for the 2-month social anxiety symptom measure as a mediator-outcome confounder (L variable). Similarly, the second model included 2-month daily alcohol use mediators predicting the 6-month daily alcohol use outcome, adjusting for the 2-month alcohol use measure as a mediator-outcome confounder (L variable). The inclusion of a continuous measure as a mediator-outcome confounder warranted the use of the g-formula approach for these models (Robins, 1986).

4.2.8 Power considerations

The primary RCT was designed with 80% power to detect a moderate main treatment effect of 0.5 on efficacy of outcomes (Stapinski et al., 2019). As the current study is an ad-hoc analysis, the trial was not designed to be powered to detect specific mediation effects. More recent methods have been developed for determining power for causal mediation analyses, however, these have not been extended to multiple mediation or longitudinal causal mediation study designs (Qin, 2024). Using the methods for single mediation, a sample size of 123 would yield 84% power to detect a small total indirect effect of 0.2, from small-medium standardised path coefficients of 0.3 for paths X➔M, M➔Y, and X➔Y (Qin, 2024). However, power is likely to be reduced in the multiple mediator models examined in the current study, as estimating several indirect pathways simultaneously increases model complexity and typically requires larger sample sizes to detect effects of comparable magnitude.

4.2.9 Ethical approval

Ethical approval was granted by the University of New South Wales (HC17185) and University of Sydney (2018/877) Human Research Ethics Committees, and the trial was prospectively registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12617001609347). All participants provided informed consent via the *Inroads* study website.

4.3 Results

4.3.1 Participants

At baseline, anxiety symptoms were high with 72% reporting moderate (score >10) to severe (>15) generalised anxiety per the GAD-7, and 75% meeting criteria for a probable SAD per the SIAS-6 (score ≥7). High levels of alcohol use were also seen across the sample with participants consuming an average of 3.5 standard drinks per day (SD = 3.1) or 104 standard drinks in the past month, and 60% reporting alcohol use behaviours, per the AUDIT, indicative of alcohol dependence (score ≥20). Additional participant characteristics are reported in the primary outcomes paper (Stapinski, Prior, et al., 2021). No significant differences were seen at baseline between the intervention and control group on any symptom, sociodemographic, or outcome variable of interest for this study.

4.3.2 Effects of intervention on anxiety outcome

Results for the causal multiple mediation for both the anxiety and alcohol models can be seen in Table 4.1. Based on the potential outcomes framework, a significant total effect was observed for the anxiety model, indicating a five-point decrease (95% CI = -1.509 to -8.191) in social anxiety symptom scores for individuals in the *Inroads* condition compared to the control group. The significant total effect in the model was primarily driven by the Pure Natural Direct Effect (PNDE). Specifically, the *Inroads* intervention had a direct effect of reducing social anxiety symptoms by five points (95% CI = -1.337 to -8.137), independent of any indirect effects mediated through increases in cognitive reappraisal and decreases in suppressive emotion regulation and alcohol use. No significant TNIE was observed via the hypothesised mediators.

4.3.3 Effects of intervention on alcohol outcome

A significant total effect was observed for the alcohol model, indicating that individuals in the *Inroads* condition consumed, on average, one standard drink per day less than those in the control group. Within this total effect, the Pure Natural Direct Effect (PNDE) but not the Total Natural Indirect Effect (TNIE) were found to be significant. Specifically, the *Inroads* intervention had a significant direct effect of decreasing individuals' alcohol use by 0.5 standard drinks per day (95% CI = -0.050 to -1.116). The TNIE indicated a non-significant decrease of 0.3 standard drinks per day (95% CI= 0.009 to -0.551) for *Inroads* individuals compared to controls. Since the 95% confidence interval for the TNIE includes zero, there was insufficient evidence of a mediated effect through the combined increase in cognitive

reappraisal and decrease in suppressive emotion regulation, drinking to cope with anxiety motives, drinking for enhancement motives, tension reduction alcohol expectancies, and social lubricant alcohol expectancies.

Table 4.1: Estimates of causal multiple mediation effects of the Inroads intervention on social anxiety and alcohol outcomes.

	Total Effect (TE)				**Pure Natural Direct Effect (PNDE)**				**Total Natural Indirect Effect (TNIE)**			
	Estimate	***p***	**95% Confidence Interval**		**Estimate**	***p***	**95% Confidence Interval**		**Estimate**	***p***	**95% Confidence Interval**	
Social anxiety symptoms outcome	-4.907	**<0.001**	-1.509	-8.191	-4.967	**<0.001**	-1.337	-8.137	0.060	0.908	1.701	-1.024
Mean standard drinks per day outcome	-0.807	**<0.001**	-0.415	-1.271	-0.515	**0.032**	-0.050	-1.116	-0.292	0.068	0.009	-0.551

Note: Estimates are reported on the mean difference scale with effects with *p* values <0.05 bolded. Models include age, sex, and the respective outcome at baseline as confounders.

4.3.4 Sensitivity analyses

The E-values for unmeasured confounding in both models are presented in Table 4.2. The PNDE E-values for the anxiety and alcohol models were 2.6 and 2.0, respectively. Given the inclusion of theoretically supported covariates in each model, it is unlikely that unmeasured confounders of this magnitude would fully explain the observed associations. However, the TNIE E-values for both models are close to one, suggesting reduced confidence in the adequacy of the models to account for all potential confounders. Specifically, the E-value of 1.1 for the anxiety model suggests that an unmeasured confounder with a weak association with the multiple mediators and outcome could have explained away the TNIE. In contrast, the E-value of 1.6 for the alcohol model suggests an unmeasured confounder with a moderate association with the multiple mediators and drinking outcome would be needed to have explained away the TNIE.

Table 4.2: E-values for unmeasured confounding and 95% Confidence Intervals associated with the anxiety and alcohol models

	Pure Natural Direct Effect (PNDE)			**Total Natural Indirect Effect (TNIE)**		
	E-value	**95% Confidence Interval**		**E-value**	**95% Confidence Interval**	
Social anxiety symptoms outcome	2.572	1.634	1.0	1.081	1.0	1.0
Mean standard drinks per day outcome	1.992	1.101	1.0	1.630	1.075	1.0

Note: E-values are reported on the risk ratio scale.

Results of the sensitivity analysis exploring potential mediation of short-term treatment effects or mediator-outcome confounding can be seen in supplementary material (Appendix F: Table F2 and Table F3). In these analyses, the significant effects ($p < .05$) for the anxiety model remained across both sensitivity analyses, although the observed estimates were slightly smaller. For the alcohol models, the mediator-outcome confounding sensitivity analyses also showed slightly smaller estimates, but the pattern of significance remained consistent with the

primary analyses. However, in the sensitivity analyses examining mediators of short-term (2-month) alcohol reductions, there was no evidence of a significant PNDE or a significant total effect (Appendix F: Table F2). The lack of significant PNDE and total effect in the supplementary model predicting short term (2-month) alcohol outcomes is consistent with the main RCT findings, where intervention versus control effects on drinking were only observed at the 6-month follow-up.

4.4 Discussion

This study aimed to examine whether hypothesised behavioural, cognitive, and motivational mechanisms jointly mediate the effectiveness of the *Inroads* intervention in reducing anxiety and daily alcohol use among young adults. As the first online intervention designed to promote coping skills for managing anxiety, hazardous alcohol use, and their interconnections, it is important to test the potential mechanisms driving these effects. The findings of this current study demonstrated evidence of a total effect of the *Inroads* program on reducing social anxiety symptoms and mean daily alcohol use at six months post-intervention, even when accounting for mediating factors. Contrary to hypotheses though, no significant mediated indirect effect was found based on measured values of mediators at time 2 and social anxiety or alcohol outcomes at time 3 whilst accounting for baseline covariates.

The *Inroads* anxiety-alcohol treatment did not appear to reduce social anxiety symptoms via the hypothesised mediators, notably one of which was reducing alcohol use. This is at odds with current theoretical models of co-occurring anxiety and alcohol use, where a reduction in alcohol use would in turn be presumed to also reduce anxiety symptoms (Smith & Randall, 2012). Alcohol has been shown to exacerbate anxiety by triggering symptoms, creating additional psychosocial stressors, and/or reinforcing threat expectancies, leading to the "vicious cycle of comorbidity", with both disorders reinforcing one another (Baillie & Sannibale, 2007). As the current study looked at joint causal mediation, further research is needed to elucidate the causal role of specific mediators, like alcohol use, in reducing anxiety symptoms. Furthermore, whilst there wasn't evidence for the hypothesised mediators of symptom change, it is possible that the detection of mediation effects was limited by the delay between assessment of mediators at 2-months post baseline and outcomes at 6-months. The four-month lag between the measurement of mediators and the social anxiety outcome may not have appropriately captured how changes in the proposed mechanisms subsequently account

for reductions in social anxiety seen among intervention participants. In the context of intervention participants also observing the greatest reductions in social anxiety symptoms from baseline to 2-months post intervention, additional measurement time points, throughout the 2-month treatment duration, could further elucidate the role of mediator timing on treatment outcomes. Given the current study did not find significant effects, however, for the hypothesised mediators at the measured timepoints, the question regarding what is driving the efficacy of the *Inroads* intervention on reducing social anxiety symptoms remains. Outside of online interventions, perceived social self-efficacy, estimated social cost, and avoidance have been identified as mediators in SAD treatments (Hedman et al., 2013; Rukmini et al., 2021). Future research is needed to determine the role these psychological mechanisms may play in the role of online anxiety-alcohol treatments.

There was not statistical evidence in the current study that reductions in drinking, within the context of co-occurring anxiety and hazardous alcohol use, were mediated by the hypothesised mechanisms of positive expectancies and motives about the effects alcohol, and maladaptive emotion regulation. While the joint mediation estimate of the total natural indirect effect did not reach statistical significance (b = -0.292, CI: 0.009 to -0.551, $p = 0.068$), the current study had only 84% power to detect small-medium effects. Furthermore, power analyses were based on single mediator models, with power likely reduced for the multiple mediation models conducted in the current study. Future research, with greater statistical power, may help identify potential small indirect effects through these hypothesised multiple mediators. Further work is needed to clarify whether significant mediation effects would be observed if mediators and outcomes were measured closer (rather than with a 4-month lag), or whether it is additional mechanisms entirely that contribute to the intervention's overall impact on alcohol use. This is particularly important given the significant pure natural direct effect observed (b = -0.515, CI: -0.050 to -1.116, $p = 0.032$). As with the anxiety model, joint causal mediation analysis limits the ability to identify the specific effects of individual mediators; but findings suggest the presence of additional pathways influencing the observed reductions. When compared to other studies investigating mechanisms of change among alcohol-only online interventions, similar (i.e., null, or weak) effects are seen. An online alcohol education course for college students found no mediating effect of positive alcohol expectancies on drinking behaviours (Paschall et al., 2014). Similarly, a personalised feedback alcohol intervention for 18-25 year olds found no effect of decreases in drinking to cope motives mediating reduced alcohol use (Lau-Barraco et al., 2018). These education courses, however, were preventative interventions which may not

be directly comparable to treatment and intervention mechanisms of change. Additionally, other psychological mechanisms, such as self-efficacy, confidence, and knowledge of how to change, have been found to mediate outcomes in online and telehealth alcohol treatments (Bendtsen et al., 2023; Brincks et al., 2024). Although not considered the key mechanistic drivers in the motivation and maintenance of co-occurring anxiety and alcohol use specifically, further research is needed to understand whether these are also potential mechanistic targets for *integrated* anxiety-alcohol interventions.

The current study has several strengths including its use of modern causal mediation methods, and longitudinal study design allowing for temporal precedence and causality to be inferred. There are, however, several limitations which must be considered. Firstly, is the likelihood of residual or unmeasured confounding. Despite including sex, age, and baseline outcome measures as potential confounders in each model, the observed E-values suggests effects could still be influenced by other unmeasured covariates. Further research is needed to elucidate the robustness of the observed causal relationships and whether there are additional confounding factors, on the mediator-outcome relationship, which should be considered in the context of integrated anxiety-alcohol treatments, and other psychological treatments more broadly. Specifically, this may also include mediator-outcome confounders which are affected by the exposure, like post-treatment levels of alcohol use. Sustained changes in alcohol use are highly correlated with alcohol use reduction immediately post treatment, and these early alcohol reductions could also influence the hypothesised mediators. For example, reduced alcohol use at post intervention might lead to reduced coping-motives for drinking. This possibility of a reverse causation relationship means that levels of anxiety/alcohol use at 2 months may confound the observed association between the mediators and outcomes at 6 months. We conducted sensitivity analyses to estimate mediation effects controlling for this potential mediator-outcome confounding, which suggested a slight reduction in effects sizes but no substantiative change to the study conclusions. Secondly, despite being the first online intervention targeting co-occurring anxiety and hazardous alcohol use in young adults, the modest trial sample size (n =123) and subsequent attrition at follow-up assessments may have introduced bias to the estimated effects. This, attrition, however was mitigated in the current study through gold standard missing data imputation approaches. Future evaluation of the *Inroads* program will address potential sample size and attrition bias through a RCT with a larger sample. This trial aims to recruit a sample of n = 500, which will be powered to detect between-group differences when comparing the *Inroads* integrated alcohol-anxiety program

(plus telehealth and email support from a non-specialist support person) to a brief alcohol-feedback control program, with an effect size of d = 0.3 and 0.9 power (Prior et al., 2024). Lastly, there are potential limitations, as alluded to earlier in this discussion, related to the measurement of the mediating variables, both in terms of their theoretical basis and timing of measurement. Whilst the measures chosen were well validated, there is the possibility that they did not adequately capture the psychological and behavioural constructs which were hypothesised to be mechanisms of change. Additionally, the mediating variables were measured 2-months post-baseline and the outcomes 6-months post-baseline. The length of time between the measurement of mediating mechanisms and outcomes may not have been appropriate to capture these psychological and behavioural factors. Measuring the hypothesised mediators immediately post treatment and at additional timepoints throughout treatment, combined with an earlier follow-up measurement of outcomes, may provide greater insight into how the anxiety-alcohol intervention was efficacious. Finally, given the lack of evidence for the hypothesised mediators in the social anxiety and alcohol use models, unmeasured or incorrectly measured mediators remain a limitation in the current study. Additional studies would benefit from testing refined measures which more accurately capture the constructs pertaining to the mechanisms of change for anxiety-alcohol early interventions and treatments.

4.4.1 Conclusion

The aim of this study was to identify the mechanistic drivers of an efficacious treatment for co-occurring anxiety and alcohol use in young people. Whilst there was evidence of an overall effect of treatment on the anxiety and alcohol use outcomes, the study did not find sufficient evidence that these effects were jointly mediated by the hypothesised processes of maladaptive emotion regulation and alcohol use for social anxiety reductions, or maladaptive emotion regulation, positive alcohol expectancies, and coping or enhancement alcohol use motives for reductions in alcohol use. Like other treatment and intervention mediation studies (Greenberg et al., 2023; Moskowitz et al., 2023; Sunderland et al., 2024), this reflects the challenge of delineating the psychological processes that underlie effective interventions. Our results may reflect that the hypothesised mediators were inadequately captured by the study measures, or alternatively that there are different psychological processes driving effects. Further research is needed to better understand *how* integrated anxiety-alcohol interventions, like *Inroads*,

achieve their effects so these mechanisms can continue to be refined and built upon in future online interventions.

Chapter 5

Logged in, dropped out? A mixed-methods study exploring young adults' experiences and engagement with an online program for co-occurring anxiety and hazardous alcohol use

Preface

Online interventions hold immense potential to transform early intervention for co-occurring anxiety and alcohol use concerns by providing accessible, low cost, and scalable support. However, ensuring that these programs are designed and implemented in ways that meet the unique needs of individuals with this comorbidity is essential. This study builds upon the findings of **Chapter 4**, which focused on elucidating *how* an efficacious anxiety-alcohol early intervention works, by shifting focus to user engagement and experience with the intervention. As outlined in **Chapter 1**, there is currently no evidence on the barriers and enablers to online intervention engagement among young adults with co-occurring anxiety and alcohol use concerns.

To address this gap, this study employed a rigorous mixed methods design to understand the factors that influence engagement with an efficacious online intervention for co-occurring anxiety and hazardous alcohol use (Gückel, Radmall et al., 2025; Stapinski, Prior, et al., 2021). Specifically, data were derived from a naturalistic trial of the *Inroads* program in which all eligible participants were provided access to a fully self-guided version of the intervention. Examining user experience, particularly barriers and enablers of engagement, in this context is highly pertinent as it offers insight into how early interventions function in real-world settings. Purposeful effort was made to sample participants for qualitative interviews who did and did not engage with program content and those who dropped out, ensuring a diverse range of experiences were captured. These qualitative findings are triangulated with quantitative data to delineate key program elements that may facilitate engagement. Findings of this study can be used to inform the design, refinement, and implementation of online early interventions targeting co-occurring anxiety and alcohol use concerns among young adults, to ensure they meet the needs and preferences of this population.

This chapter addresses the fourth objective of this thesis, which was to:

Identify barriers and enablers to the delivery of, and user engagement with, an online intervention for young adults experiencing co-occurring anxiety and hazardous alcohol use.

This study will be submitted to *Internet Interventions.*

Supplementary materials for **Chapter 5** are provided in Appendix H.

Abstract

Online programs hold great promise for scalable intervention of mental health and substance use concerns; however, facilitating uptake and engagement remains a significant challenge. This study explored participants' experiences and engagement with *Inroads*, an integrated online early intervention program targeting anxiety and alcohol use. Using a mixed-methods design, young adults enrolled in a self-guided, naturalistic one-arm trial and provided quantitative data via follow-up surveys (n = 28) and qualitative data through semi-structured interviews (n = 11) and open-text responses (n = 28). Reflexive thematic analysis was used to analyse qualitative data, and descriptive analyses reported percentage agreement with survey items. Overall, participants rated the program positively (46.4% 'good', 25.0% 'very good') and found elements such as real-life character examples helpful (42.9% 'somewhat agree' and 32.1% 'fully agree' they aided engagement). Qualitative findings highlighted enablers to engagement, including the online format and practical skills. Barriers to engagement were more likely to be individual-level factors, such as competing priorities and forgetting about the program. Thematic analysis identified three key themes: (i) Creating the "right" online format and mode of program delivery, with subthemes of fostering motivation and accountability through program factors and balancing participant preferences and theoretical foundations; (ii) Participants' program expectations and (mis)alignment; and (iii) Intersection of an online program with an individual's offline world. Together, these findings underscore the importance of motivation and accountability in online interventions. As suggested by participants, these challenges may be partially addressed through additional human support and guidance to enhance engagement.

5.1 Introduction

5.1.1 The allure of online interventions for mental health and substance use concerns

The rise in online interventions has shown great promise for treating mental health concerns, such as anxiety (Eilert et al., 2021; Richards et al., 2015) and substance use concerns including hazardous alcohol use (Ndulue & Naslund, 2024). Importantly, online interventions may be particularly beneficial for individuals experiencing co-occurring mental and substance use disorders, who often face significant structural and systemic barriers to accessing integrated care, including limited availability of specialised services and stigma-related concerns (Kaufmann et al., 2014; Priester et al., 2016). By reducing geographical, financial, and logistical constraints, online interventions have the potential to transform how, and for whom, care is delivered (Andersson & Titov, 2014; Andersson et al., 2019). As such, a growing body of work has aimed to delineate the optimal form(s) of delivery and understand how best to engage (and retain) users. This is in light of persistent challenges in engagement and retention, with Eysenbach (2005) first highlighting the "law of attrition" in relation to high discontinuation of use and dropout within online trials nearly two decades ago. While this concept was initially applied to trial contexts, poor usage and uptake in real-world settings remains a critical issue (Baumel et al., 2019; Boucher & Raiker, 2024; Cross et al., 2025; Fleming et al., 2018). One key factor influencing engagement is the level of human guidance within a program, which has been proposed as a significant determinant of user experience and treatment outcomes (C. Morgan et al., 2017; Opie et al., 2024). Given self-guided programs that do not involve human support tend to have lower engagement and higher attrition, it is critical to understand the factors that impede engagement with these programs. Examining factors that impair and facilitate engagement with online interventions will inform the future refinement and delivery of online interventions for co-occurring mental and substance use concerns.

5.1.2 The online 'Inroads' anxiety and alcohol program and naturalistic trial

Inroads is the first online early intervention program to concurrently address transdiagnostic anxiety symptoms, hazardous alcohol use, and their interconnections among young adults aged 17-30 (Stapinski et al., 2019). Given the high co-occurrence of anxiety and hazardous alcohol

use (Anker & Kushner, 2019; Grant et al., 2004; Lai et al., 2015), and poorer treatment responses associated with single-disorder interventions, *Inroads* aims to support young adults during a life stage marked by increased vulnerability to the onset and escalation of these concerns (LeBlanc et al., 2020; Legerstee et al., 2019; Leggat et al., 2022). Drawing on evidence from adult samples receiving face-to-face integrated treatments (Kushner et al., 2013; Stapinski, Sannibale, et al., 2021), the program comprises five online, self-guided CBT modules (see Appendix H: Table H1 for program content overview). These modules incorporate a range of engaging content including written text, images, infographics, "real-life" case examples, audio, quizzes, and open text fields for goal setting and reflection. In addition to the online content, the program was originally delivered alongside low-intensity psychologist support consisting of weekly emails providing feedback and personalised suggestions aligned to module content, and a 30-minute telephone and/or chat session after modules 1 and 4 (Stapinski et al., 2019). In a RCT of the psychologist-supported program, *Inroads* demonstrated beneficial effects relative to an assessment plus alcohol information control. Participants who received the *Inroads* intervention reported sustained reductions in alcohol consumption, hazardous alcohol use, and social anxiety symptoms at the 6-month follow-up compared to the control condition (Stapinski, Prior, et al., 2021). Given its efficacy and online format, *Inroads* holds strong potential for wide dissemination and impact across two commonly co-occurring and burdensome conditions.

To increase scalability and feasibility, the program was updated to be delivered in a fully self-guided format, without psychologist support. These updates were implemented during the COVID-19 pandemic, which presented a unique opportunity to roll out the program at a time when many young adults were reporting heightened anxiety and harmful alcohol use behaviours, and waitlists were long for psychologists (Foundation for Alcohol Research & Education, 2020; Manfield, 2020; Stanton et al., 2020). In the self-guided version, low-intensity psychologist support and manual emails were replaced with automated, tailored weekly feedback emails. These emails reflected the module content and participants' goals and progress. The email content was customised using rule-based algorithms according to the participant-reported goals and progress within the modules, for example participants were provided with encouragement and suggestions if they did not meet their weekly goals for alcohol reduction. Participants also received automated reminder emails and text messages encouraging them to log in and continue working through the program.

The self-guided *Inroads* program was made available as part of a single-arm naturalistic trial, where all eligible individuals were given access to the program. Beneficial effects were again observed; however, engagement was low and attrition rates were high (Gückel, Radmall et al., 2025). Significant reductions from baseline in hazardous drinking, binge drinking frequency, social anxiety and generalised anxiety symptoms were observed at 2- and 6- month follow-up, with comparable effect sizes to those observed in the psychologist-supported RCT (Gückel, Radmall et al., 2025). However, of the 115 enrolled participants, 103 (89.6%) commenced module one and 27 (23.5%) completed at least 1 module. Twelve participants (10.4%) completed at least 3 modules, a rate considerably lower than in the psychologist-guided trial where 51% completed at least three modules. High attrition was also observed across the follow-ups with only 25.2% and 30.4% completing the 2- and 6-month surveys, respectively. Several factors may have contributed to low engagement and retention, including the initial use of a prize-draw incentive for follow-up completion, which was later replaced with guaranteed individual reimbursements; following this change, follow-up rates increased nearly ninefold (Gückel, Radmall et al., 2025). The COVID-19 pandemic may have further affected program engagement and follow-up, with widespread digital fatigue and reduced motivation to participate in research reported during this period (Cardel et al., 2020; Gregersen et al., 2023). Nonetheless, while the self-guided format clearly offers benefits for young adults with anxiety and alcohol use concerns, further research is needed to improve engagement and retention of youth, with self-guided online interventions. Understanding the barriers and enablers to program engagement is critical for delivering scalable and efficacious interventions capable of disrupting the early developmental trajectory of co-occurring anxiety and alcohol use.

5.1.3 The current study

Given the importance of understanding how online mental health programs are taken up in real-world settings, the present study aims to explore the experiences and engagement of young adults with co-occurring anxiety and alcohol use concerns who accessed the self-guided *Inroads* online early intervention program. The low adherence seen in the naturalistic trial of the self-guided *Inroads* program highlights the challenges of interventions without some level of human support, and this study presents an opportunity to build a greater understanding of what the limitations but also enablers are to this program delivery to inform program refinements and improve engagement. Specifically, we seek to identify key themes related to

barriers and facilitators of user engagement, as well as participants' experiences and preferences regarding specific program components. A mixed-methods design will be employed, combining quantitative and qualitative data to address the study's aims. This approach allows for quantitative findings to be contextualised and enriched through in-depth qualitative interviews with *Inroads* participants. Whilst the current study is in the context of an online program for co-occurring anxiety and alcohol use, understanding factors that enhance or detract from user engagement can help inform and refine online interventions for mental health, substance use, and their co-occurrence more broadly.

5.2 Methods and methodology

5.2.1 Study design and context

The mixed-method study design was fixed, meaning the use of quantitative and qualitative methods was planned and decided a priori. Specifically, a convergent parallel design was used where the quantitative and qualitative component were performed independently and results were brought together in the overall discussion and study conclusions (Creswell & Plano-Clark, 2011). The current study was designed and implemented shortly after enrolment to the original trial of the self-guided program had begun.

5.2.2 Participants and recruitment

Participants were drawn from the naturalistic, single-arm *Inroads* trial of the self-guided program run from April 2021 to July 2023. Recruitment occurred via organic and minimal paid social media advertising, media coverage, cross-promotion from relevant mental health or drug and alcohol organisations (e.g., Alcohol and Drug Foundation), and youth service referrals. Young Australians aged 17-30 reporting hazardous alcohol use and at least mild generalised or social anxiety symptoms were eligible for the trial. Full eligibility criteria, including symptom thresholds for alcohol use and anxiety, and detailed recruitment procedures can be found in the trial's main outcomes paper (Gückel, Radmall et al., 2025). A total of 115 young adults were eligible and consented to participate. They all received access to the *Inroads* intervention and invited to complete assessments at baseline, and 2- and 6-month post intervention. Depending on enrolment timing, participants either received a $30 e-gift card or were entered into a $150 e-gift card prize draw for completing follow-ups. The current study focuses on the subsample

of participants who completed the quantitative (n = 28) or qualitative study components (open-ended questions n =28 and semi-structured interviews n = 11), as detailed below. Table 5.1 presents demographic characteristics for participants included in these analyses.

5.2.3 Quantitative data and analysis

5.2.3.1 Data source

Quantitative data was derived from the 2-month post-intervention assessment, administered online via the *Inroads* study website. These quantitative were embedded part-way through the trial, and one participant had completed the survey prior to the questions being added. In total, 28 participants completed the quantitative measures of interest and were included in analyses (i.e., all but the one participant who had already completed the follow-up; 24.3% of the total n = 115 sample).

5.2.3.2 Measures

For the current study, the quantitative measures of interest focused on i) feedback on specific *Inroads* program elements (i.e. the videos or real-life case examples), ii) general feedback about the *Inroads* program, and iii) barriers and enablers to online program engagement. In the context of this study, we use engagement to broadly encompass *any* user interaction with the program including logging into the program, completing a module, interacting with a program element, and reading program emails and SMS messages.

Feedback on i) specific program elements and ii) general program experiences: A series of bespoke items were used to assess which components participants completed, their perceived usefulness, and overall impressions of program quality and utility. For example, program element questions included "Did you watch any of the videos?" with a binary yes/no response option and "How useful were the videos?" with response options on a 5-point Likert scale ranging from 0 (not at all) to 4 (extremely). General program feedback items included "On average, how motivated did you feel when doing the program?" with response options on a 5-point Likert ranging from 0 (not at all motivated) to 4 (extremely motivated) and "Would you recommend the program to others with anxiety and/or harmful alcohol use?" with a no/maybe/yes response option.

iii) Barriers and enablers: We developed a nine-item measure to assess program enablers and an 11-item measure to assess program barriers. Measurement and item development was informed by previous reviews on user engagement, barriers, facilitators, enablers, and

implementation in the context of online, digital, or eHealth interventions (Borghouts et al., 2021; Schreiweis et al., 2019). Items were broadly categorised into individual/user, program, and technology/environment domains. Participants responded to each item using a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). The enabler items were introduced with the prompt: "How much do you agree with the following statements about things that helped you engage with/complete the *Inroads* program?" and the barrier items with: "How much do you agree with the following statements about things that got in the way of engaging with/completing the *Inroads* program?". The full measures can be seen in Appendix H.

5.2.3.3 Analysis

All quantitative data analyses were conducted using R version 4.5.1 (R Core Team, 2025). Descriptive analyses were carried out to summarise responses to survey items and levels of agreement with potential barriers and enablers using the *Tidyverse* package (Wickham et al., 2019).

5.2.4 Qualitative data and analysis

5.2.4.1 Data source

Qualitative data were derived from open-ended questions included in the 2-month post-intervention assessment (completed by $n = 28$ as described above) and from semi-structured interviews. For this sub-study, participants who had enrolled from July 2022 onwards were invited to participate in the semi-structured interview. Of 26 participants invited, 11 expressed interest and subsequently completed an interview; all 11 had also completed the post-intervention assessment. Participants were encouraged to participate in the interview regardless of their level of program engagement; this resulted in a diverse range of perspectives (27.3% completed no modules, 27.3% completed 1 module, and 45.5% completed >1 module).

5.2.4.2 Data

Survey open ended questions: Aligned with the study aims, open-ended questions captured what participants felt was i) most helpful in the program, ii) least helpful in the program, iii) facilitated engagement with the program, iv) negatively impacted/dissuaded engagement with the program, and v) any other general comments.

Semi-structured interviews: Interviews were conducted via Zoom audio calls, with participants receiving a $70 e-gift card for their participation. Interviews were semi-structured and conducted by one researcher (TG). At the start of interviews it was reiterated to participants that the study team was welcome to and interested in all feedback, positive or negative. The full interview guide can be seen in Appendix H: Supplementary material H3, with questions covering motives for joining the program, experiences with the program, and preferences for online programs more broadly.

5.2.4.3 Analysis

Qualitative responses from the 2-month survey and interviews were analysed using reflexive thematic analysis (Braun et al., 2022). As both sources provided insights into participants' experiences and engagement with the program, they were treated as a single dataset for the purposes of analysis. Reflexive thematic analysis was chosen for its flexibility and its alignment with the study's aim to explore subjective experiences, while acknowledging the active and interpretive role of the researcher in theme development. Analysis was primarily inductive with theme development guided by the content of the data rather than by pre-existing theories or frameworks (Braun & Clarke, 2006). Coding and theme generation were conducted at a semantic level, focused on participants' explicit statements, to understand participants' direct experiences and engagement with the *Inroads* program. The analysis process was guided by Braun and Clarkes 6 phases of thematic analysis (Braun & Clarke, 2006; Braun et al., 2022) as detailed below.

Initially, the primary researcher (TG) familiarised herself with the data by re-listening to the interview audio and editing the transcripts which had first been automatically transcribed using Microsoft Word's speech-to-text function. Edited transcripts and open-ended survey responses were then imported into NVivo 14, where all subsequent coding and analysis were managed. Once in NVivo, the qualitative data were read and re-read so the researcher was further immersed in the full dataset, with initial reflections and potential codes noted during this phase. TG then manually coded each data file line-by-line, assigning codes to any content considered meaningful in relation to participants' experiences or engagement with the program. Following the initial round of coding, the data assigned to each code were reviewed, and overlapping codes were collapsed where appropriate (e.g., "friend or family expectations to drink" was collapsed into "friends or family (mis)aligning with their drinking"). Code names were refined, and the dataset was revisited and re-coded where necessary. During this stage initial theme generation also began. TG engaged in reflexive practice through written reflections to ensure

that theme development was grounded in the data. Theme development was iterative, and codes were appraised in the context of the full dataset to ensure that the themes reflected the diversity of participants' experiences with the program. Theme refinement and definition were supported by the creation of thematic maps and discussions with other researchers (LAS, KP, and NCN), which helped clarify the meaning and scope of each theme. In the final phase of analysis and write-up, the boundaries of some themes were adjusted and theme names further refined.

Researcher's positionality and reflexivity

An important aspect of reflexive thematic analysis is consideration of the researchers' background and the active role they play in generating qualitative findings. The primary researcher (TG) who conducted and coded the interviews was involved with the coordination of the naturalistic trial, and subsequent trials i.e., Prior et al. (2024), as well as updates to the program. She was, however, not involved with the initial development of the program. The familiarity with program content enabled probing during interviews which would not have been possible by an outsider less familiar with the program's content or aims. However, this context inherently shaped the researcher's coding and theme generation, with the researcher aware of the significant buy-in they have with the *Inroads* program. Throughout coding and theme development, the researcher remained conscious of her vested interest in the program and actively challenged her own perspectives. TG's shared age group and Australian background with participants meant she could at times relate to their experiences of anxiety, alcohol use, and everyday life. Whilst the researcher knew she had this insider position; she may have been perceived as an outsider by all study participants who completed qualitative interviews as this personal, insider, perspective was not disclosed (Berger, 2015).

5.2.5 Ethical approval

Ethical approval for the *Inroads* naturalistic trial of the self-guided program, including participant interviews, were provided by the University of Sydney Human Research Ethics Committee (2020/HE000319).

5.3 Results

Table 5.1: Demographic and program related characteristics of the study sample

	Participants providing quantitative data and open-ended qualitative data from the post-intervention assessment	Participants providing semi-structured interview data
	n = 28	*n* = 11
Age (years), *M (SD)*	24.6 (3.5)	23.6 (3.6)
Gender, *n (%)*		
Male	14 (50%)	6 (54.5%)
Female	14 (50%)	5 (45.5%)
Baseline generalised anxiety (GAD-7 severity category), *n (%)*		
Mild (5-9)	9 (32.1%)	3 (27.3%)
Moderate (10-14)	9 (32.1%)	2 (18.2%)
Severe (15-21)	10 (35.7%)	6 (54.5%)
Baseline social anxiety (Mini-SPIN possible anxiety disorder), *n (%)*		
No diagnosis (<6)	8 (28.6%)	4 (36.4%)
Possible diagnosis (≥6)	20 (71.4%)	7 (63.6%)
Baseline total drink past month, *M (SD)*	109.6 (74.3)	126.7 (56.0)
Baseline total drinking days past month, *M (SD)*	17.2 (7.7)	20.9 (6.2)
Baseline hazardous alcohol use severity category (AUDIT), *n (%)*		
Risky/hazardous (8-15)	5 (17.9%)	0 (0%)
High-risk/harmful	6 (21.4%)	3 (27.3%)
Possible dependence (≥20)	17 (60.7%)	8 (72.7%)
Baseline self-reported primary concern, *n (%)*		
Generalised anxiety	8 (28.6%)	0 (0%)
Social Anxiety	6 (21.4%)	3 (27.3%)
Alcohol use	7 (25.0%)	4 (36.4%)
Depression	7 (25.0%)	4 (36.4%)
Modules completed, *n (%)*		
0	7 (25.0%)	3 (27.3%)
1	10 (35.7%)	3 (27.3%)
2	5 (17.9%)	2 (18.2%)
3	2 (7.1%)	1 (9.1%)
4	2 (7.1%)	0 (0.0%)
5	2 (7.1%)	2 (18.2%)

GAD-7 = Generalised Anxiety Disorder Questionnaire; Mini-SPIN = Mini-Social Phobia Inventory; AUDIT = Alcohol Use Disorders Identification Test

5.3.1 Quantitative findings

5.3.1.1 Program element feedback

Feedback on specific elements in the *Inroads* program is presented in Table 5.2. Overall, there was mixed engagement with these elements, with 57.1% of individuals watching module videos, 42.8% reading most or all real-life examples, and 25% listening to most or all of real-life audio examples. A third of participants (35.7%) reported spending 1-15 minutes a week completing tasks to help their anxiety or alcohol, with 53.6% reporting >15 minutes. Despite variable engagement, intervention elements were generally perceived as useful. Real-life examples received the most favourable rating, with 57.7% of participants reporting them to be at least moderately useful. In contrast, the daily anxiety and alcohol check-in tracker had the least favourable ratings, with 46.4% describing this element as only “a little bit" useful. Given that self-monitoring and tracking are well-established techniques for alcohol use and behaviour change more broadly (Howlett et al., 2022) this finding is somewhat unexpected. However, the mandatory nature, upon program login, of the check-in tracker may have negatively influenced participants’ perceptions of this feature.

Table 5.2: Quantitative feedback on specific elements in the Inroads online program

Program element survey measure	N	Response options	n (%)
Videos			
Did you watch any of the videos in the modules?	28		
		No	12 (42.9%)
		Yes	16 (57.1%)
How useful were these videos?	16		
		Not at all	0 (0.0%)
		A little bit	4 (25.0%)
		Moderately	4 (25.0%)
		Quite a bit	1 (6.2%)
		Extremely	0 (0.0%)
		Missing	7 (43.8%)
Real-life examples and its accompanying audio			
How many of the real-life examples did you read?	28		
		None	2 (7.1%)
		A few	10 (35.7%)
		Some	4 (4.3%)
		Most	3 (10.7%)
		All	9 (32.1%)
How useful were these examples?	26		
		Not at all	0 (0.0%)
		A little bit	1 (3.8%)
		Moderately	5 (19.2%)

Program element survey measure	N	Response options	n (%)
		Quite a bit	6 (23.1%)
		Extremely	4 (15.4%)
		Missing	10 (38.5%)
How much of the audio (below the real-life examples) did you listen to?	28		
		None	9 (32.1%)
		A few	12 (42.9%)
		Some	0 (0.0%)
		Most	5 (17.9%)
		All	2 (7.1%)
How useful was the audio option?	19		
		Not at all	2 (10.5%)
		A little bit	6 (31.6%)
		Moderately	2 (10.5%)
		Quite a bit	4 (21.1%)
		Extremely	5 (26.3%)
		Missing	0
Daily check-in (compulsory following program log-in)			
How useful was the daily check-in for anxiety and alcohol?	28		
		Not at all	6 (21.4%)
		A little bit	13 (46.4%)
		Moderately	4 (14.3%)
		Quite a bit	1 (3.6%)
		Extremely	4 (14.3%)
Program tasks			
On average, how much time did you spend doing tasks to help your anxiety or drinking each week?	28		
		None	3 (10.7%)
		1-15 minutes	10 (35.7%)
		16-30 minutes	6 (21.4%)
		31-45 minutes	5 (17.9%)
		46-60 minutes	1 (3.6%)
		+61 minutes	3 (10.7%)
Were the tasks…?	28		
		Very difficult	0 (0.0%)
		Difficult	8 (28.6%)
		Neutral	12 (42.9%)
		Easy	8 (28.6%)
		Very easy	0 (0.0%)

5.3.1.2 General program feedback

General feedback on the *Inroads* program is presented in Table 5.3. Overall, the program was rated positively by participants with the majority rating the program as 'good' (46.4%) or 'very good' (25.0%). Participants who completed 0 or 1 module were more likely to select the 'neutral' rating for their overall opinion. Regarding perceived usefulness, at least half of the sample saw improvements in their anxiety and/or alcohol use. Most participants (57.2%)

reported moderate to major improvements to entering anxiety-provoking situations or dealing with negative emotions, with those reporting little or no change typically completing 0-2 modules. Improvements in general feelings of worry and anxiety were slightly lower, with 43.0% reporting moderate to major improvements. When it came to improvements in alcohol use, half of participants (50.1%) reported moderate to major improvements, with lesser improvement again more common among those who completed 2 or fewer modules. Motivation when doing the program was a notable challenge for participants, with 57.1% reporting to feel a 'little motivated' and a further 17.9% 'not at all motivated'. Most participants in this low-motivation group (69%) had completed 0-1 module. Participants were divided in their reported ability to put ideas into practice outside of modules, with 28.6% finding this difficult and a further 28.6% finding it easy. Although reported benefits varied between participants, they all answered 'yes' (64.3%) or 'maybe' (35.7%) to recommending the program to others with similar concerns.

Table 5.3: Quantitative feedback on the Inroads online program generally

Survey measure	**Response options**	**n (%)**
What is your overall opinion on the quality of the program?		
	Very poor	0 (0.0%)
	Poor	0 (0.0%)
	Neutral	8 (28.6%)
	Good	13 (46.4%)
	Very good	7 (25.0%)
What is your opinion on the usefulness of the program for yourself?		
	Not useful	1 (3.6%)
	A little useful	10 (35.7%)
	Useful	10 (35.7%)
	Very useful	4 (14.3%)
	Extremely useful	3 (10.7%)
On average, how motivated did you feel when doing the program?		
	Not at all motivated	5 (17.9%)
	A little motivated	16 (57.1%)
	Motivated	3 (10.7%)
	Very motivated	4 (14.3%)
	Extremely motivated	0 (0.0%)
How difficult or easy was it to understand the content of the modules?		
	Very difficult	0 (0.0%)
	Difficult	2 (7.1%)
	Neutral	3 (10.7%)
	Easy	18 (64.3%)
	Very Easy	5 (17.9%)

Survey measure	Response options	n (%)
How difficult or easy was it to put the ideas into practice outside the modules?		
	Very difficult	0 (0.0%)
	Difficult	8 (28.6%)
	Neutral	11 (39.3%)
	Easy	8 (28.6%)
	Very Easy	1 (3.6)
How much improvement have your noticed in your feelings of worry and anxiety?		
	None/worse	6 (21.4%)
	Small	10 (35.7%)
	Moderate	8 (28.6%)
	Significant	3 (10.7%)
	Major	1 (3.6%)
How much improvement have your noticed in your willingness to enter anxiety provoking situations or to deal with negative emotion?		
	None/worse	4 (14.3%)
	Small	8 (28.6%)
	Moderate	10 (35.7%)
	Significant	5 (17.9%)
	Major	1 (3.6%)
How much improvement have your noticed in your ability to control your drinking?		
	None/worse	4 (14.3%)
	Small	10 (35.7%)
	Moderate	8 (28.6%)
	Significant	5 (17.9%)
	Major	1 (3.6%)
Would you recommend the program to others with anxiety and/or harmful alcohol use?		
	No	0 (0.0%)
	Maybe	10 (35.7%)
	Yes	18 (64.3%)

5.3.1.3 Program enablers

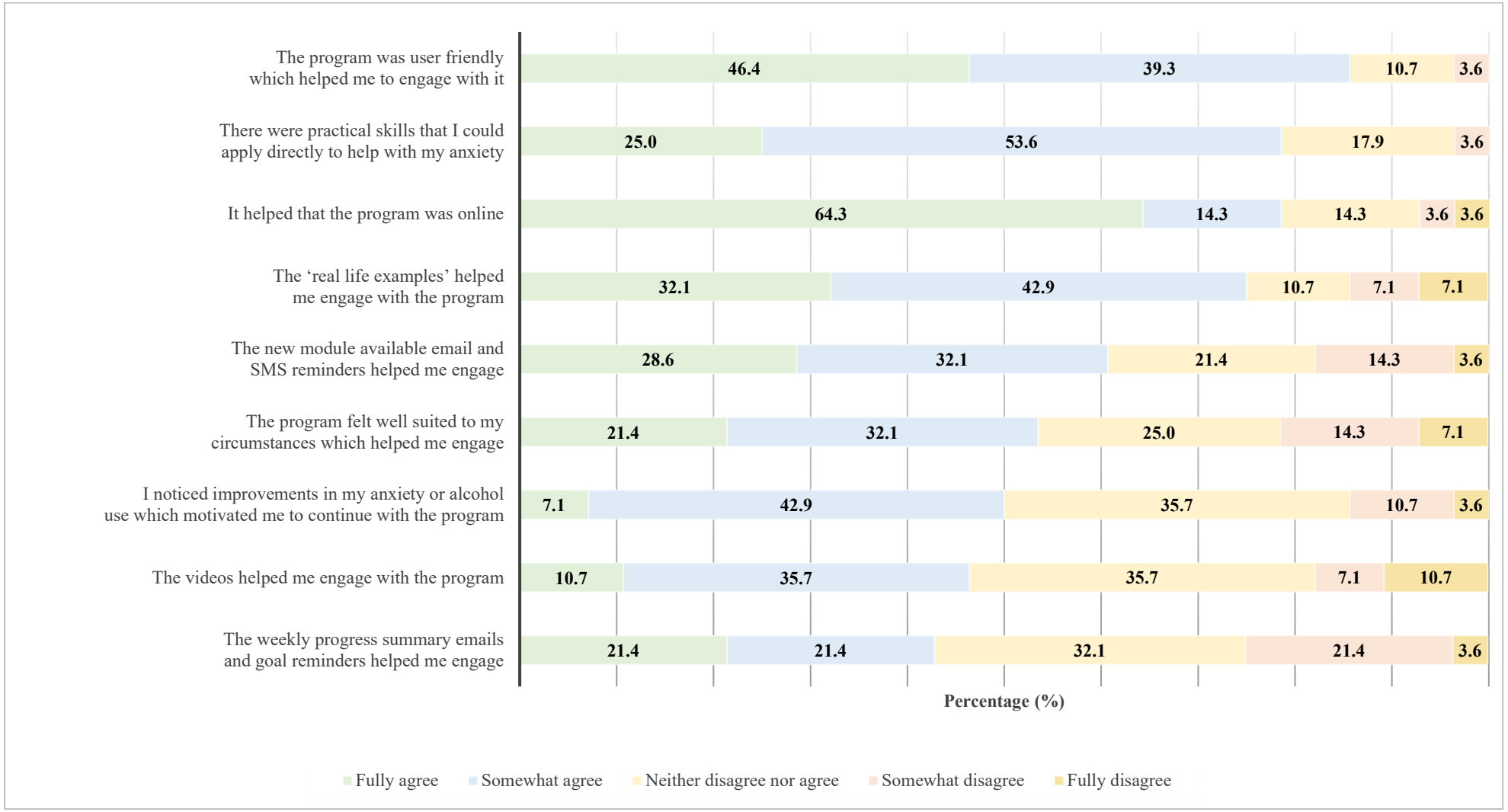
Participants' agreement with potential program enablers is presented in Figure 5.1. Overall, *'It helped that the program was online'* was the most strongly endorsed enabling factor, with 64.3% of participants indicating they 'fully agree' that this helped them engage. Other highly endorsed factors included the user-friendly design of the program (46.4% 'fully agree'; 39.3% 'somewhat agree'), the usefulness of practical skills for managing anxiety (25.0% 'fully agree'; 53.6% 'somewhat agree'), and the inclusion of real-life examples (32.1% 'fully agree'; 42.9% 'fully agree'. Together, these findings identified varied enablers across program-specific, individual-level, and technological/environmental domains. The least endorsed enablers were

video-based content and noticing improvements in their anxiety or alcohol use. One key program feature, namely the weekly feedback emails and goal reminders, received mixed feedback. While 21.4% of participants 'somewhat agreed' that these helped them engage, an equal proportion (21.4%) 'somewhat disagreed', indicating variability in how this component was experienced.

5.3.1.4 Program barriers

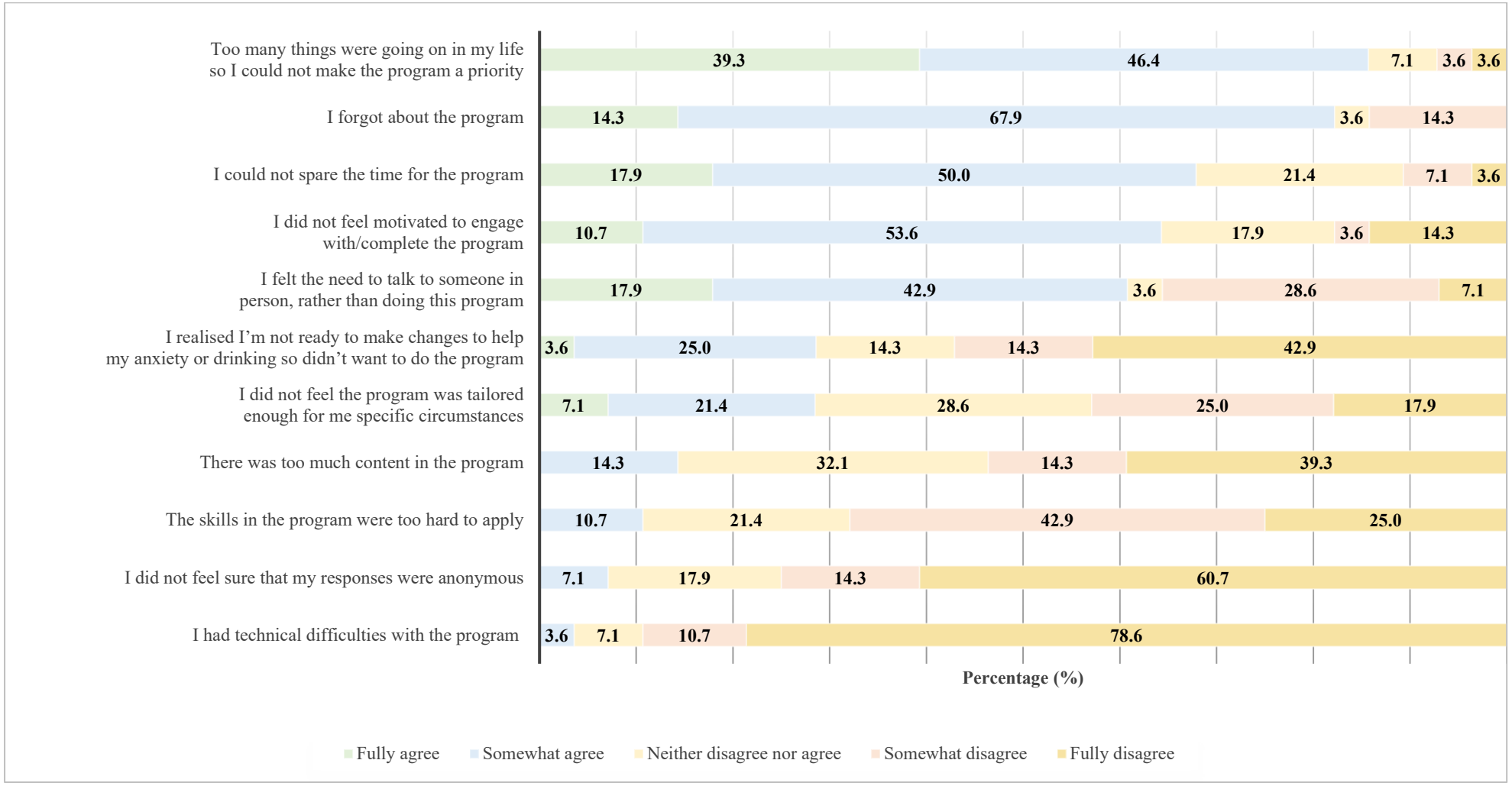
Participants' agreement with potential program barriers is presented in Figure 5.2. A majority (85.7%) reported that they 'fully agree' or 'somewhat agree' with the statement '*Too many things were going on in my life so I could not make the program a priority'*, and 67.9% similarly agreed that '*I could not spare the time for the program'*. Similarly, 82.2% said they forgot about the program. These findings highlight that individual-level factors related to time constraints and competing priorities were key barriers to engagement. Other potential barriers, such as whether the program was sufficiently tailored to individual circumstances, and whether participants felt ready to make changes to their anxiety or alcohol use, received a broader mix of endorsement levels, suggesting variability in how these factors influenced engagement. In contrast, concerns about anonymity of responses and technical difficulties (the two technology and environment barriers) were least likely to be endorsed, and were not significant concerns for participation in the *Inroads* program.

Figure 5.1: Agreement with specific factors which helped individuals engage with the Inroads program, sorted by greatest agreement.



Note: *n = 28*

Figure 5.2: Agreement with specific factors which got in the way of individuals engaging with the Inroads program, sorted by greatest agreement.

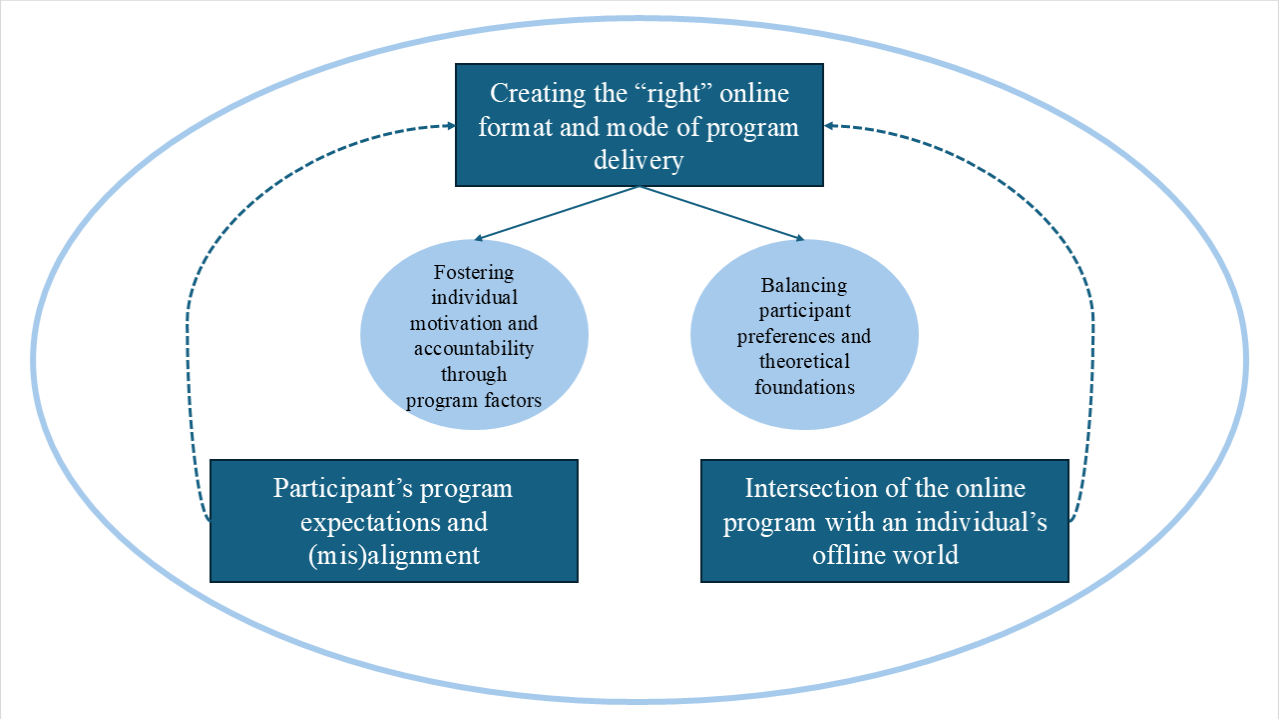


Note: *n = 28*

5.3.2 Qualitative findings

Participants offered diverse accounts of their experiences and engagement with the *Inroads* program including feedback on how the program could be updated. Three overarching themes captured these perspectives: *Creating the "right" online format and mode of program delivery; Participant's program expectations and (mis)alignment;* and *Intersection of an online program with an individual's offline world.* These themes are detailed below and illustrated in Figure 5.3.

Figure 5.3: Overview of the three qualitative themes and how they intersect and feed into one another



5.3.2.1 Creating the "right" online format and mode of program delivery

This theme describes the central role of program format and delivery in encouraging participant engagement with the program, with subthemes of *Fostering individual motivation and accountability through program factors* and *Balancing participant preferences and evidence-based components.*

Fostering individual motivation and accountability through program factors.

This subtheme captures the role of the program format and delivery itself in supporting participants to optimally engage (and stay engaged) with the *Inroads* program.

Whilst the program was self-guided, many participants expressed that some form of human support or guidance, alongside the online program, would enhance their motivation and/or accountability:

> *"[I] need more direct support to be kept accountable" (Survey)*

> *"I would have loved to work through the program with a psychologist or family member as it was hard to be motivated by myself." (Survey)*

Participants suggested a range of ways that they would prefer/like to receive support They suggested digital modalities: "back and forth email conversations" and "one session [phone call] with a research person would be good", as well as traditional avenues of support: "more formal like a psychologist". However, many felt that support needed to be mandatory to be effective:

> *"Some mandatory aspect of that [support] though would be necessary. I couldn't imagine myself booking a phone call without someone else pushing it." (Interview)*

At the same time, the balance between improving accountability (by adding a level of human support) but not deterring participants was also acknowledged:

> *"I feel like maybe the phone support would make me more anxious. I think like if I got lots of phone calls, I'd likely be nervous… It would maybe make me not want to do it... But then if it was self-paced, I wouldn't have the motivation to do it maybe." (Interview).*

This highlights the challenge of designing a program that fosters accountability while remaining sensitive to the needs of an anxious population. This point may also be relevant to the role of SMS text and email reminders sent to participants throughout the duration of the program. For many participants these were highlighted as a key program factor facilitating engagement. However, for some participants, these reminders led to feelings of guilt or shame that they weren't using the program, further increasing disengagement:

> *"I think they helped remind me, but I started to feel really guilty that I procrastinated it so hard that I then started to feel more guilty when they kept coming through being like "just a reminder, you haven't done this" and I'm like I know. I haven't done this. I'm sorry." (Interview)*

Evidently, ensuring program elements help but also don't hinder engagement is a nuanced balance which may look different for each individual.

Balancing participant preferences and theoretical foundations.

This subtheme explores the competing priorities between participants' preferences and the theoretical foundations of the program, as well as the diversity of views among participants themselves. A clear example of participant-to-participant divergence was in the perceived (un)relatability or usefulness of the 'real-life' character examples within the *Inroads* program. For some participants the examples and their accompanying audio were highly regarded:

> *"I think the different characters and voices helped way much more than I ever expected... I just feel a bit more trusting in both the verbal written and visual communications because my brain goes, "oh, that makes sense". And I can learn quicker. And it made me think, OK, well, I didn't feel like I'm not the only affluent bloke in Australia, that doesn't want to have a bloody drink at the pub." (Interview)*

Whereas others found the examples overly simplistic or unrelatable:

> *"The case studies I didn't find particularly useful. I remember reading it and thinking it was a bit kind of oversimplified like it felt like you were kind of reading like a kids book in a funny way." (Interview).*

Similar, conflicting sentiments were seen for other program elements, including the preferred platform for delivery, which is currently accessed by web browser via a computer, or mobile phone. Whilst some participants liked website-based delivery others felt a mobile phone app would have helped them engage with the program:

> *"I think for me [most helpful is] actually a website. I'm used to getting notifications from apps and stuff, and I just leave them… I get sick of reading things on my phone."* (*Interview*)

> *"Yeah, I'd be more likely to access it through an app."* (*Interview*)

Participants also demonstrated awareness of the practical limitations of their suggestions:

> *"I imagine if you've got, you know, thousands of people doing the program, it's difficult to check-in with everyone" (Interview)*

> *"It's hard to make an app, but I think an app would be really cool because it's like super easy to get on to…" (Interview)*

The push and pull between participant preferences and theoretical underpinnings were especially evident in relation to the program content and length. Some participants found the repetition and length of modules the greatest barrier to engaging with the program:

> *"The repetition of the same things." (Survey)*

> *"Wordy." (Survey)*

However, *Inroad*s was developed based on theoretical underpinnings of treating co-occurring anxiety and alcohol use concerns e.g. Stapinski et al. (2024); Stapinski et al. (2015). Providing efficacious, integrated treatment for these co-occurring concerns involves integration and repetition of therapeutic skills which, for some participants, clashed with preferences for brevity and simplicity. Interestingly, one participant identified the "short modules" as the least helpful aspect, further illustrating the individuality of preferences.

Some participants, however, recognised that challenging program elements were integral to the therapeutic process:

> *"I found the open ended tasks around setting goals and writing stuff down really challenging. And then when I got stuck on that I'd just be like, well, I can't keep doing it because I haven't done this thing so I'm just going to leave it…I can see the benefit and why it's an important part of it. It's you know, the fact that it's a challenging thing to do is probably why it's worth doing." (Interview)*

Despite these competing preferences, many participants spoke highly of the program, and the positive changes to their anxiety and alcohol use they were able to make. While these sentiments were common across many of the interviews, the below quotes are from two engaged participants who completed 4 modules and 3 modules, respectively:

> *"… One of the best things I've ever done for myself and I enjoyed the process of change. I got heaps out of this program and it honestly feels life changing." (Survey)*

> *"I really gained some practical skills and insights into my own drinking behaviour and ways I can hope to combat my worries and anxiety…. As someone who has battled with binge drinking and its negative and destructive nature I would really recommend it to other people in the same boat... I was surprised how realistic, thoughtful and practical it was." (Survey)*

5.3.2.2 Participant's program expectations and (mis)alignment

This theme explores the varying expectations participants held about the *Inroads* program and how these intersected with the program's intended aims and objectives.

For some, signing up was driven by curiosity "just keen to see what it was about" while others were drawn to the program with a more specific goal, often related to reducing alcohol use rather than addressing anxiety.

> *"Probably mainly just because I'd been drinking far too much alcohol and didn't really like know how to cut down…I didn't want to reach out in person, I suppose, to anyone about it." (Survey)*

Only a few participants explicitly mentioned the dual focus on anxiety and alcohol, in their motivation to sign-up.

> *"I really liked that it was a free program. And that it addressed anxiety and alcohol rather than depression and alcohol because so many things I've seen that [depression] is more what it talks about." (Interview)*

However, despite the program being framed around co-occurring anxiety and alcohol use, some participants did not find this dual focus beneficial, as reflected by a participant in the follow-up survey:

> *[What did you find most helpful about the program?]*
>
> *"Anxiety tools"*
>
> *[What did you find least helpful about the program?]*
>
> *"Alcohol focus"*
>
> *(Survey)*

This highlights the importance of clearly communicating the program's dual focus and overall objectives to ensure alignment with participant needs. This also extends to setting expectations around program length and time commitment. While *Inroads* is designed as a 5-week program, with a new module available weekly, users are able to go in at any time and complete the modules even after the 5 weeks have passed. However, this flexibility was not always clear, leading to perceived misalignment:

"I misread or misunderstood that I was supposed to check in daily and do the modules in a set time. I was taking my own time, and enjoying it, and it seemed to finish rather quickly." (Survey)

Another participant reflected that difficulty adhering to the weekly structure was a personal issue rather than a flaw in the program design:

"It seems like the way it's meant to be completed is that you do a module a week…I just didn't stick to that. And just wasn't sure, like if it was still beneficial without that, like because I didn't continue. But I don't think that's an issue with the way that it's set up. I think that's just more about me." (Interview)

The online format of the program was another example of (mis)alignment. While many participants appreciated the convenience of online delivery, others found it less helpful. In some cases, this misalignment only became apparent after engaging with the program.

Overall, participants' expectations were often met, and in many cases exceeded. This may reflect the minimal expectations some held when first joining:

"It was probably better than I thought, hey, like, as I said, like I didn't really know much about it coming in and but I'm a good learner like uh sitting down in my own time, you know, and sort of taking my time through things which really helped me out through this. And just all the little things like the daily check-ins or whatever every time I log in like that was really helpful. You know, like the site was easy to manage and I thought the modules were all really helpful, it definitely was better than I thought." (Interview).

5.3.2.3 Intersection of the online program with an individual's offline world

This theme explores how participants' offline lives shape their engagement and experiences with an online program.

Participants frequently referenced a lack of time, or competing life priorities, as barriers to engaging with or completing the program:

"My life got extremely busy during the program, I found it hard to set time aside for it." (Survey)

Some participants framed the challenge of dedicating time to the program as a reflection of "them" rather than a program related issue:

"I just honestly didn't really make time to do it, which is definitely my fault …, I would, you know, try and do it again, and make time for it. But yeah, it's. I just didn't make time for it." (Interview).

Whilst online programs can partially circumvent some barriers related to time, such as providing 24/7 access, incorporating additional elements to address time as a barrier may be challenging. This was reflected by one participant who reported "probably the lack of time" as the greatest barrier to engaging, but when what could be done to help time poor individuals engage with the modules they said "No, I'm not sure". Time constraints were, however, often mentioned alongside other related factors like motivation or accountability. As discussed in subtheme "Fostering individual motivation and accountability through program factors", these elements may be more amenable to program refinements, such as increased guidance or reminders.

Another offline factor influencing engagement was the role of other people in participants' lives. For some, encouragement from others prompted them to sign up:

"She [my girlfriend] was aware of all that and stuff too [seeing a psychologist for anxiety and drinking]. And then she just saw this pop up and thought it would be relevant for me." (Interview)

Support from friends and family during the program was also identified as an enabling factor for participants, reinforcing the value of social support in enhancing engagement:

"Talking with friends and sharing goals with them about the program [helped me engage]." (Survey)

Participants also reflected on how social expectations around drinking, from their personal circles and broader society, interacted with their program experience. The *Inroads* content addresses these dynamics, and some participants noted real-life changes in their relationships as a result of reducing alcohol use:

"I have lost a lot of friends that I realised, maybe they were just drinking acquaintances." (Interview)

Interestingly, whilst the *Inroads* naturalistic trial was run during COVID-19, few participants mentioned it directly. For some, however, lockdowns posed a barrier to applying skills learned in the program:

"I really gained some practical skills and insights into my own drinking behaviour and ways I can hope to combat my worries and anxiety. Unfortunately, lockdown in Sydney happened in the middle of it all so I have not had the chance to really test these skills/ideas." (Survey)

5.4 Discussion

The aim of this study was to understand participants' experience with a self-guided online anxiety and alcohol use early intervention program, including barriers and enablers to program engagement. A rigorous mixed-methods design was employed, with quantitative results capturing the strength and magnitude of sentiment towards program elements and qualitative findings providing contextual meaning and deeper understanding of program experiences. The results demonstrate that in general, participants found the *Inroads* program to be user friendly, applicable to their concerns, and have useful skills and tools for reducing anxiety and alcohol use. Several factors were highlighted as barriers to engagement, with time constraints and (lack of) accountability the most dominant. These barriers are not unique to the *Inroads* program, with reviews on engagement and retention in digital mental health interventions consistently highlighting time as a barrier (Borghouts et al., 2021; Boucher & Raiker, 2024; Torous et al., 2025). Time has often been framed as a "user-related" barrier, which as highlighted by participants in the qualitative interviews, is hard to address with program-related "fixes". In contrast, factors closely linked to time, such as accountability and motivation, may be more amenable to targeted program enhancements or additional design features. One commonly identified strategy for facilitating greater engagement is the inclusion of some form of human support.

To deliver the self-guided version of the *Inroads* program, several updates were made to provide feedback, accountability and encourage progress. Despite the inclusion of weekly personalised feedback emails, SMS text reminders, and email prompts, the findings in the current study demonstrate participants' desire for (human) guidance and support in addition to the online program. Support was desired for helping with accountability, adherence, or motivation, which aligns with prior research on the advantages of (human) guidance in aiding online program engagement and adherence (Andersson & Titov, 2014; Domhardt et al., 2019; Lattie et al., 2022; Mohr et al., 2011). Additionally, a meta-analysis comparing human guidance (e.g., weekly phone calls) versus technological based guidance (e.g., motivational messages

and automated reminders) also found human guidance to be superior for adherence and engagement outcomes (Koelen et al., 2022). Despite the advantages of human support for facilitating greater program engagement, advantages to clinical outcomes are more varied. For both anxiety disorders and alcohol use concerns, there is evidence that both guided and self-guided online CBT based interventions can improve therapeutic outcomes (Johansson et al., 2021; Oey et al., 2023; Riper et al., 2014; Sapkota et al., 2024), although guided interventions may be marginally more effective in the short term for anxiety (Oey et al., 2023) and in some instances overall for reducing alcohol use (Vangrunderbeek et al., 2022).

Notably, participants reported that guidance would not necessarily need to be delivered by a clinician (i.e., therapist or psychologist). A growing body of work for digital mental health interventions more broadly have shown non-clinician guided interventions can yield similar reductions in mental health symptoms to clinician guided interventions (Leung et al., 2022; Lidbetter et al., 2024). Whether similar efficacy holds for conditions with greater complexity (i.e., co-occurring mental health and substance use concerns) still requires investigation. Nonetheless, user's openness to human guidance from non-clinicians underscores the potential for more scalable models of support which, compared to clinician delivered support, could also be more cost-efficient.

Given the broad, and at times contradictory, range of perspectives and preferences expressed by participants in this study, the potential role of program personalisation and individual tailoring warrants consideration. This aligns with the evolving literature on digital mental health interventions, which have argued personalisation is essential for sustaining engagement and improving outcomes, particularly among youth (Borghouts et al., 2021; Cross et al., 2025; Hornstein et al., 2023). However, a recent review identified a gap between the anticipated benefits of personalisation and actual improvements in mental health outcomes, noting that heterogeneity across studies limited definitive conclusions (Schaeuffele et al., 2025). One potential area for personalisation within the *Inroads* program is the modality and amount of guided support. While most participants preferred phone calls, some viewed this as a barrier and favoured alternatives such as email. In the psychologist-supported *Inroads* RCT, text/email chat was offered as an alternative to the module phone calls, however, only two participants took up this modality. Relatedly, evidence from a RCT of internet-delivered depression treatment found comparable symptom reduction, therapeutic alliance, and engagement between telephone and email-based therapist guidance (Lindner et al., 2014), suggesting both formats are viable. Beyond delivery format, personalising therapeutic content offers further

opportunities. This approach aligns with transdiagnostic models of mental illness, which have gained increasing attention (Dalgleish et al., 2020). In practice, this could involve combining "core" modules targeting shared mechanisms (e.g., emotion dysregulation, motives for substance use) with "matched" modules addressing specific psychopathology (e.g., anxiety or depression). Personalisation of online interventions could achieve the benefits of aligning with the person's individual context, similar to the case formulation approach that is standard in face-to-face interventions (Cross et al., 2025). Personalisation may be particularly advantageous for co-occurring mental health and substance use concerns, as some participants reported a program mismatch despite meeting eligibility criteria. Overall, personalisation offers a promising strategy to address participant needs while maintaining, or potentially enhancing, adherence and efficacy.

5.4.1 Strengths and limitations

A key strength of this work is the mixed-methods design, which provides a depth of understanding about experiences with online interventions that neither quantitative nor qualitative approaches could offer alone. Investigating barriers and enablers has received some criticism in the past for its binary approach (Haynes & Loblay, 2024). However, our work moved beyond this dichotomy by using reflexive thematic analysis for the qualitative data. Unlike a deductive approach or other methods of thematic analysis that would simply look for "barriers" or "enablers" in interview responses, *reflexive* thematic analysis allowed us to explore patterns, meanings, and nuances in participants' experiences, generating richer, insights. The use of two sources for qualitative data (semi-structured interviews and open-text survey responses) was another strength of the study. Survey responses allowed greater anonymity for participants to share (negative) sentiments towards program factors which otherwise may not have been elicited during interviews due to power dynamic between the researcher and participants. In an attempt to overcome potential power relationships during the semi-structured interviews, the researcher explicitly stated at the beginning of interviews that the *Inroads* team welcomes both positive and negative feedback and attempted to create a casual and non-confrontational flow to interviews. Despite the steps put in place to foster comfortability of participants to honestly share their experiences, power imbalances should still be considered a potential limitation particularly in the context of the study's anxious sample. Another potential limitation is the low follow-up rate and generalisability of findings to all

participants in the *Inroads* program. The current findings should be considered a reflection of individuals who completed the follow-up surveys and agreed to an interview, therefore may not be representative of the true experiences of all individuals enrolled in the program. There was, however, representation from both participants who engaged with program modules and those who completed little to none of the program following enrolment. Finally, this study was conducted during the COVID-19 pandemic, which may have affected participant engagement and follow-up due to widespread digital fatigue (Gregersen et al., 2023). The low levels of engagement observed may therefore have been exacerbated by the pandemic context. Future research is needed to replicate these findings and to re-examine conclusions regarding the need for, or desirability of, additional human support outside of the pandemic setting.

5.4.2 Conclusion

This study is the first to quantitatively and qualitatively examine individuals' experiences with an online intervention targeting co-occurring anxiety and alcohol use concerns. Findings highlight key program elements that participants found helpful for engagement, including practical skills, the online format, real-life character examples, and a user-friendly design. While user-related factors such as accountability and lack of time were commonly identified as barriers, qualitative findings suggest these could be mitigated through the addition of human-guided support alongside self-guided program content. Notably, participants did not feel this support needed to be provided by a clinician. Overall, these findings contribute to the limited user experience and engagement evidence-base for online interventions addressing co-occurring mental health and substance use concerns, and provide actionable guidance for development and refinement of future interventions in this space.

Chapter 6

General discussion

Anxiety and alcohol use typically emerge during adolescence and young adulthood and often co-occur. When they do co-occur, these difficulties can interact in ways that heighten risk for future harm and contribute to substantial individual, social, and economic burden (Anker & Kushner, 2019; Bartoli et al., 2021; Burns et al., 2005; Smith & Randall, 2012). Critically, these trajectories are preventable. Early symptoms, maladaptive coping patterns, and contextual influences provide multiple opportunities to intervene before problems become entrenched and debilitating.

Significant advances have been made in treating co-occurring anxiety and alcohol problems through integrated approaches; however, waiting until these difficulties reach diagnostic thresholds for intervention represents a missed opportunity. To meaningfully reduce the burden of anxiety-alcohol use comorbidity, prevention and early intervention efforts must be prioritised. While current intervention efforts show promise, research on mechanisms, optimal targets, and implementation strategies for preventing or mitigating co-occurring anxiety and alcohol problems remains limited.

To provide much needed evidence on the developmental relationship between anxiety and alcohol use, and to strengthen early intervention efforts, this thesis had two overarching aims: i) to disentangle the anxiety alcohol-relationship and ii) to enhance early interventions for co-occurring anxiety and alcohol concerns. These aims were addressed through four novel empirical studies designed to advance both theoretical understanding and clinical practice by addressing the following research objectives:

1. Systematically review the evidence identifying factors that longitudinally a) *mediate* and b) *moderate* the bidirectional relationship between anxiety → alcohol use and alcohol use → anxiety.
2. Examine developmental associations between, and moderators of, anxiety and hazardous alcohol use across multiple timepoints from early adolescence through to young adulthood.

3. Investigate the causal mechanisms responsible for reducing social anxiety and hazardous drinking within an efficacious online early intervention program for young adults.
4. Identify barriers and enablers to the delivery of, and user engagement with, an online intervention for young adults experiencing co-occurring anxiety and hazardous alcohol use.

Overall, this thesis offers a methodologically rigorous approach to advancing understanding of co-occurring anxiety and alcohol use, which has utility to inform the development and refinement of prevention and early intervention approaches. This final chapter synthesises the overall findings of this thesis (section 6.1), before addressing the strengths and limitations of this body of work (section 6.2). The theoretical and clinical implications of the thesis findings are then discussed (section 6.3), followed by recommendation for future research (section 6.4).

6.1 Summary and synthesis of key findings

A summary of the key findings across the four empirical chapters of this thesis, based on the knowledge gaps identified in **Chapter 1** Table 1.2**,** are outlined below.

6.1.1 Addressing knowledge gap 1a: Insufficient understanding of underlying mediating factors driving the bidirectional anxiety-alcohol association.

In recent decades, researchers have increasingly sought to identify mechanisms underlying the co-occurrence of anxiety and alcohol use. Until now, there has been no comprehensive synthesis of research examining these mediating factors. This synthesis is necessary, given the central role of mediators in advancing theoretical understanding of anxiety-alcohol comorbidity and in informing targets for prevention, early intervention, and treatment. By establishing temporal ordering between an exposure, mediator, and outcome, longitudinal studies are methodologically well-suited to identifying developmental and mechanistic pathways. However, the existing longitudinal literature in this area remains limited and fragmented. **Chapter 2** synthesised existing knowledge with the first systematic review of longitudinal studies examining mediators of both the anxiety → alcohol and alcohol → anxiety

pathways. The aims of this systematic review were twofold: i) to identify intermediate variables that mediate the relationship between anxiety and alcohol use concerns, or vice versa; and ii) to provide the first consolidated overview of the current landscape of mediation research in the context of this comorbidity.

Ten longitudinal studies met inclusion criteria, from which 34 individual effects were extracted and synthesised. These comprised 30 single-mediator models, three multiple-mediator models, and one moderated-mediation model. Consistent with the broader field, the vast majority of effects (n = 29) focused on the anxiety → alcohol pathway. The review found that research to date has concentrated almost exclusively on psychological mediators, with only one socio-environmental mediator (negative life events) examined.

From the limited longitudinal work identified in the review, few psychological variables demonstrated significant mediating effects. Regarding mediators of the anxiety → alcohol pathway, there was some evidence that emotion dysregulation, repetitive negative thinking, and subsequent anxiety symptoms functioned as intermediate variables. However, these mediating effects were small and each were identified as significant in only a singular study. Notably, models in which later anxiety showed statistical evidence of mediation offer limited insight into the specific mechanistic processes underlying the anxiety-alcohol association. Rather, such findings may reflect the persistence or progression of anxiety over time, rather than elucidating explanatory pathways linking anxiety to alcohol use. Across all psychological constructs, drinking motives were the most frequently studied mediator. Despite earlier evidence from a critical review suggesting a potential mediating role of drinking motives in the anxiety-alcohol use relationship (DeMartini & Carey, 2011), findings from the current review indicated that longitudinal studies predominantly did not observe statistically significant mediation effects. Across the studies evaluating drinking motives, sub-clinical anxiety measures (i.e. anxiety sensitivity) were commonly used as the predictor variable in models. This may in part explain the null findings, and further research is needed to determine whether drinking motives, undetected in the sub-clinical models, may mediate the relationship between anxiety *disorders* and alcohol-related problems.

Regarding the inverse pathway, alcohol → anxiety, only five longitudinal effects were identified in the review. These were predominantly derived from laboratory-based studies involving experimental manipulation of alcohol exposure, offering limited insight into longer-term developmental mechanisms linking alcohol use to anxiety. The sole non-experimental

study examined anxiety sensitivity as an intermediate variable between alcohol problems and subsequent anxiety symptoms. In this study, anxiety sensitivity was not a significant mediator of the alcohol → anxiety pathway (Paulus et al., 2021), demonstrating the necessity of future work to explore other, broader, mechanistic drivers of this pathway.

Evidently, **Chapter 2** demonstrated a critical lack of longitudinal, ecologically valid, high-quality studies testing potential causal mechanisms of the anxiety-alcohol relationship. Concerningly, all identified mediation studies were rated as having a high risk of bias. The absence of reported sample size calculations may partly explain the limited evidence of significant mediating effects, as it remains unclear whether studies were adequately powered to detect mediation. Although cross-sectional studies examining mediation exist in this research area, longitudinal designs are required to strengthen causal inference by establishing temporal ordering. Without evidence from robust longitudinal studies, the ability to *truly* understand factors which contribute to the development of alcohol concerns among individuals with anxiety or vice versa remains unknown. As discussed further in subsection 6.4.2, while **Chapter 2** synthesised the available preliminary evidence, additional work is needed to identify the causal processes underlying the development of comorbid anxiety and alcohol use concerns.

6.1.2 Addressing knowledge gap 1b: Lack of synthesis for factors which moderate the bidirectional anxiety-alcohol association.

Where mediator studies identify variables that explain *why* a relationship occurs, moderator studies seek to clarify for *whom* or *under what conditions* a relationship is stronger or weaker. **Chapter 2** synthesised evidence on moderating factors, producing an evidence map of risk and protective influences on co-occurring anxiety and alcohol use. These findings are directly relevant for informing prevention and intervention targets.

As the first systematic review and meta-analysis of moderators of the anxiety-alcohol association, **Chapter 2** provided a comprehensive overview of the current evidence base. It captured biological, psychological, and socio-environmental moderators across a wide range of anxiety and alcohol constructs. In total, 47 longitudinal studies were included, from which 258 single-moderation models and 23 three-way multiple-moderation models were extracted.

By synthesising this literature, the review highlighted both key patterns and inconsistencies in the findings.

As with the mediation literature, the majority of moderation analyses (n = 247) focused on the anxiety → alcohol pathway. Gender/sex was the most frequently examined moderator, followed by a diverse set of psychological factors (e.g., drinking motives, externalising symptoms). Across the 94 gender/sex effects reviewed, the findings consistently indicated no meaningful difference in the strength of the anxiety → alcohol association for men versus women. Similarly, although some studies identified significant moderating effects of drinking motives, the overall evidence suggested these motives do not reliably moderate the longitudinal anxiety-alcohol relationship. Far fewer studies examined moderators of the opposite association: alcohol → anxiety. From the 34 moderation effects identified two were significant: one for ethnicity (first-generation Mexican status) and one for anxiety sensitivity.

Meta-analysis was possible for 13 anxiety → alcohol moderator subthemes (67 effects) and four alcohol → anxiety moderator subthemes (9 effects). Several factors emerged as significant moderators of the association between anxiety and later alcohol use. Age and experimentally-induced anxiety tended to strengthen this association, suggesting they may act as risk-enhancing factors. In contrast, externalising symptoms, perceptions of peer alcohol use, and positive family experiences appeared to weaken or attenuate the association, operating as potential protective factors. These findings should be interpreted with caution due to the notable heterogeneity across studies. In particular, the seemingly *protective* effect of externalising symptoms warrants further clarification. Although the meta-analytic estimates suggested that anxiety was negatively associated with alcohol use at elevated levels of externalising symptoms, evidence from individual studies provides important nuance. For example, Colder et al. (2017) found that the highest probability of drinking occurred among adolescents high in externalising symptoms *and* low in anxiety symptoms, with anxiety becoming less predictive of drinking behaviour as externalising symptoms increased. Overall, this interplay between internalising problems, such as anxiety, and externalising traits underscores that prevention and early interventions should consider multiple developmental pathways to alcohol use, rather than focusing solely on anxiety in isolation.

Overall, the findings from **Chapter 2** provided the most comprehensive summary to date of potential moderators of the anxiety-alcohol association. The review highlighted evidence for very few biological, psychological, or socio-environmental factors that reliably strengthen or

alter the direction of this relationship. Importantly, most studies were conducted in non-clinical, often subthreshold populations and were predominantly based in North America, limiting generalisability. Study quality was also concerning, with 79% (37/47) of included moderation articles having a high risk of bias. These findings underscore the need for further investigation of the few promising moderators identified (e.g., externalising symptoms, perceptions of peer alcohol use) as well as the exploration of additional constructs that may meaningfully moderate anxiety-alcohol associations. Potential moderating factors which were not explored or underexplored, as identified in the review, include other internalising symptoms (i.e., depression), self-compassion, and socioeconomic status. **Chapter 3** extends the synthesis of moderators in **Chapter 2**, by examining the potential moderating effects of psychological factors in adolescence and young adulthood.

6.1.3 Addressing knowledge gap 2: Lack of clarity around the anxiety-alcohol relationship across distinct developmental periods in adolescence through to young adulthood.

As outlined in **Chapter 1**, research on the relationship between anxiety and alcohol use during youth has been mixed, with some evidence suggesting a potentially protective effect of anxiety in early adolescence on later alcohol use (Pardee et al., 2014; Peeters et al., 2024). However, findings from **Chapter 3** demonstrated a consistent, positive association between anxiety symptoms and hazardous drinking across early- to middle-adolescence. Within developmental periods there were nuances to this association, as evidenced by findings of the moderation analyses.

The longitudinal study presented in **Chapter 3** spanned seven data waves from ages 13.4 to 20.5 years. Across the first five waves (ages 13.4 to 16.4), there was strong evidence that within the same developmental period, higher anxiety symptoms were associated with greater hazardous drinking. However, this cross-sectional association was not observed at ages 19 or 20.5 years. Previous work has identified a positive association between GAD and hazardous or harmful drinking at age 18 (Dyer, Heron, et al., 2019), but it is possible that beyond age 18 the relationship diverges, weakens, or becomes less detectable using subthreshold measures of anxiety and alcohol use.

Despite consistent associations at ages 13.4, 14, 14.5, 15.4 and 16.4, these patterns generally did not translate into prospective relationships *across* waves. Specifically, anxiety symptoms at one wave generally did not predict hazardous alcohol use at the next wave (approximately 0.5 to 2.5 years later). A notable exception occurred between ages 14.5 and 15.4, during which anxiety positively predicted later hazardous drinking, highlighting middle adolescence as a particularly sensitive developmental window and target intervention age. The longitudinal findings in **Chapter 3** align with prior studies showing no consistent prospective association between anxiety and later alcohol use across adolescence and young adulthood (Dyer, Easey, et al., 2019; Dyer, Heron, et al., 2019; Malmberg et al., 2010). The absence of prospective effects suggests that anxiety may not causally drive alcohol use in youth; rather, shared developmental factors may contribute to the cross-sectional relationships observed. Nonetheless, anxiety remains a concurrent risk factor for hazardous drinking. Overall, the stronger within-developmental period associations compared with across-period effects suggest that age-specific- developmentally timed interventions may be most effective. Supporting anxious adolescents during the mid-teen years (around ages 14-16) may reduce concurrent hazardous drinking, even if such efforts do not necessarily influence drinking trajectories in later adolescence or early adulthood.

Beyond main effects, **Chapter 3** also identified several developmentally-specific moderation effects of the relationship between anxiety symptoms and hazardous alcohol use. Consistent with the age-specific patterns of main effects, the most pronounced moderation effects emerged during early- to middle-adolescence. Firstly, at ages 14 and 14.5 biological sex moderated the relationship. The association between anxiety and hazardous alcohol use was weaker among young females compared to males, further supporting female sex as a protective factor during adolescence (Rieselbach et al., 2023). Secondly, higher levels of depressive symptoms and externalising symptoms (sensation seeking and impulsivity) strengthened the anxiety-hazardous drinking association from ages 14 to 15.4. and 13.5 to 14.5, respectively. These findings highlight the compounding influence of internalising (i.e., anxiety and depression) and externalising traits on alcohol use during early adolescence. Lastly, drinking motives also moderated the association during early- to middle-adolescence. Greater conformity, coping-anxiety, and enhancement drinking motives positively moderated the anxiety-alcohol association at ages 14, 14.5 and 15.4. Greater social drinking motives also positively moderated the anxiety-alcohol association at ages 14, 14.5 and 16.4; however, at age 15.4 a negative association was seen. Why greater endorsement of social motives at this age alone acted as a

'protective' effect could be probed further in future longitudinal studies. Nonetheless, these patterns suggest that the salience of different moderating factors varies across developmental stages, which may partly explain the inconsistencies identified in the moderation literature synthesised in **Chapter 2**.

6.1.4 Addressing knowledge gap 3: Insufficient evidence regarding the mechanisms that mediate effective early intervention for social anxiety and hazardous drinking.

Chapter 4 presents the first causal mediation analysis examining how an efficacious, online early intervention for co-occurring anxiety and alcohol use concerns produces change among young people aged 17-24 years. This work directly responds to longstanding calls in psychotherapy research to identify mechanisms of therapeutic change (Kazdin, 2007; Windgassen et al., 2016) to improve understanding of *how* interventions work and inform future optimisation. Using data from an RCT of the *Inroads* early intervention for co-occurring anxiety and hazardous alcohol use, two multiple-mediator models were tested: one for reductions in social anxiety and another for reductions in hazardous alcohol use. Both mediation models assumed that no single causal pathway would account for change, given the complexity of co-occurring concerns.

The hypothesised multiple-mediation models were based on the theoretical underpinnings of anxiety-alcohol comorbidity, including factors which are thought to mutually maintain or exacerbate this self-perpetuating cycle (Stapinski et al., 2015; Stewart & Conrod, 2008). Reductions in hazardous drinking were hypothesised to occur through improvements in emotion regulation (i.e., cognitive reappraisal and expressive suppression) and decreases in positive drinking motives (i.e., coping-anxiety and enhancement motives) and alcohol outcome expectancies (i.e., tension-reduction and social-lubricant expectancies). Only weak support emerged for this model, suggesting that additional mechanisms, beyond those tested, likely drive the reductions observed in the intervention group. This study attempted to move beyond the idea that drinking reductions are simply downstream effects of reduced anxiety, instead focusing on processes targeted by integrated anxiety-alcohol interventions, such as alcohol-related expectancies. While the feed-forward cycle of comorbidity suggests that anxiety and alcohol use reinforce one another, this reciprocity does not preclude the presence of deeper, unmeasured mechanisms that drive their association as tested in the multiple mediation model.

Reductions in social anxiety symptoms were similarly hypothesised to operate through changes in maladaptive emotion regulation, as well as through decreases in daily alcohol use. Despite a significant total effect of the intervention on social anxiety, there was no evidence supporting the total natural indirect effect, indicating that the proposed mediators did not account for *how* the integrated anxiety-alcohol intervention reduced social anxiety symptoms. This aligns with the broader challenge of delineating mediators of the co-occurring anxiety and alcohol use relationship as further evidenced in **Chapter 2**. The evidence synthesis in **Chapter 2**, highlighted limited research and inconsistent support for psychological mediators of the anxiety → alcohol and alcohol → anxiety pathways. Overall, **Chapter 4** demonstrated that theoretically-informed mediators do not necessarily translate into observed mechanisms of action within integrated anxiety-alcohol interventions. This suggests that future intervention development and evaluation must move beyond traditional hypothesised mechanisms and adopt more exploratory, data-driven, and iterative approaches to mechanism discovery. Identifying the processes that genuinely drive change for co-occurring concerns remains a critical and complex area for future research, as discussed further in section 6.4.

6.1.5 Addressing knowledge gap 4: Lack of evidence regarding factors that influence engagement and retention to online interventions among youth with co-occurring anxiety and hazardous alcohol use concerns.

Online interventions have the potential to offer a scalable and feasible avenue for early intervention while also addressing barriers associated with face-to-face approaches such as cost or waitlists. Despite this promise, engagement and retention remain key challenges to their successful implementation. **Chapter 5** therefore addressed a critical gap by using a comprehensive mixed-methods design to examine the barriers and enablers to engagement and to explore participants' experiences with an efficacious self-guided online early intervention for youth with co-occurring anxiety and hazardous alcohol use, delivered within a naturalistic single-arm trial. This approach offers valuable insight into how early interventions can be implemented in real-world contexts. Program enablers were primarily program-level features (e.g., online delivery, practical skills), whereas barriers tended to reflect individual-level factors (e.g., competing priorities, forgetting to complete the program). Feedback on specific program elements suggested that real-life character examples were perceived as most useful, while videos and the compulsory anxiety-alcohol check-in were viewed as less helpful. Together,

these findings provide practical direction for refining program components and enhancing engagement in online interventions designed for young adults more broadly.

Qualitative insights from semi-structured interviews and open-ended survey responses provided deeper context and generated actionable suggestions for refining online interventions for youth with co-occurring anxiety-alcohol concerns. Reflexive thematic analysis highlighted the role of program features in fostering motivation and accountability. Many participants expressed a desire for some level of human support within an online intervention, whether via phone or email. This aligns with earlier findings, showing that human guidance is a significant determinant of user experience and treatment engagement (Morgan et al., 2016; Opie et al., 2024). Notably, the current results challenge assumptions that anxious young adults prefer minimal interpersonal contact. Importantly, participants also indicated that this support did not necessarily need to come from a clinician, highlighting the potential scalability of incorporating "lay-support" alongside self-guided modules into future online interventions. Taken together, these findings complement **Chapter 4**, extending beyond mechanism of program effectiveness to illuminate *how* integrated anxiety-alcohol interventions are experienced and what factors shape engagement. While the integrated early intervention was generally well-received, the results point to specific opportunities to enhance motivation and accountability, elements that may be especially important for young people managing co-occurring anxiety and hazardous drinking.

6.2 Strengths and limitations of the research

6.2.1 General strengths of the research

Overall, this thesis advanced knowledge on the prevention and early intervention of co-occurring anxiety and alcohol use concerns by disentangling the onset of the relationship, unpacking the mechanisms underlying and moderating it, and identifying ways to enhance early interventions among for young people. A key strength of this work is its breadth: it examines micro-level factors (i.e., mediators and moderators) that drive anxiety-alcohol comorbidity, while also taking a macro-level perspective on the real-world implementation of a scalable early intervention. Across this breadth of work, this thesis applied a range of rigorous and sophisticated methodological techniques. These included a rigorous and sizeable systematic review of the literature (**Chapter 2**), longitudinal moderation analysis (**Chapter 3**),

causal mediation analysis (**Chapter 4**), and a mixed-methods study employing robust reflexive thematic analysis of qualitative data (**Chapter 5**).

The systematic review in **Chapter 2** was conducted through a causal inference lens in order to examine and address limitations in the existing literature. Although no restrictions were placed on publication year or language, a restriction to longitudinal studies was applied to more confidently identify causal factors in the anxiety-alcohol association. **Chapter 2** not only provides the largest systematic synthesis of mediators and moderators in this relationship to date, but also makes a substantial contribution to the quality appraisal of mediation and moderation studies through the development of two purpose-built, theoretically informed risk-of-bias tools. These tools (see Appendix B and Appendix C) build on and extend prior appraisals (Pincus et al., 2011; Vo et al., 2022) and represent the most comprehensive frameworks available for reviewing mediation and moderation studies in this field. Together, these contributions contribute to both the anxiety-alcohol literature and the broader practice of systematic review quality assessment.

Relatedly, the causal mediation analysis in **Chapter 4** which uses the counterfactual framework, reflects a modern and theory-driven approach to examining therapeutic mechanisms in anxiety-alcohol interventions. This method overcomes key limitations of traditional mediation approaches, including assumptions around confounding and the inability to estimate causal, rather than purely associational, effects (MacKinnon et al., 2020). Notably, this thesis is the first to apply such causal inference techniques to understanding mechanisms of anxiety-alcohol interventions. Lastly, the mixed-method design in **Chapter 5** triangulated data from study follow-up surveys and in depth semi-structured interviews. Combining findings from quantitative and qualitative data provided a comprehensive and rich account of young adults' preferences and perspectives for delivering, designing, and refining an online early intervention targeting co-occurring anxiety and alcohol use.

Another strength of the thesis is the diversity of datasets and samples used, and the broad spectrum of anxiety and alcohol constructs examined, allowing conclusions that extend beyond clinical or disorder-based classifications. **Chapter 3** employed seven waves of data spanning adolescence through young adulthood, offering insight into the anxiety-alcohol relationship across periods of rapid developmental change. Few studies have explored longitudinal associations between anxiety symptoms and later alcohol use in Australia, and none have examined these associations while simultaneously considering moderating factors (Birrell et

al., 2015; D'Aquino et al., 2025; McKenzie et al., 2011; Swift et al., 2016). Moreover, the studies by McKenzie et al. (2011) and Swift et al. (2016) focus on AUD onset, limiting inferences about other harmful drinking patterns that may be more common during adolescence. Given that almost all (86.6%) longitudinal work investigating mediators or moderators in this area has been conducted in North America (as shown in **Chapter 2**), the current thesis offers critical contributions for the Australian context. **Chapter 4** benefited from access to a rare clinical trial sample for one of the only RCTs evaluating an integrated anxiety-alcohol early intervention. The trial was adequately powered to detect mediation effects, and its methodological rigour further strengthens the value of the dataset for addressing the study objective—examining mechanisms of change in an early intervention for anxiety and alcohol.

Collectively, the chapters within this thesis help address a longstanding gap in evidence for integrated *early interventions* for co-occurring anxiety and alcohol use, an area in which the literature has historically focused on integrated *treatment* models (i.e., (Hesse, 2009; Morley et al., 2016; Stapinski et al., 2015; Stapinski, Sannibale, et al., 2021; Wolitzky-Taylor, 2023; Wolitzky-Taylor et al., 2022)). By shifting the focus earlier in the continuum and including young people with sub-clinical as well as clinical symptoms, this thesis broadens the scope of existing research and highlights opportunities for earlier, more preventive responses to comorbidity.

Finally, the studies and aims of this thesis align closely with the priorities that young people themselves have identified for mental health and substance use research (Ross et al., 2025). Specifically, four of the nine priorities outlined by the coproduced Australian Youth Priorities Project were addressed across this thesis. These are to: i) understand and target the risk and protective factors for youth mental health (**Chapters 2** and **3**); ii) understand what makes effective prevention programs, focus on early-childhood interventions (**Chapters 3**, **4** and **5**); iii) understand and educate about behavioural factors that impact mental health (**Chapters 2** and **3**); and iv) address barriers to participation in research and accessing program for rural and remote communities (**Chapter 5**). This alignment with youth-defined research priorities underscores the relevance and applicability of the thesis findings to the population they are intended to benefit.

6.2.2 General limitations of the research

Despite the significant and original contributions of this thesis to advancing knowledge of the anxiety-alcohol association and informing prevention and early-intervention efforts, several limitations warrant consideration. Firstly, **Chapters 3** and **4** involved secondary analyses of studies not originally designed with the specific objectives of this thesis in mind. Although both studies provided access to suitable data for addressing the research aims, it remains possible that unmeasured moderating (**Chapter 3**) or mediating (**Chapter 4**) variables could have yielded additional insight into developmental pathways linking anxiety and alcohol use or the mechanisms underpinning change in the *Inroads* intervention. Furthermore, the use of the BSI anxiety measure in **Chapter 3** limited broader, non-somatic, conclusions to be drawn about social or generalised anxiety, which were of theoretical interest in this thesis.

Relatedly, across **Chapters 3**, **4**, and **5**, self-report measures were used to assess mental health and alcohol use constructs. This may have introduced recall or social desirability bias, and in turn under- or over-reporting of alcohol use. Nonetheless, self-report remains a convenient, non-stigmatising, and well-validated method for capturing alcohol (Del Boca & Darkes, 2003; McKenna et al., 2018) and anxiety (Iza-Fernández et al., 2025; Leserman & Koch, 1993) among young people. Data retention across these three chapters is also a potential limitation, as discussed within each respective study's limitation section. To minimise potential bias of the subset of participants who provided data for **Chapter 5**, efforts were made to ensure the sample comprised a broad spectrum of participants including those who completed program modules and those who did not engage with any program content.

Consideration must also be given to the generalisability of the findings. Samples in **Chapters 3**, **4**, and **5** included a larger proportion of females and were predominantly non-ethnically or racially diverse. Participants in **Chapters 4** and **5** self-selected into an early intervention for anxiety-alcohol and the overrepresentation of females reflects trends in psychiatric research and online intervention trials more broadly (Merone et al., 2022; Ong et al., 2024; Titov et al., 2020). As such, conclusions should be interpreted with this relatively homogenous sample in mind.

While a strength of **Chapter 2** is its comprehensive overview of mediating and moderating factors, the broad scope of included measures for anxiety and alcohol use may have obscured more nuanced relationships that only emerge at specific severity levels or within clinical/sub-clinical populations. Similarly, the restriction to longitudinal studies, although aligned with the

broader thesis objective of identifying causal targets and timepoints for prevention and early intervention, may have omitted potentially relevant studies, particularly regarding moderation studies. A substantial body of cross-sectional work has examined moderators of the anxiety-alcohol relationship, and these studies may have offered additional insights beyond those identified in the 47 longitudinal studies included. Additionally, notable methodological limitations were identified across the studies reviewed in **Chapter 2**. These constraints limited the strength of inferences that could be drawn and, by extension, the degree to which findings could guide subsequent chapters. Nevertheless, this review provides a clear and necessary foundation for future research directions, which are discussed further in subsection 6.4.1.

6.3 Overall implications of this thesis

The findings of this thesis significantly advance the theoretical understandings of anxiety and alcohol comorbidity and have implications for prevention (subsection 6.3.1), early intervention (subsection 6.3.2), and the delivery of online interventions (subsection 6.3.3).

6.3.1 Implications for (primary) prevention

As demonstrated by the findings of this thesis, the association between anxiety symptoms and hazardous alcohol use is already evident by age 13, underscoring the need for early prevention efforts. Primary prevention can be universal, or targeted, as outlined in **Chapter 1**, and this body of work points to potential targets across both levels. Findings from the meta-analysis of moderators indicated that positive family experiences may offer a protective effect against anxiety-alcohol comorbidity. This suggests that universal prevention approaches may be effectively directed toward parents rather than youth alone. Parents play an important and sustained role in shaping adolescent mental health more broadly, with benefits shown to continue well into midlife (Chen & Harris, 2019). The present work reinforces the value of parental factors in the specific context of co-occurring anxiety and alcohol use. An example of one such parenting program with a strong-evidence base which could be adopted as a universal prevention approach in the current context is the *Triple P: Positive Parenting Program* (Sanders, 2023). Specifically, the *Fear-Less Triple P* intervention has been developed for parents of anxious children which may have additional benefits above and beyond the universal *Triple P* intervention (Cobham et al., 2017).

The developmental persistence of the anxiety-hazardous drinking, cross-sectional, associations from early- to middle-adolescence (**Chapter 3**) highlights this period of rapid psychosocial and biological change as a critical window for prevention. This thesis identified clear groups who may benefit from targeted approaches during this stage. Prevention strategies aimed at adolescents with elevated negative affect are likely to be particularly valuable. Compounding effects of anxiety and depressive symptoms were cross-sectionally associated with increased hazardous alcohol use at ages 14-15. Moderation analyses found that drinking-to-cope motives also strengthened the cross-sectional anxiety-alcohol use relationship, further reinforcing the need for approaches that buffer against adolescent negative affect. Interventions targeting externalising vulnerabilities such as sensation seeking and impulsivity should also be considered. Whether these externalising factors remain relevant intervention targets beyond adolescence is less certain, however. Findings from **Chapter 2** and past research on the interplay between internalising and externalising symptoms in older adolescence and emerging adulthood (Colder et al., 2017) suggest the relationship is multidimensional. Despite identifying key at *risk groups*, evidence for specific *mechanisms* linking anxiety and alcohol use remains limited. The absence of robust, replicable mediators across youth samples means primary prevention efforts still lack clear, evidence-based targets for interrupting the anxiety-alcohol pathway, an area for further research, as discussed in section 6.4.2. Additionally, the limited longitudinal evidence for prospective risk pathways in **Chapter 3** demonstrate further work is still needed to understand the developmental drivers of co-occurring anxiety and alcohol use.

Evidence of internalising and externalising factors compounding hazardous drinking behaviours in **Chapter 3**, and in part **Chapter 2**, provide support for interventions that target multiple psychopathology factors, such as the *Preventure* program. *Preventure* is a brief, two-session intervention that focuses on increasing coping skills in adolescents, specific to four personality risk factors: anxiety sensitivity, impulsivity, sensation seeking, and hopelessness. Previous research has demonstrated the program to reduce multiple alcohol-related outcomes as well as anxiety symptoms (Edalati & Conrod, 2018). The moderating effects observed between anxiety and other personality profiles on hazardous drinking in this thesis further strengthen the case for such an approach. Future research is needed to determine whether *Preventure* can disrupt specific theoretical mechanisms underpinning anxiety-alcohol comorbidity, such as drinking-to-cope motives.

A long-standing focus of prior research has been the potential moderating effect of gender and/or sex on the anxiety-alcohol relationship. Findings from this thesis generally did not support such moderation, suggesting that prevention does not need to be gender-targeted for adolescent girls or boys specifically. Overall, universal prevention must begin in childhood if the goal is to reduce the emergence of both anxiety and early alcohol use. Targeted approaches during adolescence, however, need to look beyond anxiety alone and instead adopt a more holistic approach to shared psychopathology. This direction is consistent with contemporary calls in youth mental health and substance use prevention to move beyond narrow diagnostic frameworks and address emerging psychopathology more broadly (Forbes et al., 2019; Henry & Compas, 2024; Holt et al., 2026; Uhlhaas et al., 2023).

6.3.2 Implications for (secondary prevention) early intervention

Early intervention is essential for disrupting the potentially lifelong, mutually reinforcing cycle of anxiety and alcohol comorbidity. To intervene effectively, we need a clear understanding of the mechanisms that contribute to, and sustain, the co-occurrence of anxiety symptoms and harmful patterns of alcohol use. Despite substantial theoretical work proposing mechanisms underlying this relationship, findings from this thesis highlight a striking lack of longitudinal evidence examining these processes. Based on the limited available studies, factors such as worry, depressive symptoms, and emotion dysregulation appear important to address within early intervention efforts and in the clinical context.

Building on the synthesis of observational evidence, **Chapters 4** and **5** of this thesis extended understanding of how an efficacious early intervention operates in practice. Together, these chapters reaffirm both the efficacy and real-world applicability of the online, integrated *Inroads* program (both psychologist-supported and self-guided) as a scalable approach to preventing the escalation of anxiety and hazardous drinking among young adults. Integrated early interventions should continue to target emotion dysregulation, drinking-to-cope motives, and alcohol outcome expectancies to achieve reductions in alcohol use. However, the specific mechanistic targets required to reliably reduce social anxiety symptoms within integrated early interventions remain unclear. Nevertheless, **Chapter 5** demonstrated that *Inroads* could be disseminated in real-world settings with generally positive feedback from youth. To ensure there is engagement with the online format of the intervention there are several key insights for adapting the program which are expanded on in the next subsection.

Lastly, established early intervention practices, such as routine clinical screening, should not be overlooked. While emerging strategies such as digital, self-guided, or self-identification-based interventions offer promising avenues for scalable early support, the findings of this thesis reaffirm that a meaningful relationship exists between anxiety and alcohol use. As such, clinicians and service providers working with individuals presenting with anxiety should routinely screen for harmful alcohol patterns. Tools such as the AUDIT can help identify risky or hazardous drinking, as well as potential AUD (Babor et al., 2001). Identifying alcohol concerns in the context of anxiety, or vice versa, supports an integrated care approach, which, as outlined in **Chapter 1**, has been shown to yield superior outcomes compared to addressing anxiety or alcohol use in isolation.

6.3.3 Implications for online interventions

Online interventions provide a feasible and scalable approach to delivering prevention and early-intervention with this thesis supporting this approach in the context of co-occurring anxiety and alcohol use. The findings of **Chapter 5** indicate that whilst many young adults aged 17-30 years had positive experiences with a self-guided format of the *Inroads* program there are several refinements which can be made to further improve program engagement and user experience to reduce barriers to program implementation in real world settings. Specifically, the addition of some level of human guidance should be implemented in online interventions. This aligns with a growing discourse that (human) guidance can help with program engagement and adherence and potentially offer additional advantages for individuals with greater symptoms severity (Werntz et al., 2023). Young adults indicated that this support does not necessarily need to be provided by a clinician, which is favourable for the scalability of interventions. Providing non-therapist guidance is an approach adopted by other online programs which have incorporated ‘e-coaches’, ‘technicians’ or ‘lay counsellors’ as a cost effective and scalable way to improve program engagement and intervention outcomes (Leung et al., 2022).

A RCT is currently underway of the *Inroads* program which is evaluating such intervention model of self-guided program modules in conjunction with non-clinician support (Prior et al., 2024). During two brief (15-minute) phone calls throughout the program (after modules 1 and 4) the ‘*Inroads* support person’ is intended to provide program motivation and technical support. This trial will provide critical insights into whether youth-selected support preferences

produce desirable clinical outcomes as well as improved engagement and retention when compared to the fully self-guided *Inroads* program (Gückel, Radmall et al., 2025). Another point of interest for this trial is whether the lay-support version of the program delivers effects comparable to those observed in the psychologist-supported version (Stapinski, Prior, et al., 2021). Additionally, the long-term efficacy and economic evaluations embedded within the current lay-support trial will enable further insights into the sustained benefits and individual-level health and societal costs and outcomes of an integrated anxiety-alcohol intervention approach compared to an alcohol-only brief feedback program.

To inform the optimisation and broader applicability of online interventions, several program elements in **Chapter 5** may be beneficial for youth-focused interventions more generally. These elements included 'real-life' character examples to demonstrate practical skills which can be applied in everyday situations, and SMS or email reminders to complete program modules. While these elements were viewed as helpful in facilitating engagement, ensuring interventions are co-designed with the target population and intended end users is paramount. Doing so will ensure program elements, like real-life character examples, remain relevant and help (not hinder) the appeal of online interventions. Addressing the individual-level barriers to engagement that were commonly reported such as user motivation and competing priorities may require customisation and flexibility at program enrolment. Allowing users to choose their preferred communication method (e.g., SMS or email reminders), set personalised pacing, or opt in to varying levels of support may strengthen autonomy and fit with their daily routines. This personalisation, coupled with low-level human guidance, can help foster accountability and improve sustained engagement. Nonetheless, in a world of digital innovations, ensuring existing efficacious interventions, like *Inroads,* are refined and optimised for contemporary platforms is paramount for widescale change in mental health and substance use care more broadly.

6.4 Future research directions

Further to the implications across the aforementioned domains, there are also implications and recommendations for future research. The findings of this thesis highlight several directions for future research investigating the developmental trajectories (subsection 6.4.1), and causal mechanisms in observational (subsection 6.4.2) and intervention work (subsection 6.4.3) to further disentangle the anxiety-alcohol relationship.

6.4.1 Suggestions for future research investigating the anxiety-alcohol relationship across the life course

As demonstrated across this thesis, disentangling the anxiety-alcohol relationship is challenging and further work is needed to understand when and how these concerns emerge and escalate. **Chapter 3** identified positive, cross-sectional, unidirectional associations between anxiety symptoms and hazardous alcohol use in adolescence; however, this pattern did not persist into young adulthood. This is somewhat surprising given that young adulthood is a period marked by high prevalence of anxiety (Lijster et al., 2017; Xiang et al., 2024) and continued escalation of alcohol consumption (Brown et al., 2008). Moreover, although co-occurring anxiety and alcohol use disorders are commonly observed in adult samples, the developmental transition, from sub-clinical symptoms to clinical disorder onset, remain poorly understood.

To address these gaps, prospective, longitudinal studies specifically designed to measure a spectrum of sub-clinical and clinical anxiety constructs alongside multiple drinking indicators (e.g., quantity, frequency, harms/AUDIT) would be highly advantageous. Such designs would also allow researchers to examine the long-term effects of alcohol on subsequent anxiety. As highlighted in a recent systematic review, research testing the alcohol → anxiety pathway remains limited, particularly among sub-clinical populations (D'Aquino et al., 2024).

This research would be particularly timely given the current landscape of alcohol use, where declines in youth drinking have been observed across many high-income countries (Dunphy et al., 2025). Evidence of declines in youth drinking have largely focused on adolescence to date, with less known about trends in drinking among young adults (Vashishtha et al., 2020; Vashishtha et al., 2021). It remains unclear whether these declines translate into shifts in the prevalence or onset of co-occurring anxiety and alcohol use concerns.

In contrast to the growing body of work focused on young people, there is a marked lack of research examining the anxiety-alcohol relationship in middle- to later-life. This gap extends across observational studies as well as mediation and moderation research, as noted in **Chapter 2**. Only one study included in the systematic review had a mean sample age above 40 years (Carvalho et al., 2018). Given that anxiety disorders and AUD are not only disorders of the young, a whole-of-life course approach is needed to fully understand the onset, maintenance,

and nature of their interrelationship. Finally, comprehensive longitudinal datasets will be essential for identifying both mechanistic (mediating) and contextual (moderating) factors that shape comorbidity across different developmental periods and life stages.

6.4.2 Suggestions for future research investigating mechanistic drivers and context factors in the anxiety-alcohol relationship

An unequivocal conclusion emerging from this thesis is the need for more research examining the prospective risk pathways and the mechanistic drivers of the anxiety-alcohol relationship. Although there is longstanding evidence of an association between anxiety and harmful alcohol use, as outlined in **Chapter 2**, the theoretical explanations of *why* this relationship occurs remain largely unsupported in longitudinal studies testing mediating pathways. Transdiagnostic constructs such as emotion dysregulation and distress intolerance, along with alcohol-related motives and outcome expectancies, continue to be key mechanisms of interest. Potential biological mechanisms also warrant exploration, given that most existing work has focused primarily on psychological factors. Future investigations of mediation should be embedded within longitudinal, observational designs that are explicitly developed to test causal mechanisms. It would also be valuable to examine candidate mediators across multiple developmental stages, to determine whether particular mechanisms operate more strongly at specific ages. This approach would offer important insights into developmentally sensitive targets for prevention, early intervention, or treatment.

Another priority is the broader adoption of causal mediation methods within observational and epidemiological research on anxiety and alcohol use. As identified in **Chapter 2**, no longitudinal study in this area has yet applied causal mediation techniques, reflecting a pattern noted across observational research more broadly (Rijnhart et al., 2021). Although rapid advances in statistical methods may contribute to this gap, accessible worked examples e.g., Fernainy et al. (2025); Nguyen et al. (2021); Rudolph et al. (2019); Xu et al. (2023) and reporting guidelines (Lee et al., 2021) are now available and should be incorporated into future anxiety-alcohol research.

Finally, additional research examining moderating factors will help clarify the contexts and populations in which the anxiety-alcohol relationship is most pronounced. Given the findings of this thesis, future studies should move beyond testing gender (or sex) alone as a moderator

and instead explore broader, modifiable biopsychosocial factors that can inform the identification of subgroups most likely to benefit from targeted prevention and early intervention strategies.

6.4.3 Suggestions for future research examining interventions and improving online intervention design in the anxiety-alcohol context

The findings from **Chapter 4** of this thesis demonstrate the need for further research to understand the mechanisms of change in early interventions that concurrently target anxiety and hazardous alcohol use. In the context of the *Inroads* program, the processes driving reductions in hazardous drinking are becoming clearer, yet the mechanisms underpinning reductions in anxiety symptoms remain largely unknown. A recent investigation of mediators of anxiety treatment response in a transdiagnostic online intervention did not find evidence that repetitive negative thinking, worry, or rumination explained improvements in anxiety (Upton et al., 2025). These constructs warrant further investigation though in the anxiety-alcohol context given their theoretical links to this comorbidity (Harwell et al., 2011; Kushner et al., 2000; Moulds & McEvoy, 2025; Wolitzky-Taylor et al., 2021).

Intervention research more broadly needs to move beyond only investigating whether programs "work" and instead focus on *how* they work, and for *whom*. Understanding mechanisms of change is critical for ensuring that prevention, early intervention, and treatment approaches translate effectively into real-world settings. It is important to emphasise, however, that an intervening variable may statistically account for the association between treatment condition (independent variable) and an outcome (e.g., anxiety or alcohol use), but may not necessarily explain the true process through which change occurs (Kazdin, 2007). For this reason, future intervention studies should be purposely designed to measure not only intended outcomes but also the theorised processes of change (i.e., mediating mechanisms).

To do this well, studies should incorporate appropriate measures *and* appropriate timing. Temporal sequencing is essential for establishing whether change processes genuinely precede outcome change (Cashin & Lee, 2021). This may involve assessing hypothesised mechanisms both during treatment and following treatment completion. Such designs will also strengthen the ability to apply causal inference methods to intervention research.

Future work may also benefit from using ecological momentary assessment to capture real-time shifts in anxious mood, coping motives, and drinking behaviour. Prior ecological momentary assessment research has shown that daytime negative mood predicts nighttime drinking via heightened coping motives (Dvorak & Simons, 2014). Testing whether the same pattern holds specifically for anxious symptomatology could inform new intervention models, including just-in-time adaptive interventions (Nahum-Shani et al., 2018; von Lützow et al., 2025).

Together, these directions for future research will help further clarify *when* anxiety-alcohol comorbidity emerges, *how* it unfolds (mediators), *who* is most vulnerable (moderators), and *what* can be done to intervene early and disrupt the feed-forward cycle of comorbidity.

6.5 Conclusions

This thesis offers a rigorous and multifaceted approach to advancing our understanding of co-occurring anxiety and alcohol use concerns to inform prevention and early intervention efforts. Across the empirical studies, several key conclusions emerged which provide actionable recommendations for the timing, targets, and delivery of approaches aimed at reducing the burden of anxiety-alcohol comorbidity. Firstly, preventive approaches must begin in early adolescence. Evidence from this thesis demonstrates that greater anxiety symptoms are already cross-sectionally associated with hazardous alcohol use by age 13. Secondly, the moderating effect of externalising symptoms (i.e., sensation seeking and impulsivity) as well as heightened negative affect (i.e., depression and drinking to cope) highlight which youth may require more intensive or tailored prevention and intervention strategies. Adolescents with both anxiety and elevated externalising traits or additional negative affect should receive targeted, prevention approaches. Thirdly, online early intervention programs, like *Inroads*, offer a scalable, efficacious, and acceptable model for delivering early intervention among youth, however, appropriate supports must be put in place to facilitate and retain engagement. For youth with co-occurring anxiety-alcohol concerns non-clinical, low-intensity guidance alongside self-guided online modules appears to be a preferred and feasible option. Further to these recommendations, this thesis synthesised the current evidence on mechanisms driving anxiety-alcohol comorbidity and the need for further work to understand causal drivers of this common relationship. In sum, while the anxiety-alcohol relationship is complex, this must not prohibit attempts to prevent and intervene early to halt or stop a potentially vicious cycle of comorbidity.

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Appendix A

Supplementary materials for Chapter 2

Preface

This Appendix includes supplementary material for **Chapter 2**. Supplementary materials include: database search strategies (Table A1 to Table A6), original and Fisher's *Z* transformed statistics for mediation and moderation effects (Table A7 to Table A11), counts and magnitude of effect size classification including studies without reported estimates (Table A12 to Table A16), full meta-analytic calculations for moderation meta-estimate results (Table A17 and Table A18), GRADE moderation subtheme results (Table A19), and risk of bias results (Table A20 and Table A21).

Table A1:Medline search strategy

Database: Medline (via OVID)		
Anxiety	1	*Anxiety/
	2	*anxiety disorders/ or *agoraphobia/ or *panic disorder/
	3	(Anxiety disorder or separation anxiety disorder or selective mutism or SM or specific phobia or SP or social phobia or social anxiety or SA or panic disorder or PD or agoraphobia or generali?ed anxiety disorder or GAD).tw.
	4	(Anxiety sensitivity or AS).tw.
	5	(Internali*ing disorder or internali*ing).tw.
	6	(Social-emotional disorder* or emotional disorder*).tw.
	7	1 or 2 or 3 or 4 or 5 or 6
Alcohol	8	exp Alcohol Drinking/ or exp Alcohol-Related Disorders/
	9	((alcohol* or drink*) adj3 (misuse* or initiat* or abus* or problem or heavy or binge or disorder* or dependen* or frequen*)).tw.
	10	8 or 9
Mediator/Moderator	11	(mediat* or moderat*).mp.
	12	(associat* or relat* or role*).ti.
	13	(Risk factor* or protective factor* or indirect* or direct*).mp.
	14	11 or 12 or 13
	15	7 and 10 and 14

Table A2: APA PsycInfo search strategy

Database: APA PsycInfo (via OVID)		
Anxiety	1	exp anxiety/
	2	*anxiety disorders/ or *generalized anxiety disorder/ or *panic attack/ or *panic disorder/ or *separation anxiety disorder/
	3	(Anxiety disorder or separation anxiety disorder or selective mutism or SM or specific phobia or SP or social phobia or social anxiety or SA or panic disorder or PD or agoraphobia or generali?ed anxiety disorder or GAD).tw.
	4	(Anxiety sensitivity or AS).tw.
	5	(Internali*ing disorder or internali*ing).tw.
	6	(Social-emotional disorder* or emotional disorder*).tw.
	7	1 or 2 or 3 or 4 or 5 or 6
Alcohol	8	exp alcohol drinking patterns/
	9	exp "alcohol use disorder"/
	10	((alcohol* or drink*) adj3 (misuse* or initiat* or abus* or problem or heavy or binge or disorder* or dependen* or frequen*)).tw.
	11	8 or 9 or 10
Mediator/Moderator	12	(mediat* or moderat*).mp.
	13	(associat* or relat* or role*).ti.
	14	(Risk factor* or protective factor* or indirect* or direct*).mp.
	15	12 or 13 or 14
	16	7 and 11 and 15

Table A3: Embase search strategy.

Database: Embase (via OVID)		
Anxiety	1	*anxiety/ or *social anxiety/
	2	*anxiety disorder/ or *generalized anxiety disorder/ or *panic/ or *separation anxiety/
	3	(Anxiety disorder or separation anxiety disorder or selective mutism or SM or specific phobia or SP or social phobia or social anxiety or SA or panic disorder or PD or agoraphobia or generali?ed anxiety disorder or GAD).tw.
	4	(Anxiety sensitivity or AS).tw.
	5	(Internali*ing disorder or internali*ing).tw.
	6	(Social-emotional disorder* or emotional disorder*).tw.
	7	1 or 2 or 3 or 4 or 5 or 6
Alcohol	8	exp alcohol abuse/
	9	*alcoholism/
	10	*alcohol consumption/
	11	((alcohol* or drink*) adj3 (misuse* or initiat* or abus* or problem or heavy or binge or disorder* or dependen* or frequen*)).tw.
	12	8 or 9 or 10 or 11
Mediator/Moderator	13	(mediat* or moderat*).mp.
	14	(associat* or relat* or role*).ti.
	15	(Risk factor* or protective factor* or indirect* or direct*).mp.
	16	13 or 14 or 15
	17	7 and 12 and 16

Table A4: Cochrane Central Register of Controlled trials (CENTRAL) search strategy.

Database: Cochrane Central Register of Controlled trials (CENTRAL) (via OVID)		
Anxiety	1	anxiety.mp.
	2	(Anxiety disorder or separation anxiety disorder or selective mutism or SM or specific phobia or SP or social phobia or social anxiety or SP or panic disorder or PD or agoraphobia or generali?ed anxiety disorder or GAD).tw.
	3	(Anxiety sensitivity or AS).tw.
	4	(Internali*ing disorder or internali*ing).tw.
	5	(Social-emotional disorder* or emotional disorder*).tw.
	6	1 or 2 or 3 or 4 or 5
Alcohol	7	alcohol.mp.
	8	((alcohol* or drink*) adj3 (misuse* or initiat* or abus* or problem or heavy or binge or disorder* or dependen* or frequen*)).tw.
	9	7 or 8
Mediator/Moderator	10	(mediat* or moderat*).mp.
	11	(associat* or relat* or role*).ti.
	12	(Risk factor* or protective factor* or indirect* or direct*).mp.
	13	10 or 11 or 12
	14	6 and 9 and 13

Table A5: Scopus search strategy

Database: Scopus		
Anxiety	1	(TITLE (anxiety OR anxious) OR TITLE-ABS-KEY ("anxiety disorder" OR "separation anxiety disorder" OR "selective mutism" OR "specific phobia" OR "social phobia" OR "social anxiety" OR "panic disorder" OR "agoraphobia" OR "generali?ed anxiety disorder" OR "gad"))
Alcohol	2	(TITLE (alcohol)) OR (TITLE-ABS-KEY (((alcohol* OR drink*) W/3 (misuse* OR initiat* OR abus* OR problem* OR heavy OR binge OR disorder* OR dependen* OR frequen*))))
Mediator/Moderator	3	(TITLE-ABS-KEY (mediat* OR moderat*) OR TITLE (associat* OR relat* OR role OR "risk factor" OR "protective factor" OR indirect* OR direct))
		1 AND 2 AND 3

Table A6: Web of Science search strategy

Database: Web of science (core collection)		
Anxiety	1	TI=(anxiety OR anxious)
	2	TS=("anxiety disorder" OR "separation anxiety disorder" OR "selective mutism" OR "specific phobia" OR "social phobia" OR "social anxiety" OR "panic disorder" OR "agoraphobia" OR "generali?ed anxiety disorder" OR "gad")
	3	#2 OR #1
Alcohol	4	TI=(alcohol)
	5	TS=((alcohol* OR drink*) NEAR/3 (misuse* OR initiat* OR abus* OR problem* OR heavy OR binge OR disorder* OR dependen* OR frequen*))
	6	#4 OR #5
Mediator/Moderator	7	TS=(mediat* OR moderat*)
	8	TI=(associat* OR relat* OR role OR "risk factor" OR "protective factor" OR indirect* OR direct)
	9	#7 OR #8
	10	#3 AND #6 AND #9

Table A7: Complete mediation effects in the anxiety → alcohol relationship (n =25). Original and transformed statistics

Mediator (Author, Year)	Predictor	Outcome	Metric of mediation	Mediation metric (type)	Measure of variance	Variance metric (type)	Sig./ Not sig.	N	Conversion from un/standardised regression		Conversion from OR	
									R	Fisher's Z With CI	R	Fisher's Z With CI
Anxiety (wave 2) (Paulus et al. 2021)	Anxiety sensitivity	Alcohol problems (continuous)	0.01	Standardised coefficient	0.003, 0.02	CI	Sig.	3396	0.040	0.040 (0.006 to 0.073)	--	--
Anxiety (wave 3) (Paulus et al. 2021)	Anxiety sensitivity	Alcohol problems (continuous)	0.01	Standardised coefficient	0.003, 0.03	CI	Sig.	3396	0.025	0.025 (-0.009 to 0.058)	--	--
Depressive symptoms (McCarty et al. 2023)	Anxiety sensitivity	Alcohol use frequency (continuous)	0.02	Standardised coefficient	-0.01, 0.05	CI	Not sig.	361	0.069	0.069 (-0.035 to 0.171)	--	--
Depressive symptoms (McCarty et al. 2023)	Anxiety sensitivity	Alcohol use quantity (continuous)	0.04	Standardised coefficient	-0.01, 0.08	CI	Not sig.	361	0.091	0.091 (-0.012 to 0.193)	--	--
Depressive symptoms (McCarty et al. 2023)	Anxiety sensitivity	Alcohol use problems (continuous)	0.06	Standardised coefficient	0.01, 0.10	CI	Sig.	361	0.136	0.136 (0.034 to 0.236)	--	--
Drinking motives- conformity (Collins et al. 2018)	Social avoidance	Alcohol problems (continuous)	0.03	Standardised coefficient	-0.03, 0.09	CI	Not sig.	219	0.066	0.066 (-0.067 to 0.197)	--	--
Drinking motives- conformity (between-subject model) (Mackinnon et al. 2014)	Anxiety sensitivity	Alcohol problems (continuous)	0.039	Unstandardised coefficient	-0.002, 0.09	CI	Not sig.	302	0.095	0.095 (-0.018 to 0.206)	--	--
Drinking motives- conformity (within-subject model) (Mackinnon et al. 2014)	Anxiety sensitivity	Alcohol problems (continuous)	0.006	Unstandardised coefficient	-0.01, 0.01	CI	Not sig.	302	0.068	0.068 (-0.046 to 0.179)	--	--
Drinking motives- Drinking to cope with anxiety (Collins et al. 2018)	Social avoidance	Alcohol problems (continuous)	-0.07	Standardised coefficient	-0.07, 0.06	CI	Not sig.	219	-0.141	-0.141 (-0.269 to -0.009)	--	--
Drinking motives- Drinking to cope with anxiety (between-subject model) (Mackinnon et al. 2014)	Anxiety sensitivity	Alcohol problems (continuous)	-0.005	Unstandardised coefficient	-0.05, 0.03	CI	Not sig.	302	-0.014	-0.014 (-0.127 to 0.099)	--	--
Drinking motives- Drinking to cope with anxiety (within-subject model) (Mackinnon et al. 2014)	Anxiety sensitivity	Alcohol problems (continuous)	-0.003	Unstandardised coefficient	-0.01, 0.004	CI	Not sig.	302	-0.048	-0.048 (-0.160 to 0.065)	--	--
Drinking motives- Drinking to cope with depression (Collins et al. 2018)	Social avoidance	Alcohol problems (continuous)	0.15	Standardised coefficient	0.02, 0.33	CI	Sig.	219	0.127	0.127 (-0.006 to 0.255)	--	--
Drinking motives- Drinking to cope with depression (between-subject model) (Mackinnon et al. 2014)	Anxiety sensitivity	Alcohol problems (continuous)	0.039	Unstandardised coefficient	-0.01, 0.04	CI	Not sig.	302	0.173	0.173 (0.062 to 0.281)	--	--
Drinking motives- Drinking to cope with depression (within-subject model) (Mackinnon et al. 2014)	Anxiety sensitivity	Alcohol problems (continuous)	0.004	Unstandardised coefficient	-0.004, 0.02	CI	Not sig.	302	0.038	0.038 (-0.076 to 0.150)	--	--
Drinking motives- enhancement (Collins et al. 2018)	Social avoidance	Alcohol problems (continuous)	0.02	Standardised coefficient	-0.01, 0.06	CI	Not sig.	219	0.075	0.075 (-0.058 to 0.206)	--	--
Drinking motives- social (Collins et al. 2018)	Social avoidance	Alcohol problems (continuous)	0.01	Standardised coefficient	0.01, 0.04	CI	Not sig.	219	0.088	0.088 (-0.045 to 0.218)	--	--
Emotion dysregulation (Goldstein et al. 2019)	Anxious attachment	Alcohol problems (continuous)	0.16	Standardised coefficient	0.009, 0.316	CI	Sig.	203	0.142	0.142 (0.004 to 0.274)	--	--
Expectancies for not drinking (Bekman et al. 2010)	Social anxiety symptoms	Initiation of alcohol use	0.87	OR	0.05	SE	Sig.	677	--	--	-0.107	-0.107 (-0.180 to -0.031)
Expectancies for not drinking (Bekman et al. 2010)	Social anxiety symptoms	Initiation of alcohol use	0.98	OR	0.07	SE	Not sig.	591	--	--	-0.012	-0.012 (-0.092 to 0.069)
Interpersonal difficulties (Goldstein et al. 2019)	Anxious attachment	Alcohol problems (continuous)	0.095	Standardised coefficient	0.0025, 0.203	CI	Sig.	203	0.129	0.129 (-0.009 to 0.262)	--	--
Perceptions of peer alcohol use (Bekman et al. 2010)	Social anxiety symptoms	Initiation of alcohol use	0.96	OR	0.03	SE	Not sig.	677	--	--	-0.052	-0.052 (-0.127 to 0.023)
Perceptions of peer alcohol use (Bekman et al. 2010)	Social anxiety symptoms	Initiation of alcohol use	0.95	OR	0.05	SE	Not sig.	591	--	--	-0.042	-0.042 (-0.122 to 0.039)

Mediator (Author, Year)	Predictor	Outcome	Metric of mediation	Mediation metric (type)	Measure of variance	Variance metric (type)	Sig./ Not sig.	N	Conversion from un/standardised regression		Conversion from OR	
									R	Fisher's Z With CI	R	Fisher's Z With CI
Rumination (Wolitzky-Taylor et al. 2021)	Anxiety disorder severity	Alcohol use disorder symptoms severity (continuous)	0.03	Unstandardised coefficient	0.002, 0.06	CI	Sig.	232	0.132	0.132 (0.003 to 0.256)	--	--
Worry (Wolitzky-Taylor et al. 2021)	Anxiety disorder severity	Alcohol use disorder symptoms severity (continuous)	0.01	Unstandardised coefficient	-0.01, 0.04	CI	Not sig.	232	0.051	0.051 (-0.078 to 0.179)	--	--
Negative life events (Buckner et al. 2009)	Social anxiety disorder	Alcohol use disorder (binary)	4.43	OR	1.29, 15.22	CI	Not sig.	544	--	--	-0.116	-0.116 (-0.199 to -0.033)

Table A8: Complete mediation effects in the alcohol → anxiety relationship (n =5). Original and transformed statistics.

Mediator (Author, Year)	Predictor	Outcome	Metric of mediation	Mediation metric (type)	Measure of variance	Variance metric (type)	Sig./ Not sig.	N	Conversion from un/standardised regression		Conversion from OR	
									R	Fisher's Z With CI		Fisher's Z With CI
Anxiety (wave 2) (Paulus et al. 2021)	Alcohol problems (wave 1)	Anxiety sensitivity (wave 3)	-0.01	Standardised coefficient	-0.01	S.E	Not sig.	3396	0.017	0.017 (-0.016 to 0.051)	- -	--
Anxiety (wave 3) (Paulus et al. 2021)	Alcohol problems (wave 2)	Anxiety sensitivity (wave 4)	-0.01	Standardised coefficient	-0.01	S.E	Not sig.	3396	0.017	0.017 (-0.016 to 0.051)	- -	--
Sustained attention (Sher et al. 2007)	Alcohol dose (placebo vs control)	Anxiety symptoms	Not reported	Unstandardised coefficient	Not reported	S.E	Not sig.	101	--	--	- -	--
Change in negative thoughts (Abrams et al. 2002)	Alcohol beverage group (alcohol expected, alcohol not expected, placebo)	Anxiety symptoms	Not reported	Unknown type	Not reported	S.E	Sig.	61	--	--	- -	--
Change in positive thoughts (Abrams et al. 2002)	Alcohol beverage group (alcohol expected, alcohol not expected, placebo)	Anxiety symptoms	Not reported	Unknown type	Not reported	S.E	Sig.	61	--	--	- -	--

Table A9: Complete moderation effects in the anxiety → alcohol relationship (n =224). Original and transformed statistics.

									Conversion From un/standardised regression		Conversion from OR	
Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
Age (Cerda et al. 2013)	Anxiety symptoms (recent)	Alcohol use initiation	Not reported	-	Not reported	-	Not sig.	460	--	--	--	--
Age (Cerda et al. 2013)	Anxiety symptoms (cumulative)	Alcohol use initiation	Not reported	-	Not reported	-	Not sig.	460	--	--	--	--
Age (Colder et al. 2017)	Generalised anxiety symptoms	Drinks per year (continuous)	0.02	Unstandardised coefficient	0	S.E	Sig.	387	--	--	--	--
Age (Colder et al. 2017)	Social anxiety symptoms	Drinks per year (continuous)	0.01	Unstandardised coefficient	0	S.E	Sig.	387	--	--	--	--
Age (Colder et al. 2017)	Social anxiety symptoms	Alcohol problems (continuous)	-0.03	Unstandardised coefficient	0.01	S.E	Sig.	387	-0.151	-0.151 (-0.247 to -0.052)	--	--
Age (Cheng et al. 2004)	Anxiety disorder	Alcohol use disorder	3.03	OR	0.60, 15.31	CI	Not sig.	491	--	--	-0.142	-0.142 (-0.228 to -0.055)
Age (Cheng et al. 2004)	Anxiety disorder	Alcohol use disorder	16.86	OR	3.98, 71.41	CI	Sig.	491	--	--	-0.280	-0.280 (-0.359 to -0.196)
Gender (Colder et al. 2019)	Social anxiety symptoms	Alcohol use quantity (continuous)	Not reported	-	Not reported	-	Not sig.	387	--	--	--	--
Gender (Dahne et al. 2014)	Social phobia symptoms	Alcohol use (binary)	Not reported	-	Not reported	-	Not sig.	277	--	--	--	--
Gender (Parrish et al. 2016)	Anxiety symptoms	Frequency of alcohol use	Not reported	-	Not reported	-	Not sig.	620	--	--	--	--
Gender (Parrish et al. 2016)	Anxious arousal symptoms	Frequency of alcohol use	Not reported	-	Not reported	-	Not sig.	620	--	--	--	--
Gender (Schimdt et al. 2007)	Anxiety sensitivity-Cognitive concerns	Alcohol use disorder (binary)	0.28	Stand. Coef.	0.3	S.E	Not sig.	404	0.046	0.046 (-0.051 to 0.143)	--	--
Gender (Schimdt et al. 2007)	Anxiety sensitivity-Physical concerns	Alcohol use disorder (binary)	0.15	Stand. Coef.	0.33	S.E	Not sig.	404	0.023	0.023 (-0.075 to 0.120)	--	--
Gender (Schimdt et al. 2007)	Anxiety sensitivity-Social concerns	Alcohol use disorder (binary)	0.13	Stand. Coef.	0.6	S.E	Not sig.	404	0.011	0.011 (-0.087 to 0.108)	--	--
Gender (Schimdt et al. 2007)	Anxiety sensitivity	Alcohol use disorder (binary)	0.11	Stand. Coef.	0.09	S.E	Not sig.	404	0.061	0.061 (-0.037 to 0.157)	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Regular alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	3021	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Hazardous alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	3021	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Alcohol use disorder: abuse without dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	3021	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Alcohol use disorder: dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	3021	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Alcohol use disorder: any (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	3021	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic attack	Regular alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	3021	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic attack	Hazardous alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	3021	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic attack	Alcohol use disorder: abuse without dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	3021	--	--	--	--

										Conversion From un/standardised regression		Conversion from OR	
Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
Gender (Zimmermann et al. 2003)	Panic attack	Alcohol use disorder: dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic attack	Alcohol use disorder: any (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Regular alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Hazardous alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Alcohol use disorder: abuse without dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Alcohol use disorder: dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Alcohol use disorder: any (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Regular alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Hazardous alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Alcohol use disorder: abuse without dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Alcohol use disorder: dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Alcohol use disorder: any (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Specific phobia	Regular alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Specific phobia	Hazardous alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Specific phobia	Alcohol use disorder: abuse without dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Specific phobia	Alcohol use disorder: dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Specific phobia	Alcohol use disorder: any (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Regular alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Hazardous alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Alcohol use disorder: abuse without dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Alcohol use disorder: dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Alcohol use disorder: any (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Regular alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Hazardous alcohol use (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--

										Conversion From un/standardised regression		Conversion from OR	
Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Alcohol use disorder: abuse without dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Alcohol use disorder: dependence (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Alcohol use disorder: any (onset/progression at follow-up)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Regular alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Hazardous alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Alcohol use disorder: abuse without dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Alcohol use disorder: dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic disorder with or without agoraphobia	Alcohol use disorder: any (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic attack	Regular alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic attack	Hazardous alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic attack	Alcohol use disorder: abuse without dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic attack	Alcohol use disorder: dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Panic attack	Alcohol use disorder: any (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Regular alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Hazardous alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Alcohol use disorder: abuse without dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Alcohol use disorder: dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Agoraphobia without panic disorder	Alcohol use disorder: any (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Regular alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Hazardous alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Alcohol use disorder: abuse without dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Alcohol use disorder: dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Social phobia	Alcohol use disorder: any (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Specific phobia	Regular alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Specific phobia	Hazardous alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Specific phobia	Alcohol use disorder: abuse without dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--

									Conversion From un/standardised regression		Conversion from OR	
Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
Gender (Zimmermann et al. 2003)	Specific phobia	Alcohol use disorder: dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Specific phobia	Alcohol use disorder: any (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Hazardous alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Alcohol use disorder: abuse without dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Alcohol use disorder: dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Alcohol use disorder: any (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Regular alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Hazardous alcohol use (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Alcohol use disorder: abuse without dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Alcohol use disorder: dependence (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Generalised anxiety disorder	Alcohol use disorder: any (persistence of lifetime)	Not reported	-	Not reported	-	Not sig.	30 21	--	--	--	--
Gender (Zimmermann et al. 2003)	Phobia (not otherwise specified)	Regular alcohol use (persistence of lifetime)	0	OR	0.0, 0.2	CI	Sig.	30 21	--	--	--	--
Gender male/female (Mackie et al. 2011)	Anxiety symptoms	Alcohol use (continuous)	0.73	Unstandardised coefficient	0.52	S.E	Not sig.	39 3	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Alcohol consumption escalation (vs maintenance) early pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Alcohol consumption reduction (vs maintenance) early pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Alcohol consumption initiation (vs abstinence) early pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Alcohol consumption escalation (vs maintenance) late pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Alcohol consumption reduction (vs maintenance) late pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Alcohol consumption initiation (vs abstinence) late pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Binge drinking escalation (vs maintenance) early pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Binge drinking reduction (vs maintenance) early pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Binge drinking initiation (vs abstinence) early pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Binge drinking escalation (vs maintenance) late pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Binge drinking reduction (vs maintenance) late pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Gohari et al. 2023)	Anxiety symptoms	Binge drinking initiation (vs abstinence) late pandemic (binary)	Not reported	-	Not reported	-	Not sig.	19 01	--	--	--	--
Sex (Kaplow et al. 2001)	Separation anxiety symptoms	Initiation of alcohol use (binary)	1.47	OR	0.81, 2.73	CI	Not sig.	93 6	--	--	0.041	0.041 (-0.024 to 0.104)

									Conversion From un/standardised regression		Conversion from OR	
Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
Sex (Kaplow et al. 2001)	Anxiety symptoms (general & separation)	Initiation of alcohol use (binary)	0.97	OR	0.84, 1.12	CI	Not sig.	936	--	--	-0.014	-0.014 (-0.078 to 0.051)
Sex (Kaplow et al. 2001)	Anxiety symptoms	Initiation of alcohol use (binary)	0.91	OR	0.74, 1.11	CI	Not sig.	936	--	--	-0.030	-0.030 (-0.094 to 0.034)
Generational status (Mexican) (Parrish et al. 2016)	Anxiety symptoms	Frequency of alcohol use	Not reported	-	Not reported	-	Not sig.	620	--	--	--	--
Generational status (Mexican) (Parrish et al. 2016)	Anxious arousal symptoms	Frequency of alcohol use	Not reported	-	Not reported	-	Not sig.	620	--	--	--	--
Race (Black/white) (Schleider et al. 2019)	Anxiety severity	Alcohol use (binary)	Not reported	-	Not reported	-	Not sig.	2100	--	--	--	--
Race/ethnicity (Nichter et al. 2015)	Worry	Typical quantity of drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Race/ethnicity (Nichter et al. 2015)	Worry	Frequency of binge drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Race/ethnicity (Nichter et al. 2015)	Worry	Alcohol dependence symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Race/ethnicity (Nichter et al. 2015)	Physiological anxiety symptoms	Typical quantity of drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Race/ethnicity (Nichter et al. 2015)	Physiological anxiety symptoms	Frequency of binge drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Race/ethnicity (Nichter et al. 2015)	Physiological anxiety symptoms	Alcohol dependence symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Race/ethnicity (Black/other) (Cerda et al. 2013)	Anxiety symptoms (recent)	Alcohol use initiation	1.19	Hazard ratio	1.10, 1.29	CI	Not sig.	460	--	--	0.196	0.196 (0.107 to 0.282)
Race/ethnicity (Black/other) (Cerda et al. 2013)	Anxiety symptoms (cumulative)	Alcohol use initiation	Not reported	-	Not reported	-	Not sig.	460	--	--	--	--
Impairment alcohol expectancies (daily) (Richton et al. 2017)	Social anxiety symptoms	Drinks per drinking day (count)	0	Unstandardised coefficient	0.01	S.E	Not sig.	515	--	--	--	--
Impairment alcohol expectancies (daily) (Richton et al. 2017)	Yearly social anxiety symptoms	Drinks per drinking day (count)	0	Unstandardised coefficient	0.02	S.E	Not sig.	515	--	--	--	--
Impairment alcohol expectancies (daily) (Richton et al. 2017)	Social anxiety symptoms	Any drinking (binary)	-0.02	Unstandardised coefficient	0.02	S.E	Not sig.	537	--	--	--	--
Impairment alcohol expectancies (daily) (Richton et al. 2017)	Yearly social anxiety symptoms	Any drinking (binary)	0.05	Unstandardised coefficient	0.04	S.E	Not sig.	537	--	--	--	--
Impairment alcohol expectancies (yearly) (Richton et al. 2017)	Social anxiety symptoms	Drinks per drinking day (count)	-0.01	Unstandardised coefficient	0.01	S.E	Not sig.	515	--	--	--	--
Impairment alcohol expectancies (yearly) (Richton et al. 2017)	Social anxiety symptoms	Any drinking (binary)	0.05	Unstandardised coefficient	0.04	S.E	Not sig.	537	--	--	--	--
Alcohol outcome expectancies-Positive (Borges et al. 2018)	Anxiety sensitivity	Alcohol use (in past year)	0.01	Unstandardised coefficient	0.01	S.E	Sig.	246	--	--	--	--
Tension-reduction alcohol expectancies (daily) (Richton et al. 2017)	Social anxiety symptoms	Drinks per drinking day (count)	-0.01	Unstandardised coefficient	0.01	S.E	Not sig.	515	--	--	--	--
Tension-reduction alcohol expectancies (daily) (Richton et al. 2017)	Yearly social anxiety symptoms	Drinks per drinking day (count)	-0.03	Unstandardised coefficient	0.02	S.E	Not sig.	515	--	--	--	--
Tension-reduction alcohol expectancies (daily) (Richton et al. 2017)	Social anxiety symptoms	Any drinking (binary)	0	Unstandardised coefficient	0.02	S.E	Not sig.	537	--	--	--	--
Tension-reduction alcohol expectancies (daily) (Richton et al. 2017)	Yearly social anxiety symptoms	Any drinking (binary)	0.06	Unstandardised coefficient	0.04	S.E	Not sig.	537	--	--	--	--
Tension-reduction alcohol expectancies (yearly) (Richton et al. 2017)	Social anxiety symptoms	Drinks per drinking day (count)	0.01	Unstandardised coefficient	0.02	S.E	Not sig.	515	--	--	--	--
Tension-reduction alcohol expectancies (yearly) (Richton et al. 2017)	Social anxiety symptoms	Any drinking (binary)	0.03	Unstandardised coefficient	0.04	S.E	Not sig.	537	--	--	--	--

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Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
1st trimester alcohol use (Leis et al. 2012)	Anxiety symptoms	Any alcohol use at 32 weeks gestation (binary)	1	OR	0.98, 1.03	CI	Not sig.	12,824	--	--	0.000	0.000 (-0.017 to 0.017)
1st trimester alcohol use (Leis et al. 2012)	Anxiety symptoms	Binge drinking at 32 weeks gestation (binary)	0.99	OR	0.97, 1.02	CI	Not sig.	12,824	--	--	-0.007	-0.007 (-0.024 to 0.010)
Means drinks (quantity x frequency) (Armeli et al. 2014)	Anxiety symptoms	Drinking related problems (continuous)	0.019	Unstandardised coefficient	0.02	S.E	Not sig.	844	--	--	--	--
Means drinks (quantity x frequency) (Armeli et al. 2014)	Anxiety symptoms (monthly)	Drinking related problems (continuous)	-0.003	Unstandardised coefficient	0.065	S.E	Not sig.	844	--	--	--	--
Anxiety sensitivity (Mackie et al. 2011)	Anxiety symptoms	Alcohol use (continuous)	0.97	Unstandardised coefficient	0.37	S.E	Sig.	393	--	--	--	--
Delinquency (Marmorstein et al. 2010)	Anxiety symptoms	Age at first use of alcohol (continuous)	Not reported	-	Not reported	-	Not sig.	503	--	--	--	--
Delinquency (Marmorstein et al. 2010)	Social anxiety symptoms	Age at first use of alcohol (continuous)	Not reported	-	Not reported	-	Not sig.	503	--	--	--	--
Hopelessness (Mackie et al. 2011)	Anxiety symptoms	Alcohol use (continuous)	0.34	Unstandardised coefficient	0.24	S.E	Not sig.	393	--	--	--	--
Drinking motives- conformity (Grant et al. 2009)	Daily anxious mood	Daily alcohol use, capped at 6 (continuous)	0.45	Unstandardised coefficient	0.11	S.E	Sig.	142	0.325	0.325 (0.169 to 0.465)	--	--
Drinking motives- drinking to cope depression (Grant et al. 2009)	Daily anxious mood	Daily alcohol use, capped at 6 (continuous)	-0.22	Unstandardised coefficient	0.14	S.E	Not sig.	142	-0.131	-0.131 (-0.289 to 0.035)	--	--
Drinking motives- drinking to cope anxiety (Grant et al. 2009)	Daily anxious mood	Daily alcohol use, capped at 6 (continuous)	0.23	Unstandardised coefficient	0.11	S.E	Sig.	142	0.173	0.173 (0.008 to 0.328)	--	--
Drinking motives- drinking to cope (Armeli et al. 2014)	Anxiety symptoms	Drinking related problems (continuous)	0.102	Unstandardised coefficient	0.024	S.E	Sig.	844	0.145	0.145 (0.078 to 0.210)	--	--
Drinking motives- drinking to cope (Armeli et al. 2014)	Anxiety symptoms (monthly)	Drinking related problems (continuous)	-0.006	Unstandardised coefficient	0.047	S.E	Not sig.	844	-0.004	-0.004 (-0.072 to 0.063)	--	--
Drinking motives- drinking to cope (Dyer et al. 2019)	Generalised anxiety disorder	Harmful drinking, AUDIT, age 18 (binary)	0.86	OR	0.23, 3.13	CI	Not sig.	3452	--	--	-0.004	-0.004 (-0.037 to 0.030)
Drinking motives- drinking to cope (Dyer et al. 2019)	Generalised anxiety disorder	Harmful drinking, AUDIT, age 21 (binary)	0.73	OR	0.28, 1.87	CI	Not sig.	3452	--	--	-0.011	-0.011 (-0.044 to 0.022)
Drinking motives- drinking to cope (Dyer et al. 2019)	Generalised anxiety disorder	Frequent bingeing, AUDIT, age 18 (binary)	1.66	OR	0.67, 4.12	CI	Not sig.	3452	--	--	0.019	0.019 (-0.015 to 0.052)
Drinking motives- drinking to cope (Dyer et al. 2019)	Generalised anxiety disorder	Hazardous drinking, AUDIT, age 21 (binary)	0.84	OR	0.38, 1.85	CI	Not sig.	3452	--	--	-0.007	-0.007 (-0.041 to 0.026)
Drinking motives- drinking to cope (Dyer et al. 2019)	Generalised anxiety disorder	Frequent bingeing, AUDIT, age 21 (binary)	0.95	OR	0.43, 2.09	CI	Not sig.	3452	--	--	-0.002	-0.002 (-0.036 to 0.031)
Drinking motives- drinking to cope (Dyer et al. 2019)	Generalised anxiety disorder	Frequent drinking, AUDIT, age 21 (binary)	1	OR	0.48, 2.11	CI	Not sig.	3452	--	--	0.000	0.000 (-0.033 to 0.033)
Drinking motives- drinking to cope (Dyer et al. 2019)	Generalised anxiety disorder	Frequent drinking, AUDIT, age 18 (binary)	1.8	OR	0.90, 3.62	CI	Not sig.	3452	--	--	0.028	0.028 (-0.005 to 0.061)
Drinking motives- drinking to cope (Dyer et al. 2019)	Generalised anxiety disorder	Hazardous drinking, AUDIT, age 18 (binary)	0.96	OR	0.50, 1.82	CI	Not sig.	3452	--	--	-0.002	-0.002 (-0.035 to 0.031)
Drinking motives- drinking to cope (Armeli et al. 2008)	Anxiety daily mood symptoms	Weekly drinking onset (time to drink)	0.38	Unstandardised coefficient	Not reported	-	Sig.	458	--	--	--	--

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Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
Drinking motives- drinking to cope (Armeli et al. 2008)	Anxiety same day symptoms	Weekly drinking onset (time to drink)	0.18	Unstandardised coefficient	Not reported	-	Sig.	458	--	--	--	--
Drinking motives- drinking to cope (Armeli et al. 2008)	Anxiety symptoms Sunday only	Weekly drinking onset (time to drink)	0.24	Unstandardised coefficient	Not reported	-	Sig.	458	--	--	--	--
Drinking motives- drinking to cope (Armeli et al. 2008)	Anxiety daily symptoms	Any drinking (binary)	0.06	Unstandardised coefficient	Not reported	-	Not sig.	458	--	--	--	--
Drinking motives- drinking to cope (Armeli et al. 2008)	Anxiety daily symptoms	Heavy drinking (binary)	0.008	Unstandardised coefficient	Not reported	-	Not sig.	458	--	--	--	--
Drinking motives- drinking to cope (Armeli et al. 2010)	Mean daily diary anxiety	Month-level drinking frequency (continuous)	-0.031	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking motives- drinking to cope (Armeli et al. 2010)	Retrospective anxiety	Month-level drinking frequency (continuous)	-0.444	Unstandardised coefficient	Not reported	-	Sig.	530	--	--	--	--
Drinking motives- drinking to cope (Armeli et al. 2010)	Mean daily diary anxiety	Drinking quantity (drinks per drinking day) (continuous)	0.076	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking motives- drinking to cope (Armeli et al. 2010)	Retrospective anxiety	Drinking quantity (drinks per drinking day) (continuous)	-0.176	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking motives- drinking to cope (Armeli et al. 2010)	Mean daily diary anxiety	Any drinking (binary)	0.008	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking motives- drinking to cope (Armeli et al. 2010)	Mean daily diary anxiety	Drinks consumed per drinking day (count)	-0.058	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking motives- drinking to cope (Littlefield et al. 2012)	Anxiety symptoms	Onset of any drinking (binary)	Not reported	-	Not reported	-	Not sig.	1152	--	--	--	--
Drinking motives- drinking to cope (Littlefield et al. 2012)	Anxiety symptoms	Onset of heavy episodic drinking (binary)	Not reported	-	Not reported	-	Not sig.	1152	--	--	--	--
Drinking motives- drinking to cope (Littlefield et al. 2012)	Anxiety symptoms	Onset of intoxication (binary)	Not reported	-	Not reported	-	Not sig.	1152	--	--	--	--
Drinking motives- drinking to socialise or enhance (Armeli et al. 2010)	Mean daily diary anxiety	Month-level drinking frequency (continuous)	0.06	Unstandardised coefficient	Not reported	-	Sig.	530	--	--	--	--
Drinking motives- drinking to socialise or enhance (Armeli et al. 2010)	Retrospective anxiety	Month-level drinking frequency (continuous)	0.463	Unstandardised coefficient	Not reported	-	Sig.	530	--	--	--	--
Drinking motives- drinking to socialise or enhance (Armeli et al. 2010)	Mean daily diary anxiety	Drinking quantity (drinks per drinking day) (continuous)	-0.51	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking motives- drinking to socialise or enhance (Armeli et al. 2010)	Retrospective anxiety	Drinking quantity (drinks per drinking day) (continuous)	0.159	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking motives- drinking to socialise or enhance (Armeli et al. 2010)	Mean daily diary anxiety	Any drinking (binary)	-0.009	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking motives- drinking to socialise or enhance (Armeli et al. 2010)	Mean daily diary anxiety	Drinks consumed per drinking day (count)	-0.078	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking motives- drinking to socialise or enhance (Grant et al. 2009)	Daily anxious mood	Daily alcohol use, capped at 6 (continuous)	-0.31	Unstandardised coefficient	0.11	S.E	Sig.	142	-0.230	-0.230 (-0.380 to -0.068)	--	--
Drinking motives- drinking to socialise or enhance (Grant et al. 2009)	Daily anxious mood	Daily alcohol use, capped at 6 (continuous)	0.07	Unstandardised coefficient	0.1	S.E	Not sig.	142	0.059	0.059 (-0.107 to 0.221)	--	--
Drinking motives- drinking to socialise or enhance (Littlefield et al. 2012)	Anxiety symptoms	Onset of any drinking (binary)	Not reported	-	Not reported	-	Not sig.	1152	--	--	--	--
Drinking motives- drinking to socialise or enhance (Littlefield et al. 2012)	Anxiety symptoms	Onset of heavy episodic drinking (binary)	Not reported	-	Not reported	-	Not sig.	1152	--	--	--	--
Drinking motives- drinking to socialise or enhance (Littlefield et al. 2012)	Anxiety symptoms	Onset of intoxication (binary)	Not reported	-	Not reported	-	Not sig.	1152	--	--	--	--
Embarrassing event (O'Grady et al. 2011)	Social anxiety symptoms	Same day drinking (continuous)	0.02	Unstandardised coefficient	0.04	S.E	Not sig.	476	0.023	0.023 (-0.067 to 0.113)	--	--
Embarrassing event (O'Grady et al. 2011)	Social anxiety symptoms	Same evening drinking (continuous)	-0.02	Unstandardised coefficient	0.01	S.E	Sig.	476	-0.091	-0.091 (-0.180 to -0.001)	--	--
Embarrassing event (O'Grady et al. 2011)	Social anxiety symptoms	Next day drinking (continuous)	-0.01	Unstandardised coefficient	0.04	S.E	Not sig.	476	-0.011	-0.011 (-0.101 to 0.079)	--	--

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Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
Embarrassing event (O'Grady et al. 2011)	Social anxiety symptoms	Next evening drinking (continuous)	-0.01	Unstandardised coefficient	0.01	S.E	Not sig.	476	-0.046	-0.046 (-0.135 to 0.044)	--	--
Conduct disorder symptoms (Pardini et al. 2007)	Anxiety and withdrawal symptoms	Alcohol use disorder symptoms (binary)	0.817	OR	0.581, 1.149	CI	Not sig.	506	--	--	-0.052	-0.052 (-0.138 to 0.036)
Conduct disorder symptoms (Pardini et al. 2007)	Anxiety and withdrawal symptoms	Alcohol use disorder symptoms (count)	0.978	Incident rate ratio	0.889, 1.078	CI	Not sig.	506	--	--	--	--
Conduct disorder symptoms (Pardini et al. 2007)	Anxiety and withdrawal symptoms	Alcohol abuse disorder only (binary)	1.138	Relative Risk Ratio	0.826, 1.567	CI	Not sig.	506	--	--	--	--
Conduct disorder symptoms (Pardini et al. 2007)	Anxiety and withdrawal symptoms	Alcohol dependence disorder only (binary)	1.048	Relative Risk Ratio	0.795, 1.384	CI	Not sig.	506	--	--	--	--
Anticipatory anxiety (Cloutier et al. 2019)	Social anxiety symptoms	Alcohol use initiation onset (binary)	0.03	Unstandardised coefficient	0.01	S.E	Sig.	104	0.282	0.282 (0.095 to 0.450)	--	--
Post task anxiety (Cloutier et al. 2019)	Social anxiety symptoms	Alcohol use initiation onset (binary)	0.02	Unstandardised coefficient	0.01	S.E	Not sig.	104	0.192	0.192 (0.000 to 0.371)	--	--
Externalising symptoms (Colder et al. 2017)	Generalised anxiety symptoms	Drinks per year (binary)	-0.19	Unstandardised coefficient	0.06	S.E	Sig.	387	-0.159	-0.159 (-0.255 to -0.060)	--	--
Externalising symptoms (Colder et al. 2017)	Generalised anxiety symptoms	Drinks per year (continuous)	-0.15	Unstandardised coefficient	0.02	S.E	Sig.	387	-0.356	-0.356 (-0.440 to -0.266)	--	--
Externalising symptoms (Colder et al. 2017)	Generalised anxiety symptoms	Alcohol problems (continuous)	-0.08	Unstandardised coefficient	0.01	S.E	Sig.	387	-0.377	-0.377 (-0.459 to -0.288)	--	--
Externalising symptoms (Colder et al. 2017)	Social anxiety symptoms	Drinks per year (continuous)	-0.16	Unstandardised coefficient	0.01	S.E	Sig.	387	-0.631	-0.631 (-0.687 to -0.567)	--	--
Externalising symptoms (Colder et al. 2017)	Social anxiety symptoms	Alcohol problems (continuous)	0.08	Unstandardised coefficient	0.04	S.E	Sig.	387	0.101	0.101 (0.001 to 0.199)	--	--
Impulsivity (Bilevicius et al. 2021)	Social anxiety symptoms	Weekly alcohol use (quantity x frequency) (continuous)	-0.005	Stand. Coef.	0.013	S.E	Not sig.	297	-0.022	-0.022 (-0.136 to 0.092)	--	--
Impulsivity (Bilevicius et al. 2021)	Social anxiety symptoms	Alcohol related problems	0.01	Stand. Coef.	0.003	S.E	Sig.	297	0.190	0.190 (0.078 to 0.297)	--	--
Impulsivity (Mackie et al. 2011)	Anxiety symptoms	Alcohol use (continuous)	-0.74	Unstandardised coefficient	0.36	S.E	Not sig.	393	-0.103	-0.103 (-0.200 to -0.004)	--	--
Sensation seeking (Mackie et al. 2011)	Anxiety symptoms	Alcohol use (continuous)	-0.31	Unstandardised coefficient	0.27	S.E	Not sig.	393	-0.058	-0.058 (-0.156 to 0.041)	--	--
Urgency (Marmorstein et al. 2015)	Anxiety symptoms	Alcohol use frequency (continuous)	0	Parameter estimate	0	S.E	Not sig.	144	--	--	--	--
Urgency (Marmorstein et al. 2015)	Social anxiety symptoms	Alcohol use frequency (continuous)	0	Parameter estimate	0.01	S.E	Not sig.	144	--	--	--	--
Perceptions of peer alcohol use (Buckner et al. 2009)	Social anxiety disorder	Alcohol use disorder	0.56	OR	0.28, 1.14	CI	Not sig.	544	--	--	-0.069	-0.069 (-0.153 to 0.015)
Perceptions of peer alcohol use (Pedersen et al. 2013)	Anxiety symptoms	Alcohol related consequences (continuous)	-0.04	Unstandardised coefficient	0.02	S.E	Not sig.	193	--	--	--	--
Social familiarity with surrounding individuals (Caumiant et al. 2023)	Social anxiety symptoms	Estimated breath alcohol concentration (eBrAC) (continuous)	-0.004	Unstandardised coefficient	Not reported	-	Sig.	48	--	--	--	--
Social familiarity with surrounding individuals (Caumiant et al. 2023)	Social anxiety, fear specific symptoms	Estimated breath alcohol concentration (eBrAC) (continuous)	-0.009	Unstandardised coefficient	Not reported	-	Sig.	48	--	--	--	--
Social familiarity with surrounding individuals (Caumiant et al. 2023)	Social anxiety, avoidance specific symptoms	Estimated breath alcohol concentration (eBrAC) (continuous)	-0.005	Unstandardised coefficient	Not reported	-	Not sig.	48	--	--	--	--
Social familiarity with surrounding individuals (Caumiant et al. 2023)	Social anxiety symptoms	Quantity of alcohol consumed within drinking episode (continuous)	-0.003	Unstandardised coefficient	Not reported	-	Sig.	48	--	--	--	--
Social familiarity with surrounding individuals (Caumiant et al. 2023)	Social anxiety symptoms	Drinking versus not drinking (binary)	-0.001	Unstandardised coefficient	Not reported	-	Not sig.	48	--	--	--	--

									Conversion From un/standardised regression		Conversion from OR	
Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
Negative family interactions (Buckner et al. 2009)	Social anxiety disorder	Alcohol use disorder	0.68	OR	0.46, 1.00	CI	Sig.	544	--	--	-0.083	-0.083 (-0.166 to 0.001)
Self-reported offending (non-drug related) (Nichter et al. 2015)	Worry	Typical quantity of drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Self-reported offending (non-drug related) (Nichter et al. 2015)	Worry	Frequency of binge drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Self-reported offending (non-drug related) (Nichter et al. 2015)	Worry	Alcohol dependence symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Self-reported offending (non-drug related) (Nichter et al. 2015)	Physiological anxiety symptoms	Typical quantity of drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Self-reported offending (non-drug related) (Nichter et al. 2015)	Physiological anxiety symptoms	Frequency of binge drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Self-reported offending (non-drug related) (Nichter et al. 2015)	Physiological anxiety symptoms	Alcohol dependence symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Worry	Typical quantity of drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Worry	Frequency of binge drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Worry	Alcohol dependence symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Physiological anxiety symptoms	Typical quantity of drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Physiological anxiety symptoms	Frequency of binge drinking (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Physiological anxiety symptoms	Alcohol dependence symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	818	--	--	--	--
Partner support (Buckner et al. 2009)	Social anxiety disorder	Alcohol use disorder	1.24	OR	0.97, 1.59	CI	Not sig.	544	--	--	0.073	0.073 (-0.011 to 0.156)
Peer social support (Buckner et al. 2009)	Social anxiety disorder	Alcohol use disorder	0.82	OR	0.59, 1.13	CI	Not sig.	544	--	--	-0.051	-0.051 (-0.135 to 0.033)
Family cohesion (Buckner et al. 2009)	Social anxiety disorder	Alcohol use disorder	0.65	OR	0.44, 0.96	CI	Sig.	544	--	--	-0.093	-0.093 (-0.175 to -0.009)
Maternal support (Gorka et al. 2014)	Anxiety disorder	Alcohol use disorder (binary)	0.91	Hazard ratio	0.86, 0.96	CI	Sig.	817	--	--	-0.117	-0.117 (-0.184 to -0.049)
Parent support (Buckner et al. 2009)	Social anxiety disorder	Alcohol use disorder	0.83	OR	0.64, 1.09	CI	Not sig.	544	--	--	-0.059	-0.059 (-0.142 to 0.025)
Paternal support (Gorka et al. 2014)	Anxiety disorder	Alcohol use disorder (binary)	0.96	Hazard ratio	0.92, 1.02	CI	Not sig.	817	--	--	-0.054	-0.054 (-0.122 to 0.014)
Community cohesion (Schleider et al. 2019)	Anxiety severity	Alcohol use (binary)	Not reported	-	Not reported	-	Not sig.	2100	--	--	--	--
Low neighbourhood safety (Schleider et al. 2019)	Anxiety severity	Alcohol use (binary)	Not reported	-	Not reported	-	Not sig.	2100	--	--	--	--
Socioeconomic status (Schleider et al. 2019)	Anxiety severity	Alcohol use (binary)	Not reported	-	Not reported	-	Not sig.	2100	--	--	--	--
Time (follow-up) (Dahne et al. 2014)	Social phobia symptoms	Alcohol use (binary)	1.03	OR	0.99, 1.06	CI	Not sig.	277	--	--	0.102	0.102 (-0.016 to 0.217)

									Conversion From un/standardised regression		Conversion from OR	
Moderator (Author, Year)	**Predictor**	**Outcome**	**Metric of interaction (effect)**	**Effect size metric (type)**	**Measure of variance**	**Variance metric (Type)**	**Sig./Not sig.**	**N**	**R**	**Fisher's Z With CI**	**R**	**Fisher's Z With CI**
Time (follow-up) (Marmorstein et al. 2010)	Anxiety symptoms	Age at first use of alcohol (continuous)	Not reported	-	Not reported	-	Not sig.	503	--	--	--	--
Time (follow-up) (Marmorstein et al. 2010)	Social anxiety symptoms	Age at first use of alcohol (continuous)	Not reported	-	Not reported	-	Not sig.	503	--	--	--	--

Table A10: Complete moderation effects in the alcohol → anxiety relationship (n =34). Original and transformed statistics.

Moderator (Author, Year)	Predictor	Outcome	Metric of interaction (effect)	Effect size metric (type)	Measure of variance	Variance metric (Type)	Sig./ Not sig.	N	Conversion From un/standardised		Conversion from OR	
									R	Fisher's Z With CI	R	Fisher's Z With CI
Gender (Mackie et al. 2011)	Alcohol use	Anxiety symptoms (continuous)	0.01	Unstandardised coefficient	0.01	S.E	Not sig.	393	0.050	0.050 (-0.049 to 0.149)	- -	--
Gender (Parrish et al. 2016)	Frequency of alcohol use	Anxiety symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	620	--	--	- -	--
Gender (Parrish et al. 2016)	Frequency of alcohol use	Anxious arousal symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	620	--	--	- -	--
Sex (Carvalho et al. 2018)	Alcohol consumption level (non-drinker/light or moderate drinker/heavier drinker)	Incident anxiety (new case of anxiety) (binary)	Not reported	-	Not reported	-	Not sig.	1418	--	--	- -	--
Sex (Carvalho et al. 2018)	Alcohol consumption level (non-drinker/light or moderate drinker/heavier drinker)	Persistent anxiety	Not reported	-	Not reported	-	Not sig.	1418	--	--	- -	--
Sex (Carvalho et al. 2018)	Problem drinking (non-drinker/non-problem drinker/problem drinker)	Incident anxiety (new case of anxiety) (binary)	Not reported	-	Not reported	-	Not sig.	4461	--	--	- -	--
Sex (Carvalho et al. 2018)	Problem drinking (non-drinker/non-problem drinker/problem drinker)	Persistent anxiety	Not reported	-	Not reported	-	Not sig.	4461	--	--	- -	--
Generational status (Mexican) (Parrish et al. 2016)	Frequency of alcohol use	Anxiety symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	620	--	--	- -	--
Generational status (Mexican) (Parrish et al. 2016)	Frequency of alcohol use	Anxious arousal symptoms (continuous)	Not reported	-	Not reported	-	Sig.	620	--	--	- -	--
Alcohol outcome expectancies-tension reduction (Abrams et al. 2021)	Alcohol dose (placebo vs control)	Anxiety (state) (continuous)	0.294	Unstandardised coefficient	0.148	S.E	Not sig.	53	0.263	0.263 (-0.008 to 0.498)	- -	--
Alcohol outcome expectancies-tension reduction (Abrams et al. 2021)	Alcohol dose (placebo vs control)	Anxiety (state) (continuous)	0.336	Unstandardised coefficient	0.144	S.E	Sig.	53	0.305	0.305 (0.038 to 0.532)	- -	--
Anxiety sensitivity (Abrams et al. 2021)	Alcohol dose (placebo vs control)	Anxiety (state) (continuous)	-0.179	Unstandardised coefficient	0.079	S.E	Sig.	53	-0.297	-0.297 (-0.525 to -0.029)	- -	--
Anxiety sensitivity (Mackie et al. 2011)	Alcohol use	Anxiety symptoms (continuous)	0.01	Unstandardised coefficient	0.01	S.E	Not sig.	393	0.050	0.050 (-0.049 to 0.149)	- -	--
History of past Anxiety (Cook et al. 2024)	Alcohol use disorder (at time of type 2 diabetes diagnosis)	New episode of anxiety disorder	Not reported	-	Not reported	--	Sig.	439494	--	--	- -	--
Sustained attention (Sher et al. 2007)	Drink group (alcohol or placebo)	Subjective anxiety change (continuous)	0.08	Standardised coefficient	Not reported	-	Not sig.	101	--	--	- -	--
Attentional engagement and expectancy (Steele et al. 1986)	Alcohol beverage group (alcohol/slides/expectancy vs. alcohol/slides/no expectancy vs. alcohol/no slides)	Anxiety symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	62	--	--	- -	--
Hopelessness (Mackie et al. 2011)	Alcohol use	Anxiety symptoms (continuous)	0.01	Unstandardised coefficient	0.01	S.E	Not sig.	393	0.050	0.050 (-0.049 to 0.149)	- -	--
Major depressive disorder (Wojciechowski et al. 2024)	Heavy episodic drinking frequency	Anxiety symptoms in adolescence	-0.153	Unstandardised coefficient	-0.291, -0.014	CI	Sig.	1001	--	--	- -	--
Major depressive disorder (Wojciechowski et al. 2024)	Heavy episodic drinking frequency	Anxiety symptoms in emerging adulthood	-0.207	Unstandardised coefficient	-0.387, -0.027	CI	Sig.	1001	--	--	- -	--
Drink and stress task order (Sayette et al. 2001)	Drink group (alcohol or placebo)	State anxiety (continuous)	Not reported	-	Not reported	-	Not sig.	169	--	--	- -	--
Distracting activity (Steele et al. 1986)	Alcohol beverage group (alcohol vs placebo)	Anxiety symptoms (continuous)	Not reported	-	Not reported	-	Not sig.	71	--	--	- -	--

Moderator (Author, Year)	Predictor	Outcome	Metric of interaction (effect)	Effect size metric (type)	Measure of variance	Variance metric (Type)	Sig./ Not sig.	N	Conversion From un/standardised		Conversion from OR	
									R	Fisher's Z With CI	R	Fisher's Z With CI
Impulsivity (Mackie et al. 2011)	Alcohol use	Anxiety symptoms (continuous)	0.01	Unstandardised coefficient	0.01	S.E	Not sig.	393	0.050	0.050 (-0.049 to 0.149)	-	--
Sensation seeking (Mackie et al. 2011)	Alcohol use	Anxiety symptoms (continuous)	0.01	Unstandardised coefficient	0.01	S.E	Not sig.	393	0.050	0.050 (-0.049 to 0.149)	-	--
Drink was alone (Armeli et al. 2014)	Episode specific drinking to cope (continuous)	Anxiety symptoms the day after drinking episode (continuous)	0.011	Standardised coefficient	Not reported	-	Not sig.	142 1	--	--	-	--
Drink was alone (Armeli et al. 2014)	Episode specific drinking to cope (continuous)	Anxiety symptoms the day after drinking episode (continuous)	-0.004	Standardised coefficient	Not reported	-	Not sig.	142 1	--	--	-	--
Drinking was with others (Armeli et al. 2014)	Episode specific drinking to cope (continuous)	Anxiety symptoms the day after drinking episode (continuous)	-0.009	Standardised coefficient	Not reported	-	Not sig.	142 1	--	--	-	--
Drinking was with others (Armeli et al. 2014)	Episode specific drinking to cope (continuous)	Anxiety symptoms the day after drinking episode (continuous)	-0.017	Standardised coefficient	Not reported	-	Not sig.	142 1	--	--	-	--
Time (during experimental phase) (Stevens et al. 2014)	Alcohol beverage group (alcohol expected, alcohol not expected, placebo)	Anxiety symptoms	2.39	F-statistic	Not reported	-	Sig.	95	--	--	-	--
Time (linear) (Ferariu et al. 2024)	Low vs high alcohol sipping latent class	Anxiety symptoms	0	Unstandardised coefficient	Not reported	-	Not sig.	118 68	--	--	-	--
Time (linear) (Ferariu et al. 2024)	No vs high alcohol sipping latent class	Anxiety symptoms	-0.08	Unstandardised coefficient	Not reported	-	Not sig.	118 68	--	--	-	--
Time (pre to post beverage phase) (Abrams et al. 2001)	Alcohol beverage group (alcohol expected, alcohol not expected, placebo)	Performance anxiety: visual analogue scale	Not reported	-	Not reported	-	Sig.	61	--	--	-	--
Time (pre to post beverage phase) (Abrams et al. 2001)	Alcohol beverage group (alcohol expected, alcohol not expected, placebo)	Performance anxiety: post-speech audience anxious scale	Not reported	-	Not reported	-	Sig.	61	--	--	-	--
Time (quadratic) (Ferariu et al. 2024)	Low vs high alcohol sipping latent class	Anxiety symptoms	-0.01	Unstandardised coefficient	Not reported	-	Not sig.	118 68	--	--	-	--
Time (quadratic) (Ferariu et al. 2024)	No vs high alcohol sipping latent class	Anxiety symptoms	0	Unstandardised coefficient	Not reported	-	Not sig.	118 68	--	--	-	--

Table A11: Complete complex effects grouped by analysis type. Original and derived statistics.

Variable (Author, Year)	Predictor	Outcome	Metric of effect	Effect size metric (type)	Measure of variance	Variance metric (Type)	Sig./Not sig.	N	Conversion From un/standardised regression		Conversion from OR	
									R	Fisher's Z With CI	R	Fisher's Z With CI
Multiple mediation												
Expectancies for not drinking & Perceptions of peer alcohol use (male only model) (Bekman et al. 2010)	Social anxiety symptoms	Drinking initiation (binary)	0.81	OR	0.06	S.E	Sig.	677	--	--	-0.134	-0.134 (-0.207 to -0.059)
Expectancies for not drinking & Perceptions of peer alcohol use (female only model) (Bekman et al. 2010)	Social anxiety symptoms	Drinking initiation (binary)	0.79	OR	0.08	S.E	Sig.	591	--	--	-0.121	-0.121 (-0.199 to -0.040)
Rumination & Worry (Wolitzky-Taylor et al. 2012)	Anxiety disorder severity	Alcohol use disorder symptoms severity (continuous)	Not reported	-	Not reported	-	Not sig.	232	--	--	--	--
Moderated-mediation effects												
Anxiety symptoms (mediator) & Race/ethnicity (moderator) (Paulus et al. 2016)	Anxiety sensitivity	Alcohol problems (continuous)	Not reported	-	Not reported	-	Not sig.	3396	--	--	--	--
Moderated moderation effects (3-way interactions)												
Drinking to cope & Drinking to socialise or enhance motives (Armeli et al. 2010)	Anxiety symptoms-daily mean	Drinking frequency- monthly (diary)	0.046	Unstandardised coefficient	Not reported	-	Sig.	530	--	--	--	--
Drinking to cope & Drinking to socialise or enhance motives (Armeli et al. 2010)	Anxiety symptoms-daily mean	Drinking frequency- monthly (retrospective)	0.23	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking to cope & Drinking to socialise or enhance motives (Armeli et al. 2010)	Anxiety symptoms-daily mean	Drinking quantity-monthly (diary)	-0.068	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking to cope & Drinking to socialise or enhance motives (Armeli et al. 2010)	Anxiety symptoms-daily mean	Drinking quantity-monthly (retrospective)	-0.08	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking to cope & Drinking to socialise or enhance motives (Armeli et al. 2010)	Anxiety symptoms-daily	Any drinking (binary)	-0.004	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Drinking to cope & Drinking to socialise or enhance motives (Armeli et al. 2010)	Anxiety symptoms-daily	Drinks per drinking day	0.055	Unstandardised coefficient	Not reported	-	Not sig.	530	--	--	--	--
Externalising symptoms & Age (Colder et al. 2017)	Anxiety symptoms	Drinks per year (count)	0.01	Unstandardised coefficient	0	S.E	Sig.	387	--	--	--	--
Externalising symptoms & Age (Colder et al. 2017)	Social anxiety symptoms	Drinks per year (count)	0.02	Unstandardised coefficient	0	S.E	Sig.	387	--	--	--	--
Externalising symptoms & Age (Colder et al. 2017)	Social anxiety symptoms	Drinking problems (count)	-0.02	Unstandardised coefficient	0.01	S.E	Sig.	387	-0.101	-0.101 (-0.199 to -0.001)	--	--
Task switching & Age (Dvorak et al. 2014)	Daytime anxious mood	Drinking likelihood (binary)	1.1	OR	Not reported	-	Sig.	100	--	--	--	--
Task switching & Age (Dvorak et al. 2014)	Daytime anxious mood	Level of intoxication (continuous)	-0.004	Unstandardised coefficient	Not reported	-	Not sig.	100	--	--	--	--
Sustained attention & Age (Dvorak et al. 2014)	Daytime anxious mood	Drinking likelihood (binary)	5.646	OR	Not reported	-	Sig.	100	--	--	--	--
Sustained attention & Age (Dvorak et al. 2014)	Daytime anxious mood	Level of intoxication (continuous)	0.201	Unstandardised coefficient	Not reported	-	Sig.	100	--	--	--	--
Perceptions of peer alcohol use & Year (O'Grady et al. 2011)	Social anxiety symptoms	Drinking quantity	-0.01	Unstandardised coefficient	0	S.E	Not sig.	574	--	--	--	--

Tension reduction alcohol outcome expectancies & Sex (Richton et al. 2017)	Social anxiety symptoms	Any drinking (binary)	0.21	Unstandardised coefficient	0.09	S.E	Sig.	537	0.100	0.100 (0.016 to 0.183)	--	--
Drinking to cope motives & past month drinking (Armeli et al. 2014)	Anxiety symptoms	Drinking related problems (continuous)	0.05	Unstandardised coefficient	0.019	S.E	Sig.	844	0.090	0.090 (0.023 to 0.157)	--	--
Drinking to cope motives & past month drinking (Armeli et al. 2014)	Anxiety symptoms monthly changes	Drinking related problems (continuous)	0.025	Unstandardised coefficient	0.072	S.E	Not sig.	844	0.012	0.012 (-0.056 to 0.079)	--	--
Social anxiety & Time (Stevens et al. 2014)	Alcohol beverage group (alcohol expected, alcohol not expected, placebo)	Trait anxiety	2.68	F-statistic	Not reported	-	Sig.	95	0.166	0.167 (-0.036 to 0.357)	--	--
Drink-activity order & gender (Abrams et al. 2002)	Anxiety activity session (anxiety vs reading challenge)	Alcoholic drink choice (weak, moderate or strong)	4.24	F-statistic	Not reported	-	Sig.	44	0.296	0.306 (0.010 to 0.552)	--	--
Distracted or non-distracted activity group & State anxiety measurement timepoints (4) (Steele et al. 1988)	Alcohol beverage group (alcohol vs placebo)	State anxiety	9.367	F-statistic	Not reported	-	Sig.	40	0.436	0.467 (0.182 to 0.679)	--	--
Distracted or non-distracted activity group & State anxiety measurement timepoints(2) (Steele et al. 1988)	Alcohol beverage group (alcohol vs placebo)	State anxiety	18.11	F-statistic	Not reported	-	Sig.	40	0.558	0.630 (0.397 to 0.787)	--	--
Distracted or non-distracted activity group & State anxiety measurement timepoint (4) (Steele et al. 1988)	Alcohol beverage group (alcohol vs placebo)	State anxiety	3.65	F-statistic	Not reported	-	Sig.	37	0.300	0.309 (-0.017 to 0.576)	--	--
Distracted or non-distracted activity group & State anxiety measurement timepoint (2) (Steele et al. 1988)	Alcohol beverage group (alcohol vs placebo)	State anxiety	6.27	F-statistic	Not reported	-	Sig.	37	0.381	0.401 (0.088 to 0.642)	--	--

Table A12: Mediation anxiety → alcohol significance counts and magnitude of effect size classification.

Mediator super-ordinate theme	Mediator subtheme	Effect label assigned *Predictor → Outcome | Mediator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
Psychological	Anxiety sensitivity/ Anxiety	Anxiety sensitivity → Alcohol problems | Anxiety (wave 2) (Paulus et al. 2021)	Significant	0.040 (0.006 to 0.073)	Small Positive
		Anxiety sensitivity → Alcohol problems | Anxiety (wave 3) (Paulus et al. 2021)	Significant	0.025 (-0.009 to 0.058)	Small Positive
		Subtheme total	*0 neg / 0 not sig / 2 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 0 NS : 2 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Depression	Anxiety sensitivity → Alcohol use frequency | Depressive symptoms (McCarty et al. 2023)	Not Significant	0.069 (-0.035 to 0.171)	NS
		Anxiety sensitivity → Alcohol use quantity | Depressive symptoms (McCarty et al. 2023)	Not Significant	0.091 (-0.012 to 0.193)	NS
		Anxiety sensitivity → Alcohol use problems | Depressive symptoms (McCarty et al. 2023)	Significant	0.136 (0.034 to 0.236)	Small Positive
		Subtheme total	*0 neg / 2 not sig / 1 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 1 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Drinking motives: conformity	Social avoidance → Alcohol problems | Drinking motives: conformity (Collins et al. 2018)	Not Significant	0.066 (-0.067 to 0.197)	NS
		Anxiety sensitivity → Alcohol problems | Drinking motives: conformity (between-subject model) (Mackinnon et al. 2014)	Not Significant	0.095 (-0.018 to 0.206)	NS
		Anxiety sensitivity → Alcohol problems | Drinking motives: conformity (within-subject model) (Mackinnon et al. 2014)	Not Significant	0.068 (-0.046 to 0.179)	NS
		Subtheme total	*0 neg / 3 not sig / 0 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 3 NS : 0 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Drinking motives: drinking to cope	Social avoidance → Alcohol problems | Drinking motives: Drinking to cope with anxiety (Collins et al. 2018)	Not Significant	-0.141 (-0.269 to -0.009)	NS
		Anxiety sensitivity → Alcohol problems | Drinking motives: Drinking to cope with anxiety (between-subject model) (Mackinnon et al. 2014)	Not Significant	-0.014 (-0.127 to 0.099)	NS
		Anxiety sensitivity → Alcohol problems | Drinking motives: Drinking to cope with anxiety (within-subject model) (Mackinnon et al. 2014)	Not Significant	-0.048 (-0.160 to 0.065)	NS
		Social avoidance → Alcohol problems | Drinking motives: Drinking to cope with depression (Collins et al. 2018)	Significant	0.127 (-0.006 to 0.255)	Small Positive
		Anxiety sensitivity → Alcohol problems | Drinking motives: Drinking to cope with depression (between-subject model) (Mackinnon et al. 2014)	Not Significant	0.173 (0.062 to 0.281)	NS
		Anxiety sensitivity → Alcohol problems | Drinking motives: Drinking to cope with depression (within-subject model) (Mackinnon et al. 2014)	Not Significant	0.038 (-0.076 to 0.150)	NS
		Subtheme total	*0 neg / 5 not sig / 1 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 5 NS : 1 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Drinking motives: drinking to socialise or enhance	Social avoidance → Alcohol problems | Drinking motives: enhancement (Collins et al. 2018)	Not Significant	0.075 (-0.058 to 0.206)	NS
		Social avoidance → Alcohol problems | Drinking motives: social (Collins et al. 2018)	Not Significant	0.088 (-0.045 to 0.218)	NS
		Subtheme total	*0 neg / 2 not sig / 0 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 0 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Emotion dysregulation	Anxious attachment → Alcohol problems | Emotion dysregulation (Goldstein et al. 2019)	Significant	0.142 (0.004 to 0.274)	Small Positive
		Subtheme total	*0 neg / 0 not sig / 1 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 0 NS : 1 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Expectancies for not drinking	Social anxiety symptoms → Initiation of alcohol use | Expectancies for not drinking (Bekman et al. 2010)	Significant	-0.107 (-0.180 to -0.031)	Small Negative
		Social anxiety symptoms → Initiation of alcohol use | Expectancies for not drinking (Bekman et al. 2010)	Not Significant	-0.012 (-0.092 to 0.069)	NS

Mediator super-ordinate theme	Mediator subtheme	Effect label assigned *Predictor → Outcome | Mediator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
Socio-environmen-		***Subtheme total***	*1 neg / 1 not sig / 0 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 1 SNeg : 1 NS : 0 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Interpersonal difficulties	Anxious attachment → Alcohol problems | Interpersonal difficulties (Goldstein et al. 2019)	Significant	0.129 (-0.009 to 0.262)	Small Positive
		Subtheme total	*0 neg / 0 not sig / 1 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 0 NS : 1 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Perceptions of peer alcohol use	Social anxiety symptoms → Initiation of alcohol use | Perceptions of peer alcohol use (Bekman et al. 2010)	Not Significant	-0.052 (-0.127 to 0.023)	NS
		Social anxiety symptoms → Initiation of alcohol use | Perceptions of peer alcohol use (Bekman et al. 2010)	Not Significant	-0.042 (-0.122 to 0.039)	NS
		Subtheme total	*0 neg / 2 not sig / 0 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 0 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Repetitive negative thinking	Anxiety disorder severity → Alcohol use disorder symptoms severity | Rumination (Wolitzky-Taylor et al. 2021)	Significant	0.132 (0.003 to 0.256)	Small Positive
		Anxiety disorder severity → Alcohol use disorder symptoms severity | Worry (Wolitzky-Taylor et al. 2021)	Not Significant	0.051 (-0.078 to 0.179)	NS
		Subtheme total	*0 neg / 1 not sig / 1 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 1 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Negative life events	Social anxiety disorder → Alcohol use disorder | Negative life events (Buckner et al. 2009)	Not Significant	-0.116 (-0.199 to -0.033)	NS
		Subtheme total	*0 neg / 1 not sig / 0 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 0 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
Grand total			1 neg / 17 not sig / 7 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 1 SNeg : 17 NS : 7 Spos : 0 MPos : 0 LPos / 0 Sig w/o z	

Table A13: Mediation alcohol → anxiety significance counts and magnitude of effect size classification.

Mediator super-ordinate theme	Mediator subtheme	Effect label assigned ***Predictor → Outcome | Mediator***	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
Psychological	**Anxiety sensitivity/ Anxiety**	Alcohol problems (wave 1) → Anxiety sensitivity (wave 3) | Anxiety (wave 2) (Paulus et al. 2021)	Not Significant	0.017 (-0.016 to 0.051)	NS
		Alcohol problems (wave 2) → Anxiety sensitivity (wave 4) | Anxiety (wave 3) (Paulus et al. 2021)	Not Significant	0.017 (-0.016 to 0.051)	NS
		Subtheme total	*0 neg / 2 not sig / 0 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 0 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Attentional processes	Alcohol dose (placebo vs control) → Anxiety symptoms | Sustained attention (Sher et al. 2007)	Not Significant	N/A	NS
		Subtheme total	*0 neg / 1 not sig / 0 pos / 0 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 0 Spos : 0 MPos : 0 LPos / 0 Sig w/o z*	
	Other	Alcohol beverage group (alcohol expected, alcohol not expected, placebo) → Anxiety symptoms | Change in negative thoughts (Abrams et al. 2002)	Significant	N/A	Sig w/o Z
		Alcohol beverage group (alcohol expected, alcohol not expected, placebo) → Anxiety symptoms | Change in positive thoughts (Abrams et al. 2002)	Significant	N/A	Sig w/o Z
		Subtheme total	*0 neg / 0 not sig / 0 pos / 2 sig w/o value*	*0 LNeg : 0 MNeg : 0 SNeg : 0 NS : 0 Spos : 0 MPos : 0 LPos / 2 Sig w/o z*	
Grand total			0 neg / 3 not sig / 0 pos / 2 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 3 NS : 0 Spos : 0 MPos : 0 LPos / 2 Sig w/o z	

Table A14: Moderation anxiety → alcohol significance counts and magnitude of effect size classification.

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
Biological	Age	Anxiety symptoms (recent) → Alcohol use initiation | Age (Cerda et al. 2013)	Not Significant	N/A	NS
		Anxiety symptoms (cumulative) → Alcohol use initiation | Age (Cerda et al. 2013)	Not Significant	N/A	NS
		Generalised anxiety symptoms → Drinks per year (continuous) | Age (Colder et al. 2017)	Significant	N/A	Sig w/o Z
		Social anxiety symptoms → Drinks per year (continuous) | Age (Colder et al. 2017)	Significant	N/A	Sig w/o Z
		Social anxiety symptoms → Alcohol problems (continuous) | Age (Colder et al. 2017)	Significant	-0.151 (-0.247 to -0.052)	Small Negative
		Anxiety disorder → Alcohol use disorder | Age (Cheng et al. 2004)	Not Significant	-0.142 (-0.228 to -0.055)	NS
		Anxiety disorder → Alcohol use disorder | Age (Cheng et al. 2004)	Significant	-0.280 (-0.359 to -0.196)	Small Negative
		Subtheme total	1 neg / 3 not sig / 3 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 2 SNeg : 3 NS : 0 SPos : 0 MPos : 0 LPos / 2 Sig w/o z	
	Gender/ sex	Social anxiety symptoms → Alcohol use quantity (continuous) | Gender (Colder et al. 2019)	Not Significant	N/A	NS
		Social phobia symptoms → Alcohol use (binary) | Gender (Dahne et al. 2014)	Not Significant	N/A	NS
		Anxiety symptoms → Frequency of alcohol use | Gender (Parrish et al. 2016)	Not Significant	N/A	NS
		Anxious arousal symptoms → Frequency of alcohol use | Gender (Parrish et al. 2016)	Not Significant	N/A	NS
		Anxiety sensitivity- Cognitive concerns → Alcohol use disorder (binary) | Gender (Schimdt et al. 2007)	Not Significant	0.046 (-0.051 to 0.143)	NS
		Anxiety sensitivity- Physical concerns → Alcohol use disorder (binary) | Gender (Schimdt et al. 2007)	Not Significant	0.023 (-0.075 to 0.120)	NS
		Anxiety sensitivity- Social concerns → Alcohol use disorder (binary) | Gender (Schimdt et al. 2007)	Not Significant	0.011 (-0.087 to 0.108)	NS
		Anxiety sensitivity → Alcohol use disorder (binary) | Gender (Schimdt et al. 2007)	Not Significant	0.061 (-0.037 to 0.157)	NS
		Panic disorder with or without agoraphobia → Regular alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic disorder with or without agoraphobia → Hazardous alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic disorder with or without agoraphobia → Alcohol use disorder: abuse without dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic disorder with or without agoraphobia → Alcohol use disorder: dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic disorder with or without agoraphobia → Alcohol use disorder: any (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic attack → Regular alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic attack → Hazardous alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome* | *Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
		Panic attack → Alcohol use disorder: abuse without dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic attack → Alcohol use disorder: dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic attack → Alcohol use disorder: any (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Regular alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Hazardous alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Alcohol use disorder: abuse without dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Alcohol use disorder: dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Alcohol use disorder: any (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Social phobia → Regular alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Social phobia → Hazardous alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Social phobia → Alcohol use disorder: abuse without dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Social phobia → Alcohol use disorder: dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Social phobia → Alcohol use disorder: any (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Regular alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Hazardous alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Alcohol use disorder: abuse without dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Alcohol use disorder: dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Alcohol use disorder: any (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Regular alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Hazardous alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Alcohol use disorder: abuse without dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Alcohol use disorder: dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Alcohol use disorder: any (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
		Generalised anxiety disorder → Regular alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Generalised anxiety disorder → Hazardous alcohol use (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Generalised anxiety disorder → Alcohol use disorder: abuse without dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Generalised anxiety disorder → Alcohol use disorder: dependence (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Generalised anxiety disorder → Alcohol use disorder: any (onset/progression at follow-up) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic disorder with or without agoraphobia → Regular alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic disorder with or without agoraphobia → Hazardous alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic disorder with or without agoraphobia → Alcohol use disorder: abuse without dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic disorder with or without agoraphobia → Alcohol use disorder: dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic disorder with or without agoraphobia → Alcohol use disorder: any (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic attack → Regular alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic attack → Hazardous alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic attack → Alcohol use disorder: abuse without dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic attack → Alcohol use disorder: dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Panic attack → Alcohol use disorder: any (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Regular alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Hazardous alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Alcohol use disorder: abuse without dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Alcohol use disorder: dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Agoraphobia without panic disorder → Alcohol use disorder: any (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Social phobia → Regular alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Social phobia → Hazardous alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Social phobia → Alcohol use disorder: abuse without dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
		Social phobia → Alcohol use disorder: dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Social phobia → Alcohol use disorder: any (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Regular alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Hazardous alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Alcohol use disorder: abuse without dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Alcohol use disorder: dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Specific phobia → Alcohol use disorder: any (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Hazardous alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Alcohol use disorder: abuse without dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Alcohol use disorder: dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Alcohol use disorder: any (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Generalised anxiety disorder → Regular alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Generalised anxiety disorder → Hazardous alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Generalised anxiety disorder → Alcohol use disorder: abuse without dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Generalised anxiety disorder → Alcohol use disorder: dependence (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Generalised anxiety disorder → Alcohol use disorder: any (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Not Significant	N/A	NS
		Phobia (not otherwise specified) → Regular alcohol use (persistence of lifetime) | Gender (Zimmermann et al. 2003)	Significant	N/A	Sig w/o Z
		Anxiety symptoms → Alcohol use (continuous) | Gender (Mackie et al. 2011)	Not Significant	0.071 (-0.028 to 0.168)	NS
		Anxiety symptoms → Alcohol consumption escalation (vs maintenance) early pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Alcohol consumption reduction (vs maintenance) early pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Alcohol consumption initiation (vs abstinence) early pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Alcohol consumption escalation (vs maintenance) late pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Alcohol consumption reduction (vs maintenance) late pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Alcohol consumption initiation (vs abstinence) late pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
		Anxiety symptoms → Binge drinking escalation (vs maintenance) early pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Binge drinking reduction (vs maintenance) early pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Binge drinking initiation (vs abstinence) early pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Binge drinking escalation (vs maintenance) late pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Binge drinking reduction (vs maintenance) late pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Anxiety symptoms → Binge drinking initiation (vs abstinence) late pandemic (binary) | Sex (Gohari et al. 2023)	Not Significant	N/A	NS
		Separation anxiety symptoms → Initiation of alcohol use (binary) | Sex (Kaplow et al. 2001)	Not Significant	0.041 (-0.024 to 0.104)	NS
		Anxiety symptoms (general & separation) → Initiation of alcohol use (binary) | Sex (Kaplow et al. 2001)	Not Significant	-0.014 (-0.078 to 0.051)	NS
		Anxiety symptoms → Initiation of alcohol use (binary) | Sex (Kaplow et al. 2001)	Not Significant	-0.030 (-0.094 to 0.034)	NS
		Subtheme total	0 neg / 93 not sig / 0 pos / 1 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 93 NS : 0 SPos : 0 MPos : 0 LPos / 1 Sig w/o z	
	Race/ethnicity	Anxiety symptoms → Frequency of alcohol use | Generational status (Mexican) (Parrish et al. 2016)	Not Significant	N/A	NS
		Anxious arousal symptoms → Frequency of alcohol use | Generational status (Mexican) (Parrish et al. 2016)	Not Significant	N/A	NS
		Anxiety severity → Alcohol use (binary) | Race (Black/white) (Schleider et al. 2019)	Not Significant	N/A	NS
		Worry → Typical quantity of drinking (continuous) | Race/ethnicity (Nichter et al. 2015)	Not Significant	N/A	NS
		Worry → Frequency of binge drinking (continuous) | Race/ethnicity (Nichter et al. 2015)	Not Significant	N/A	NS
		Worry → Alcohol dependence symptoms (continuous) | Race/ethnicity (Nichter et al. 2015)	Not Significant	N/A	NS
		Physiological anxiety symptoms → Typical quantity of drinking (continuous) | Race/ethnicity (Nichter et al. 2015)	Not Significant	N/A	NS
		Physiological anxiety symptoms → Frequency of binge drinking (continuous) | Race/ethnicity (Nichter et al. 2015)	Not Significant	N/A	NS
		Physiological anxiety symptoms → Alcohol dependence symptoms (continuous) | Race/ethnicity (Nichter et al. 2015)	Not Significant	N/A	NS
		Anxiety symptoms (recent) → Alcohol use initiation | Race/ethnicity (Black/other) (Cerda et al. 2013)	Not Significant	0.196 (0.107 to 0.282)	NS
		Anxiety symptoms (cumulative) → Alcohol use initiation | Race/ethnicity (Black/other) (Cerda et al. 2013)	Not Significant	N/A	NS
		Subtheme total	0 neg / 11 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 11 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
Psychological	**Alcohol outcome expectancies: negative**	Social anxiety symptoms → Drinks per drinking day (count) | Impairment alcohol expectancies (daily) (Richton et al. 2017)	Not Significant	0.000 (-0.086 to 0.086)	NS
		Yearly social anxiety symptoms → Drinks per drinking day (count) | Impairment alcohol expectancies (daily) (Richton et al. 2017)	Not Significant	0.000 (-0.086 to 0.086)	NS
		Social anxiety symptoms → Any drinking (binary) | Impairment alcohol expectancies (daily) (Richton et al. 2017)	Not Significant	-0.043 (-0.127 to 0.042)	NS
		Yearly social anxiety symptoms → Any drinking (binary) | Impairment alcohol expectancies (daily) (Richton et al. 2017)	Not Significant	0.054 (-0.031 to 0.138)	NS

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
		Social anxiety symptoms → Drinks per drinking day (count) | Impairment alcohol expectancies (yearly) (Richton et al. 2017)	Not Significant	-0.044 (-0.130 to 0.043)	NS
		Social anxiety symptoms → Any drinking (binary) | Impairment alcohol expectancies (yearly) (Richton et al. 2017)	Not Significant	0.054 (-0.031 to 0.138)	NS
		Subtheme total	0 neg / 6 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 6 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Alcohol outcome expectancies: positive	Anxiety sensitivity → Alcohol use (in past year) | Alcohol outcome expectancies: Positive (Borges et al. 2018)	Significant	0.064 (-0.062 to 0.187)	Small Positive
		Social anxiety symptoms → Drinks per drinking day (count) | Tension-reduction alcohol expectancies (daily) (Richton et al. 2017)	Not Significant	-0.044 (-0.130 to 0.043)	NS
		Yearly social anxiety symptoms → Drinks per drinking day (count) | Tension-reduction alcohol expectancies (daily) (Richton et al. 2017)	Not Significant	-0.066 (-0.151 to 0.021)	NS
		Social anxiety symptoms → Any drinking (binary) | Tension-reduction alcohol expectancies (daily) (Richton et al. 2017)	Not Significant	0.000 (-0.085 to 0.085)	NS
		Yearly social anxiety symptoms → Any drinking (binary) | Tension-reduction alcohol expectancies (daily) (Richton et al. 2017)	Not Significant	0.065 (-0.020 to 0.148)	NS
		Social anxiety symptoms → Drinks per drinking day (count) | Tension-reduction alcohol expectancies (yearly) (Richton et al. 2017)	Not Significant	0.022 (-0.065 to 0.108)	NS
		Social anxiety symptoms → Any drinking (binary) | Tension-reduction alcohol expectancies (yearly) (Richton et al. 2017)	Not Significant	0.032 (-0.052 to 0.117)	NS
		Subtheme total	0 neg / 6 not sig / 1 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 6 NS : 1 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Alcohol use	Anxiety symptoms → Any alcohol use at 32 weeks gestation (binary) | 1st trimester alcohol use (Leis et al. 2012)	Not Significant	0.000 (-0.017 to 0.017)	NS
		Anxiety symptoms → Binge drinking at 32 weeks gestation (binary) | 1st trimester alcohol use (Leis et al. 2012)	Not Significant	-0.007 (-0.024 to 0.010)	NS
		Anxiety symptoms → Drinking related problems (continuous) | Means drinks (quantity x frequency) (Armeli et al. 2014)	Not Significant	0.033 (-0.035 to 0.100)	NS
		Anxiety symptoms (monthly) → Drinking related problems (continuous) | Means drinks (quantity x frequency) (Armeli et al. 2014)	Not Significant	-0.002 (-0.069 to 0.066)	NS
		Subtheme total	0 neg / 4 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 4 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Anxiety sensitivity/ Anxiety	Anxiety symptoms → Alcohol use (continuous) | Anxiety sensitivity (Mackie et al. 2011)	Significant	0.131 (0.033 to 0.227)	Small Positive
		Subtheme total	0 neg / 0 not sig / 1 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 0 NS : 1 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Delinquency	Anxiety symptoms → Age at first use of alcohol (continuous) | Delinquency (Marmorstein et al. 2010)	Not Significant	N/A	NS
		Social anxiety symptoms → Age at first use of alcohol (continuous) | Delinquency (Marmorstein et al. 2010)	Not Significant		NS
		Subtheme total	0 neg / 2 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Depression	Anxiety symptoms → Alcohol use (continuous) | Hopelessness (Mackie et al. 2011)	Not Significant	0.071 (-0.028 to 0.169)	NS
		Subtheme total	0 neg / 1 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Drinking motives: conformity	Daily anxious mood → Daily alcohol use, capped at 6 (continuous) | Drinking motives: conformity (Grant et al. 2009)	Significant	0.325 (0.169 to 0.465)	Moderate Positive
		Subtheme total	0 neg / 0 not sig / 1 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 0 NS : 0 SPos : 1 MPos : 0 LPos / 0 Sig w/o z	
	Drinking motives: drinking to cope	Daily anxious mood → Daily alcohol use, capped at 6 (continuous) | Drinking motives: drinking to cope depression (Grant et al. 2009)	Not Significant	-0.131 (-0.289 to 0.035)	NS
		Daily anxious mood → Daily alcohol use, capped at 6 (continuous) | Drinking motives: drinking to cope anxiety (Grant et al. 2009)	Significant	0.173 (0.008 to 0.328)	Small Positive
		Anxiety symptoms → Drinking related problems (continuous) | Drinking motives: drinking to cope (Armeli et al. 2014)	Significant	0.145 (0.078 to 0.210)	Small Positive

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome* | *Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
		Anxiety symptoms (monthly) → Drinking related problems (continuous) | Drinking motives: drinking to cope (Armeli et al. 2014)	Not Significant	-0.004 (-0.072 to 0.063)	NS
		Generalised anxiety disorder → Harmful drinking, AUDIT, age 18 (binary) | Drinking motives: drinking to cope (Dyer et al. 2019)	Not Significant	-0.004 (-0.037 to 0.030)	NS
		Generalised anxiety disorder → Harmful drinking, AUDIT, age 21 (binary) | Drinking motives: drinking to cope (Dyer et al. 2019)	Not Significant	-0.011 (-0.044 to 0.022)	NS
		Generalised anxiety disorder → Frequent bingeing, AUDIT, age 18 (binary) | Drinking motives: drinking to cope (Dyer et al. 2019)	Not Significant	0.019 (-0.015 to 0.052)	NS
		Generalised anxiety disorder → Hazardous drinking, AUDIT, age 21 (binary) | Drinking motives: drinking to cope (Dyer et al. 2019)	Not Significant	-0.007 (-0.041 to 0.026)	NS
		Generalised anxiety disorder → Frequent bingeing, AUDIT, age 21 (binary) | Drinking motives: drinking to cope (Dyer et al. 2019)	Not Significant	-0.002 (-0.036 to 0.031)	NS
		Generalised anxiety disorder → Frequent drinking, AUDIT, age 21 (binary) | Drinking motives: drinking to cope (Dyer et al. 2019)	Not Significant	0.000 (-0.033 to 0.033)	NS
		Generalised anxiety disorder → Frequent drinking, AUDIT, age 18 (binary) | Drinking motives: drinking to cope (Dyer et al. 2019)	Not Significant	0.028 (-0.005 to 0.061)	NS
		Generalised anxiety disorder → Hazardous drinking, AUDIT, age 18 (binary) | Drinking motives: drinking to cope (Dyer et al. 2019)	Not Significant	-0.002 (-0.035 to 0.031)	NS
		Anxiety daily mood symptoms → Weekly drinking onset (time to drink) | Drinking motives: drinking to cope (Armeli et al. 2008)	Significant	N/A	Sig w/o Z
		Anxiety same day symptoms → Weekly drinking onset (time to drink) | Drinking motives: drinking to cope (Armeli et al. 2008)	Significant	N/A	Sig w/o Z
		Anxiety symptoms Sunday only → Weekly drinking onset (time to drink) | Drinking motives: drinking to cope (Armeli et al. 2008)	Significant	N/A	Sig w/o Z
		Anxiety daily symptoms → Any drinking (binary) | Drinking motives: drinking to cope (Armeli et al. 2008)	Not Significant	N/A	NS
		Anxiety daily symptoms → Heavy drinking (binary) | Drinking motives: drinking to cope (Armeli et al. 2008)	Not Significant	N/A	NS
		Mean daily diary anxiety → Month-level drinking frequency (continuous) | Drinking motives: drinking to cope (Armeli et al. 2010)	Not Significant	N/A	NS
		Retrospective anxiety → Month-level drinking frequency (continuous) | Drinking motives: drinking to cope (Armeli et al. 2010)	Significant	N/A	Sig w/o Z
		Mean daily diary anxiety → Drinking quantity (drinks per drinking day) (continuous) | Drinking motives: drinking to cope (Armeli et al. 2010)	Not Significant	N/A	NS
		Retrospective anxiety → Drinking quantity (drinks per drinking day) (continuous) | Drinking motives: drinking to cope (Armeli et al. 2010)	Not Significant	N/A	NS
		Mean daily diary anxiety → Any drinking (binary) | Drinking motives: drinking to cope (Armeli et al. 2010)	Not Significant	N/A	NS
		Mean daily diary anxiety → Drinks consumed per drinking day (count) | Drinking motives: drinking to cope (Armeli et al. 2010)	Not Significant	N/A	NS
		Anxiety symptoms → Onset of any drinking (binary) | Drinking motives: drinking to cope (Littlefield et al. 2012)	Not Significant	N/A	NS
		Anxiety symptoms → Onset of heavy episodic drinking (binary) | Drinking motives: drinking to cope (Littlefield et al. 2012)	Not Significant	N/A	NS
		Anxiety symptoms → Onset of intoxication (binary) | Drinking motives: drinking to cope (Littlefield et al. 2012)	Not Significant	N/A	NS

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
		Subtheme total	1 neg / 20 not sig / 5 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 20 NS : 2 SPos : 0 MPos : 0 LPos / 4 Sig w/o z	
	Drinking motives: drinking to socialise or enhance	Mean daily diary anxiety → Month-level drinking frequency (continuous) | Drinking motives: drinking to socialise or enhance (Armeli et al. 2010)	Significant	N/A	Sig w/o Z
		Retrospective anxiety → Month-level drinking frequency (continuous) | Drinking motives: drinking to socialise or enhance (Armeli et al. 2010)	Significant	N/A	Sig w/o Z
		Mean daily diary anxiety → Drinking quantity (drinks per drinking day) (continuous) | Drinking motives: drinking to socialise or enhance (Armeli et al. 2010)	Not Significant	N/A	NS
		Retrospective anxiety → Drinking quantity (drinks per drinking day) (continuous) | Drinking motives: drinking to socialise or enhance (Armeli et al. 2010)	Not Significant	N/A	NS
		Mean daily diary anxiety → Any drinking (binary) | Drinking motives: drinking to socialise or enhance (Armeli et al. 2010)	Not Significant	N/A	NS
		Mean daily diary anxiety → Drinks consumed per drinking day (count) | Drinking motives: drinking to socialise or enhance (Armeli et al. 2010)	Not Significant	N/A	NS
		Daily anxious mood → Daily alcohol use, capped at 6 (continuous) | Drinking motives: drinking to socialise or enhance (Grant et al. 2009)	Significant	-0.230 (-0.380 to -0.068)	Small Negative
		Daily anxious mood → Daily alcohol use, capped at 6 (continuous) | Drinking motives: drinking to socialise or enhance (Grant et al. 2009)	Not Significant	0.059 (-0.107 to 0.221)	NS
		Anxiety symptoms → Onset of any drinking (binary) | Drinking motives: drinking to socialise or enhance (Littlefield et al. 2012)	Not Significant	N/A	NS
		Anxiety symptoms → Onset of heavy episodic drinking (binary) | Drinking motives: drinking to socialise or enhance (Littlefield et al. 2012)	Not Significant	N/A	NS
		Anxiety symptoms → Onset of intoxication (binary) | Drinking motives: drinking to socialise or enhance (Littlefield et al. 2012)	Not Significant	N/A	NS
		Subtheme total	1 neg / 8 not sig / 2 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 1 SNeg : 8 NS : 0 SPos : 0 MPos : 0 LPos / 2 Sig w/o z	
	Embarrassment	Social anxiety symptoms → Same day drinking (continuous) | Embarrassing event (O'Grady et al. 2011)	Not Significant	0.023 (-0.067 to 0.113)	NS
		Social anxiety symptoms → Same evening drinking (continuous) | Embarrassing event (O'Grady et al. 2011)	Significant	-0.091 (-0.180 to -0.001)	Small Negative
		Social anxiety symptoms → Next day drinking (continuous) | Embarrassing event (O'Grady et al. 2011)	Not Significant	-0.011 (-0.101 to 0.079)	NS
		Social anxiety symptoms → Next evening drinking (continuous) | Embarrassing event (O'Grady et al. 2011)	Not Significant	-0.046 (-0.135 to 0.044)	NS
		Subtheme total	1 neg / 3 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 1 SNeg : 3 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Emotion dysregulation	Anxiety and withdrawal symptoms → Alcohol use disorder symptoms (binary) | Conduct disorder symptoms (Pardini et al. 2007)	Not Significant	-0.052 (-0.138 to 0.036)	NS
		Anxiety and withdrawal symptoms → Alcohol use disorder symptoms (count) | Conduct disorder symptoms (Pardini et al. 2007)	Not Significant	N/A	NS
		Anxiety and withdrawal symptoms → Alcohol abuse disorder only (binary) | Conduct disorder symptoms (Pardini et al. 2007)	Not Significant	N/A	NS
		Anxiety and withdrawal symptoms → Alcohol dependence disorder only (binary) | Conduct disorder symptoms (Pardini et al. 2007)	Not Significant	N/A	NS
		Subtheme total	0 neg / 4 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 4 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
Socio-environmental	**Experimental manipulation of anxiety**	Social anxiety symptoms → Alcohol use initiation onset (binary) | Anticipatory anxiety (Cloutier et al. 2019)	Significant	0.282 (0.095 to 0.450)	Small Positive
		Social anxiety symptoms → Alcohol use initiation onset (binary) | Post task anxiety (Cloutier et al. 2019)	Not Significant	0.192 (0.000 to 0.371)	NS
		Subtheme total	0 neg / 1 not sig / 1 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 1 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Externalising symptoms	Generalised anxiety symptoms → Drinks per year (binary) | Externalising symptoms (Colder et al. 2017)	Significant	-0.159 (-0.255 to -0.060)	Small Negative
		Generalised anxiety symptoms → Drinks per year (continuous) | Externalising symptoms (Colder et al. 2017)	Significant	-0.356 (-0.440 to -0.266)	Moderate Negative
		Generalised anxiety symptoms → Alcohol problems (continuous) | Externalising symptoms (Colder et al. 2017)	Significant	-0.377 (-0.459 to -0.288)	Moderate Negative
		Social anxiety symptoms → Drinks per year (continuous) | Externalising symptoms (Colder et al. 2017)	Significant	-0.631 (-0.687 to -0.567)	Large Negative
		Social anxiety symptoms → Alcohol problems (continuous) | Externalising symptoms (Colder et al. 2017)	Significant	0.101 (0.001 to 0.199)	Small Positive
		Social anxiety symptoms → Weekly alcohol use (quantity x frequency) (continuous) | Impulsivity (Bilevicius et al. 2021)	Not Significant	-0.022 (-0.136 to 0.092)	NS
		Social anxiety symptoms → Alcohol related problems | Impulsivity (Bilevicius et al. 2021)	Significant	0.190 (0.078 to 0.297)	Small Positive
		Anxiety symptoms → Alcohol use (continuous) | Impulsivity (Mackie et al. 2011)	Not Significant	-0.103 (-0.200 to -0.004)	NS
		Anxiety symptoms → Alcohol use (continuous) | Sensation seeking (Mackie et al. 2011)	Not Significant	-0.058 (-0.156 to 0.041)	NS
		Anxiety symptoms → Alcohol use frequency (continuous) | Urgency (Marmorstein et al. 2015)	Not Significant	N/A	NS
		Social anxiety symptoms → Alcohol use frequency (continuous) | Urgency (Marmorstein et al. 2015)	Not Significant	N/A	NS
		Subtheme total	4 neg / 5 not sig / 2 pos / 0 sig w/o value	1 LNeg : 2 MNeg : 1 SNeg : 5 NS : 2 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Perceptions of peer alcohol use	Social anxiety disorder → Alcohol use disorder | Perceptions of peer alcohol use (Buckner et al. 2009)	Not Significant	-0.069 (-0.153 to 0.015)	NS
		Anxiety symptoms → Alcohol related consequences (continuous) | Perceptions of peer alcohol use (Pedersen et al. 2013)	Not Significant	-0.142 (-0.278 to -0.001)	NS
		Subtheme total	0 neg / 2 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Changing association over time	Social phobia symptoms → Alcohol use (binary) | Time (follow-up) (Dahne et al. 2014)	Not Significant	0.102 (-0.016 to 0.217)	NS
		Anxiety symptoms → Age at first use of alcohol (continuous) | Time (follow-up) (Marmorstein et al. 2010)	Not Significant	N/A	NS
		Social anxiety symptoms → Age at first use of alcohol (continuous) | Time (follow-up) (Marmorstein et al. 2010)	Not Significant	N/A	NS
		Subtheme total	0 neg / 3 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 3 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Criminal offending related factors	Worry → Typical quantity of drinking (continuous) | Self-reported offending (non-drug related) (Nichter et al. 2015)	Not Significant	N/A	NS
		Worry → Frequency of binge drinking (continuous) | Self-reported offending (non-drug related) (Nichter et al. 2015)	Not Significant	N/A	NS
		Worry → Alcohol dependence symptoms (continuous) | Self-reported offending (non-drug related) (Nichter et al. 2015)	Not Significant	N/A	NS
		Physiological anxiety symptoms → Typical quantity of drinking (continuous) | Self-reported offending (non-drug related) (Nichter et al. 2015)	Not Significant	N/A	NS

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
		Physiological anxiety symptoms → Frequency of binge drinking (continuous) | Self-reported offending (non-drug related) (Nichter et al. 2015)	Not Significant	N/A	NS
		Physiological anxiety symptoms → Alcohol dependence symptoms (continuous) | Self-reported offending (non-drug related) (Nichter et al. 2015)	Not Significant	N/A	NS
		Worry → Typical quantity of drinking (continuous) | Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Not Significant	N/A	NS
		Worry → Frequency of binge drinking (continuous) | Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Not Significant	N/A	NS
		Worry → Alcohol dependence symptoms (continuous) | Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Not Significant	N/A	NS
		Physiological anxiety symptoms → Typical quantity of drinking (continuous) | Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Not Significant	N/A	NS
		Physiological anxiety symptoms → Frequency of binge drinking (continuous) | Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Not Significant	N/A	NS
		Physiological anxiety symptoms → Alcohol dependence symptoms (continuous) | Time in supervised facilities (e.g. juvenile detention) (Nichter et al. 2015)	Not Significant	N/A	NS
		Subtheme total	0 neg / 12 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 12 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Drinking context	Social anxiety symptoms → Estimated breath alcohol concentration (eBrAC) (continuous) | Social familiarity with surrounding individuals (Caumiant et al. 2023)	Significant	N/A	Sig w/o Z
		Social anxiety, fear specific symptoms → Estimated breath alcohol concentration (eBrAC) (continuous) | Social familiarity with surrounding individuals (Caumiant et al. 2023)	Significant	N/A	Sig w/o Z
		Social anxiety, avoidance specific symptoms → Estimated breath alcohol concentration (eBrAC) (continuous) | Social familiarity with surrounding individuals (Caumiant et al. 2023)	Not Significant	N/A	NS
		Social anxiety symptoms → Quantity of alcohol consumed within drinking episode (continuous) | Social familiarity with surrounding individuals (Caumiant et al. 2023)	Significant	N/A	Sig w/o Z
		Social anxiety symptoms → Drinking versus not drinking (binary) | Social familiarity with surrounding individuals (Caumiant et al. 2023)	Not Significant	N/A	NS
		Subtheme total	3 neg / 2 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 0 SPos : 0 MPos : 0 LPos / 3 Sig w/o z	
	Negative family experiences	Social anxiety disorder → Alcohol use disorder | Negative family interactions (Buckner et al. 2009)	Significant	-0.083 (-0.166 to 0.001)	Small Negative
		Subtheme total	1 neg / 0 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 1 SNeg : 0 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Partner support	Social anxiety disorder → Alcohol use disorder | Partner support (Buckner et al. 2009)	Not Significant	0.073 (-0.011 to 0.156)	NS
		Subtheme total	0 neg / 1 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Peer social support	Social anxiety disorder → Alcohol use disorder | Peer social support (Buckner et al. 2009)	Not Significant	-0.051 (-0.135 to 0.033)	NS
		Subtheme total	0 neg / 1 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Positive family experiences	Social anxiety disorder → Alcohol use disorder | Family cohesion (Buckner et al. 2009)	Significant	-0.093 (-0.175 to -0.009)	Small Negative
		Anxiety disorder → Alcohol use disorder (binary) | Maternal support (Gorka et al. 2014)	Significant	-0.117 (-0.184 to -0.049)	Small Negative

Moderator super-ordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
		Social anxiety disorder → Alcohol use disorder | Parent support (Buckner et al. 2009)	Not Significant	-0.059 (-0.142 to 0.025)	NS
		Anxiety disorder → Alcohol use disorder (binary) | Paternal support (Gorka et al. 2014)	Not Significant	-0.054 (-0.122 to 0.014)	NS
		Subtheme total	2 neg / 2 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 2 SNeg : 2 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Socioeconomic factors	Anxiety severity → Alcohol use (binary) | Community cohesion (Schleider et al. 2019)	Not Significant	N/A	NS
		Anxiety severity → Alcohol use (binary) | Low neighbourhood safety (Schleider et al. 2019)	Not Significant	N/A	NS
		Anxiety severity → Alcohol use (binary) | Socioeconomic status (Schleider et al. 2019)	Not Significant	N/A	NS
		Subtheme total	0 neg / 3 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 3 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
Grand total			14 neg / 193 not sig / 16 pos / 1 sig w/o value	1 LNeg : 2 MNeg : 8 SNeg : 193 NS : 7 SPos : 1 MPos : 0 LPos / 12 Sig w/o z	

Table A15: Moderation alcohol → anxiety significance counts and magnitude of effect size classification.

Moderator superordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
Biological	Gender/sex	Alcohol use → Anxiety symptoms (continuous) | Gender (Mackie et al. 2011)	Not Significant	0.050 (-0.049 to 0.149)	NS
		Frequency of alcohol use → Anxiety symptoms (continuous) | Gender (Parrish et al. 2016)	Not Significant	N/A	NS
		Frequency of alcohol use → Anxious arousal symptoms (continuous) | Gender (Parrish et al. 2016)	Not Significant	N/A	NS
		Alcohol consumption level (non-drinker/light or moderate drinker/heavier drinker) → Incident anxiety (new case of anxiety) (binary) | Sex (Carvalho et al. 2018)	Not Significant	N/A	NS
		Alcohol consumption level (non-drinker/light or moderate drinker/heavier drinker) → Persistent anxiety | Sex (Carvalho et al. 2018)	Not Significant	N/A	NS
		Problem drinking (non-drinker/non-problem drinker/problem drinker) → Incident anxiety (new case of anxiety) (binary) | Sex (Carvalho et al. 2018)	Not Significant	N/A	NS
		Problem drinking (non-drinker/non-problem drinker/problem drinker) → Persistent anxiety | Sex (Carvalho et al. 2018)	Not Significant	N/A	NS
		Subtheme total	0 neg / 7 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 7 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Race/ethnicity	Frequency of alcohol use → Anxiety symptoms (continuous) | Generational status (Mexican) (Parrish et al. 2016)	Not Significant		NS
		Frequency of alcohol use → Anxious arousal symptoms (continuous) | Generational status (Mexican) (Parrish et al. 2016)	Significant		Sig w/o Z
		Subtheme total	0 neg / 1 not sig / 0 pos / 1 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 0 SPos : 0 MPos : 0 LPos / 1 Sig w/o z	
Psychological	Alcohol outcome expectancies: Positive	Alcohol dose (placebo vs control) → Anxiety (state) (continuous) | Alcohol outcome expectancies: tension reduction (Abrams et al. 2021)	Not Significant	0.263 (-0.008 to 0.498)	NS
		Alcohol dose (placebo vs control) → Anxiety (state) (continuous) | Alcohol outcome expectancies: tension reduction (Abrams et al. 2021)	Significant	0.305 (0.038 to 0.532)	Moderate Positive
		Subtheme total	0 neg / 1 not sig / 1 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 0 SPos : 1 MPos : 0 LPos / 0 Sig w/o z	
	Anxiety sensitivity/ Anxiety	Alcohol dose (placebo vs control) → Anxiety (state) (continuous) | Anxiety sensitivity (Abrams et al. 2021)	Significant	-0.297 (-0.525 to -0.029)	Small Negative
		Alcohol use → Anxiety symptoms (continuous) | Anxiety sensitivity (Mackie et al. 2011)	Not Significant	0.050 (-0.049 to 0.149)	NS
		Alcohol use disorder (at time of type 2 diabetes diagnosis) → New episode of anxiety disorder | History of past Anxiety (Cook et al. 2024)	Significant		Sig w/o Z
		Subtheme total	1 neg / 1 not sig / 0 pos / 1 sig w/o value	0 LNeg : 0 MNeg : 1 SNeg : 1 NS : 0 SPos : 0 MPos : 0 LPos / 1 Sig w/o z	
	Attentional processes	Drink group (alcohol or placebo) → Subjective anxiety change (continuous) | Sustained attention (Sher et al. 2007)	Not Significant		NS
		Alcohol beverage group (alcohol/slides/expectancy vs. alcohol/slides/no expectancy vs. alcohol/no slides) → Anxiety symptoms (continuous) | Attentional engagement and expectancy (Steele et al. 1986)	Not Significant		NS
		Subtheme total	0 neg / 2 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Depression	Alcohol use → Anxiety symptoms (continuous) | Hopelessness (Mackie et al. 2011)	Not Significant	0.050 (-0.049 to 0.149)	NS
		Heavy episodic drinking frequency → Anxiety symptoms in adolescence | Major depressive disorder (Wojciechowski et al. 2024)	Significant		Sig w/o Z
		Heavy episodic drinking frequency → Anxiety symptoms in emerging adulthood | Major depressive disorder (Wojciechowski et al. 2024)	Significant		Sig w/o Z
		Subtheme total	2 neg / 1 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 0 SPos : 0 MPos : 0 LPos / 2 Sig w/o z	
		Drink group (alcohol or placebo) → State anxiety (continuous) | Drink and stress task order (Sayette et al. 2001)	Not Significant		NS

Moderator superordinate theme	Moderator subtheme	Effect label assigned *Predictor → Outcome | Moderator*	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
Socio-environmental	**Experimental manipulation of anxiety**	Alcohol beverage group (alcohol vs placebo) → Anxiety symptoms (continuous) | Distracting activity (Steele et al. 1986)	Not Significant		NS
		Subtheme total	0 neg / 2 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Externalising symptoms	Alcohol use → Anxiety symptoms (continuous) | Impulsivity (Mackie et al. 2011)	Not Significant	0.050 (-0.049 to 0.149)	NS
		Alcohol use → Anxiety symptoms (continuous) | Sensation seeking (Mackie et al. 2011)	Not Significant	0.050 (-0.049 to 0.149)	NS
		Subtheme total	0 neg / 2 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 2 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
	Changing association over time	Alcohol beverage group (alcohol expected, alcohol not expected, placebo) → Anxiety symptoms | Time (during experimental phase) (Stevens et al. 2014)	Significant		Sig w/o Z
		Low vs high alcohol sipping latent class → Anxiety symptoms | Time (linear) (Ferariu et al. 2024)	Not Significant		NS
		No vs high alcohol sipping latent class → Anxiety symptoms | Time (linear) (Ferariu et al. 2024)	Not Significant		NS
		Alcohol beverage group (alcohol expected, alcohol not expected, placebo) → Performance anxiety: visual analogue scale | Time (pre to post beverage phase) (Abrams et al. 2001)	Significant		Sig w/o Z
		Alcohol beverage group (alcohol expected, alcohol not expected, placebo) → Performance anxiety: post-speech audience anxious scale | Time (pre to post beverage phase) (Abrams et al. 2001)	Significant		Sig w/o Z
		Low vs high alcohol sipping latent class → Anxiety symptoms | Time (quadratic) (Ferariu et al. 2024)	Not Significant		NS
		No vs high alcohol sipping latent class → Anxiety symptoms | Time (quadratic) (Ferariu et al. 2024)	Not Significant		NS
		Subtheme total	0 neg / 4 not sig / 0 pos / 3 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 4 NS : 0 SPos : 0 MPos : 0 LPos / 3 Sig w/o z	
	Drinking context	Episode specific drinking to cope (continuous) → Anxiety symptoms the day after drinking episode (continuous) | Drink was alone (Armeli et al. 2014)	Not Significant		NS
		Episode specific drinking to cope (continuous) → Anxiety symptoms the day after drinking episode (continuous) | Drink was alone (Armeli et al. 2014)	Not Significant		NS
		Episode specific drinking to cope (continuous) → Anxiety symptoms the day after drinking episode (continuous) | Drinking was with others (Armeli et al. 2014)	Not Significant		NS
		Episode specific drinking to cope (continuous) → Anxiety symptoms the day after drinking episode (continuous) | Drinking was with others (Armeli et al. 2014)	Not Significant		NS
		Subtheme total	0 neg / 4 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 4 NS : 0 SPos : 0 MPos : 0 LPos / 0 Sig w/o z	
Grand total			3 neg / 25 not sig / 1 pos / 5 sig w/o value	0 LNeg : 0 MNeg : 1 SNeg : 25 NS : 0 SPos : 1 MPos : 0 LPos / 7 Sig w/o z	

Table A16: Counts and magnitude of effect size classification for complex model designs.

Effect Label Assigned Predictor → Outcome | Effect	Reported significance in-text	Effect magnitude (transformed to Fisher's Z)	Effect size classification
Multiple mediation effects			
Social anxiety symptoms → Drinking initiation (binary) | Expectancies for not drinking & Perceptions of peer alcohol use (male only model) (Bekman et al. 2010) [Sig]	Significant	-0.134 (-0.207 to -0.059)	Small Negative
Social anxiety symptoms → Drinking initiation (binary) | Expectancies for not drinking & Perceptions of peer alcohol use (female only model) (Bekman et al. 2010) [Sig]	Significant	-0.121 (-0.199 to -0.040)	Small Negative
Anxiety disorder severity → Alcohol use disorder symptoms severity (continuous) | Rumination & Worry (Wolitzky-Taylor et al. 2012) [NS]	Not Significant	N/A	NS
Total	2 neg / 1 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 2 SNeg : 1 NS : 0 Spos : 0 MPos : 0 LPos / 0 Sig w/o z	
Moderated-mediation effects			
Anxiety sensitivity → Alcohol problems (continuous) | Anxiety symptoms (mediator) & Race/ethnicity (moderator) (Paulus et al. 2016) [NS]	Not Significant	N/A	NS
Total	0 neg / 1 not sig / 0 pos / 0 sig w/o value	0 LNeg : 0 MNeg : 0 SNeg : 1 NS : 0 Spos : 0 MPos : 0 LPos / 0 Sig w/o z	
Moderated moderation effects (3-way interactions)			
Anxiety symptoms- daily mean → Drinking frequency- monthly (diary) | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [Sig]	Significant	--	Sig w/o Z
Anxiety symptoms- daily mean → Drinking frequency- monthly (retrospective) | Drinking to cope & Drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	Not significant	--	NS
Anxiety symptoms- daily mean → Drinking quantity- monthly (diary) | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	Not significant	--	NS
Anxiety symptoms- daily mean → Drinking quantity- monthly (retrospective) | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	Not significant	--	NS
Anxiety symptoms- daily → Any drinking (binary) | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	Not significant	--	NS
Anxiety symptoms- daily → Drinks per drinking day | Drinking to cope & drinking to socialise or enhance motives (Armeli et al. 2010) [NS]	Not significant	--	NS
Anxiety symptoms → Drinks per year (count) | Externalising symptoms & Age (Colder et al. 2017) [Sig]	Significant	--	Sig w/o Z
Social anxiety symptoms → Drinks per year (count) | Externalising symptoms & Age (Colder et al. 2017) [Sig]	Significant	--	Sig w/o Z
Social anxiety symptoms → Drinking problems (count) | Externalising symptoms & Age (Colder et al. 2017) [Sig]	Significant	-0.101 (-0.199 to -0.001)	Small Negative
Daytime anxious mood → Drinking likelihood (binary) | Task switching & Age (Dvorak et al. 2014) [Sig]	Significant	--	Sig w/o Z
Daytime anxious mood → Level of intoxication (continuous) | Task switching & Age (Dvorak et al. 2014) [NS]	Not significant	--	NS
Daytime anxious mood → Drinking likelihood (binary) | Sustained attention & Age (Dvorak et al. 2014) [Sig]	Significant	--	Sig w/o Z
Daytime anxious mood → Level of intoxication (continuous) | Sustained attention & Age (Dvorak et al. 2014) [Sig]	Significant	--	Sig w/o Z
Social anxiety symptoms → Drinking quantity | Perceptions of peer alcohol use & Year (O'Grady et al. 2011) [NS]	Not significant	--	NS
Social anxiety symptoms → Any drinking (binary) | Tension reduction alcohol outcome expectancies & Sex (Richton et al. 2017) [Sig]	Significant	0.100 (0.016 to 0.183)	Small Positive
Anxiety symptoms → Drinking related problems (continuous) | Drinking to cope motives & past month drinking (Armeli et al. 2014) [Sig]	Significant	0.090 (0.023 to 0.157)	Small Positive
Anxiety symptoms monthly changes → Drinking related problems (continuous) | Drinking to cope motives & past month drinking (Armeli et al. 2014) [NS]	Not significant	0.012 (-0.056 to 0.079)	NS
Alcohol beverage group (alcohol expected, alcohol not expected, placebo) → Trait anxiety | Social anxiety & Time (Stevens et al. 2014) [Sig]	Significant	0.167 (-0.036 to 0.357)	Small Positive
Anxiety activity session (anxiety vs reading challenge) → Alcoholic drink choice (weak, moderate or strong) | Drink-activity order & gender (Abrams et al. 2002) [Sig]	Significant	0.306 (0.010 to 0.552)	Small Positive

Alcohol beverage group (alcohol vs placebo) → State anxiety | Activity group (distracted or not distracted) (2) & Measurement time point of STAI (4) (Steele et al. 1988) [Sig]	Significant	0.467 (0.182 to 0.679)	Moderate Positive
Alcohol beverage group (alcohol vs placebo) → State anxiety | Activity group (distracted or not distracted) (2) & Measurement time point of STAI (2) (Steele et al. 1988) [Sig]	Significant	0.630 (0.397 to 0.787)	Large Positive
Alcohol beverage group (alcohol vs placebo) → State anxiety | Activity group (distracted or not distracted) (2) & Measurement time point of STAI (4) (Steele et al. 1988) [Sig]	Significant	0.309 (-0.017 to 0.576)	Moderate Positive
Alcohol beverage group (alcohol vs placebo) → State anxiety | Activity group (distracted or not distracted) (2) & Measurement time point of STAI (2) (Steele et al. 1988) [Sig]	Significant	0.401 (0.088 to 0.642)	Moderate Positive
Total	1 neg / 8 not sig / 8 pos / 6 sig w/o value	0 LNeg : 0 MNeg : 1 SNeg : 8 NS : 4 SPos : 3 MPos : 0 LPos / 6 Sig w/o z	

Table A17: Anxiety → alcohol relationship full meta-analytic calculations for meta-estimate results, grouped by moderator subtheme.

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome* | *Moderator*	Effect Magnitude (transformed to Fisher's Z)	Fisher's Z S.E	Fixed-effect weights	Weighted effects	Mean FEz	Q	I^2	τ^2	Random weights	Random-weighted effects	Final pooled z	S.E of Pooled Estimate:	Meta LCI	Meta UCI	Meta estimate (random effect with CI)
Biological	Age	Social anxiety symptoms → Alcohol problems | Age (Colder et al. 2017) [Sig]	-0.151 (-0.247 to -0.052)	0.051	384.000	-58.335					346.120	-52.580					
		Anxiety disorder → Alcohol use disorder | Age (Cheng et al. 2004) [NS]	0.061 (-0.028 to 0.148)	0.037	716.783	43.423					595.193	36.057					
		Anxiety disorder → Alcohol use disorder | Age (Cheng et al. 2004) [Sig]	0.171 (0.084 to 0.256)	0.033	917.452	158.454					727.284	125.610					
		Age meta-estimate					0.071	28.650	0.930	0.021			0.065	0.024	0.017	0.113	**0.065 (0.017 to 0.113)**
	Gender/sex	Anxiety symptoms → Initiation of alcohol use | Sex (Kaplow et al. 2001) [NS]	-0.030 (-0.094 to 0.034)	0.003	87300.387	-2604.185					3373.142	-100.621					
		Anxiety symptoms (general & separation) → Initiation of alcohol use | Sex (Kaplow et al. 2001) [NS]	-0.014 (-0.078 to 0.051)	0.002	173417.869	-2355.043					3439.130	-46.704					
		Anxiety sensitivity- Social concerns → Alcohol use disorder | Gender (Schimdt et al. 2007) [NS]	0.011 (-0.087 to 0.108)	0.050	401.000	4.323					359.871	3.879					
		Anxiety sensitivity- Physical concerns → Alcohol use disorder | Gender (Schimdt et al. 2007) [NS]	0.023 (-0.075 to 0.120)	0.050	401.000	9.068					359.871	8.138					
		Separation anxiety symptoms → Initiation of alcohol use | Sex (Kaplow et al. 2001) [NS]	0.041 (-0.024 to 0.104)	0.010	9723.425	395.353					2578.322	104.834					
		Anxiety sensitivity- Cognitive concerns → Alcohol use disorder | Gender (Schimdt et al. 2007) [NS]	0.046 (-0.051 to 0.143)	0.050	401.000	18.614					359.871	16.705					
		Anxiety sensitivity → Alcohol use disorder | Gender (Schimdt et al. 2007) [NS]	0.061 (-0.037 to 0.157)	0.050	401.000	24.369					359.871	21.870					
		Anxiety symptoms → Alcohol use | Gender (Mackie et al. 2011) [NS]	0.071 (-0.028 to 0.168)	0.051	390.000	27.595					350.987	24.834					
		Gender/sex meta-estimate					-0.016	56.622	0.876	0.000			0.003	0.009	-0.016	0.021	0.003 (-0.016 to 0.021)
	Race/ethnicity	Anxiety symptoms → Alcohol use initiation | Race/ethnicity (Black/other) (Cerda et al. 2013) [NS]	0.196 (0.107 to 0.282)	0.002													
		Race/ethnicity meta-estimate															N/A
Psychological	Alcohol outcome expectancies: negative	Social anxiety symptoms → Drinks per drinking day | Impairment alcohol expectancies (Richton et al. 2017) [NS]	0.000 (-0.086 to 0.086)	0.044	512.000	0.000					446.802	0.000					
		Yearly social anxiety symptoms → Drinks per drinking day | Impairment alcohol expectancies (Richton et al. 2017) [NS]	0.000 (-0.086 to 0.086)	0.044	512.000	0.000					446.802	0.000					

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome* | *Moderator*	Effect Magnitude (transformed to Fisher's Z)	Fisher's Z S.E	Fixed-effect weights	Weighted effects	Mean FE z	Q	I^2	τ^2	Random weights	Random-weighted effects	Final pooled z	S.E of Pooled Estimate:	Meta LCI	Meta UCI	Meta estimate (random effect with CI)
		Social anxiety symptoms → Any drinking | Impairment alcohol expectancies (Richton et al. 2017) [NS]	-0.043 (-0.127 to 0.042)	0.043	534.000	-23.037					463.464	-19.994					
		Yearly social anxiety symptoms → Any drinking | Impairment alcohol expectancies (Richton et al. 2017) [NS]	0.054 (-0.031 to 0.138)	0.043	534.000	28.791					463.464	24.988					
		Social anxiety symptoms → Drinks per drinking day | Impairment alcohol expectancies (yearly) (Richton et al. 2017) [NS]	-0.044 (-0.130 to 0.043)	0.044	512.000	-22.554					446.802	-19.682					
		Social anxiety symptoms → Any drinking | Impairment alcohol expectancies (yearly) (Richton et al. 2017) [NS]	0.054 (-0.031 to 0.138)	0.043	534.000	28.791					463.464	24.988					
		Alcohol outcome expectancies: Negative meta-estimate					0.004	5.046	0.009	0.000			0.004	0.019	-0.034	0.041	0.004 (-0.034 to 0.041)
	Alcohol outcome expectancies: positive	Anxiety sensitivity → Alcohol use (in past year) | Alcohol outcome expectancies- Positive (Borges et al. 2018) [Sig]	0.064 (-0.062 to 0.187)	0.064	243.000	15.483					227.261	14.480					
		Social anxiety symptoms → Drinks per drinking day | Tension-reduction (Richton et al. 2017) [NS]	-0.044 (-0.130 to 0.043)	0.044	512.000	-22.554					446.802	-19.682					
		Yearly social anxiety symptoms → Drinks per drinking day | Tension-reduction expectancies (Richton et al. 2017) [NS]	-0.066 (-0.151 to 0.021)	0.044	512.000	-33.818					446.802	-29.511					
		Social anxiety symptoms → Any drinking | Tension-reduction expectancies (Richton et al. 2017) [NS]	0.000 (-0.085 to 0.085)	0.043	534.000	0.000					463.464	0.000					
		Yearly social anxiety symptoms → Any drinking | Tension-reduction expectancies (Richton et al. 2017) [NS]	0.065 (-0.020 to 0.148)	0.043	534.000	34.542					463.464	29.979					
		Social anxiety symptoms → Drinks per drinking day | Tension-reduction expectancies (yearly) (Richton et al. 2017) [NS]	0.022 (-0.065 to 0.108)	0.044	512.000	11.280					446.802	9.843					
		Social anxiety symptoms → Any drinking | Tension-reduction expectancies (yearly) (Richton et al. 2017) [NS]	0.032 (-0.052 to 0.117)	0.043	534.000	17.280					463.464	14.997					
		Alcohol outcome expectancies: Positive meta-estimate					0.007	7.110	0.156	0.000			0.007	0.018	-0.029	0.043	0.007 (-0.029 to 0.043)
	Alcohol use	Anxiety symptoms → Any alcohol use at 32 weeks gestation | 1st trimester alcohol use (Leis et al. 2012) [NS]	0.000 (-0.017 to 0.017)	0.000	79568434.494	0.000					3508.558	0.000					
		Anxiety symptoms → Binge drinking at 32 weeks gestation | 1st trimester alcohol use (Leis et al. 2012) [NS]	-0.007 (-0.024 to 0.010)	0.000	77992211.220	-5398811.173					3508.555	-24.287					
		Anxiety symptoms → Drinking related problems | Means drinks (quantity x frequency) (Armeli et al. 2008) [NS]	0.033 (-0.035 to 0.100)	0.034	841.000	27.496					678.396	22.180					

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome* | *Moderator*	Effect Magnitude (transformed to Fisher's Z)	Fisher's Z S.E	Fixed-effect weights	Weighted effects	Mean FE z	Q	I^2	τ^2	Random weights	Random-weighted effects	Final pooled z	S.E of Pooled Estimate:	Meta LCI	Meta UCI	Meta estimate (random effect with CI)
		Anxiety symptoms (monthly) → Drinking related problems | Means drinks (quantity x frequency) (Armeli et al. 2008) [NS]	-0.002 (-0.069 to 0.066)	0.034	841.000	-1.336					678.396	-1.078					
		Alcohol use meta-estimate					-0.003	1888.388	0.998	0.000			0.000	0.011	-0.022	0.021	0.000 (-0.022 to 0.021)
	Anxiety sensitivity/ Anxiety	Anxiety symptoms → Alcohol use| Anxiety sensitivity (Mackie et al. 2011) [Sig]	0.131 (0.033 to 0.227)	0.051													
		Anxiety sensitivity/ Anxiety meta-estimate															N/A
	Delinquency	--															
	Depression	Anxiety symptoms → Alcohol use | Hopelessness (Mackie et al. 2011) [NS]	0.071 (-0.028 to 0.169)	0.051													
		Depression meta-estimate															N/A
	Drinking motives: conformity	Daily anxious mood → Daily alcohol use | Drinking motives- conformity (Grant et al. 2009) [Sig]	0.325 (0.169 to 0.465)	0.085													
		Drinking motives: conformity meta-estimate															
	Drinking motives: drinking to cope	Daily anxious mood → Daily alcohol use | drinking to cope (Grant et al. 2009) [NS]	-0.131 (-0.289 to 0.035)	0.085	139.000	-18.277					133.703	-17.581					
		Generalised anxiety disorder → Harmful drinking, AUDIT, age 21 | drinking to cope (Dyer et al. 2019) [NS]	-0.011 (-0.044 to 0.022)	0.008	14702.718	-162.620					2832.705	-31.331					
		Generalised anxiety disorder → Hazardous drinking, AUDIT, age 21 | drinking to cope (Dyer et al. 2019) [NS]	-0.007 (-0.041 to 0.026)	0.007	21162.142	-155.577					3009.700	-22.126					
		Anxiety symptoms (monthly) → Drinking related problems | drinking to cope (Armeli et al. 2008) [NS]	-0.004 (-0.072 to 0.063)	0.034	841.000	-3.696					678.396	-2.981					
		Generalised anxiety disorder → Harmful drinking, AUDIT, age 18 | drinking to cope (Dyer et al. 2019) [NS]	-0.004 (-0.037 to 0.030)	0.011	7778.165	-29.989					2417.971	-9.323					
		Generalised anxiety disorder → Frequent bingeing, AUDIT, age 21 | drinking to cope (Dyer et al. 2019) [NS]	-0.002 (-0.036 to 0.031)	0.007	21205.774	-45.912					3010.581	-6.518					
		Generalised anxiety disorder → Hazardous drinking, AUDIT, age 18 | drinking to cope (Dyer et al. 2019) [NS]	-0.002 (-0.035 to 0.031)	0.006	31759.772	-66.972					3159.646	-6.663					
		Generalised anxiety disorder → Frequent drinking, AUDIT, age 21 | drinking to cope (Dyer et al. 2019) [NS]	0.000 (-0.033 to 0.033)	0.006	24181.444	0.000					3064.112	0.000					
		Generalised anxiety disorder → Frequent bingeing, AUDIT, age 18 | drinking to cope (Dyer et al. 2019) [NS]	0.019 (-0.015 to 0.052)	0.008	16070.660	299.255					2879.936	53.628					

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome | Moderator*	Effect Magnitude (transformed to Fisher's Z)	Fisher's Z S.E	Fixed-effect weights	Weighted effects	Mean FE z	Q	I^2	τ^2	Random weights	Random-weighted effects	Final pooled z	S.E of Pooled Estimate:	Meta LCI	Meta UCI	Meta estimate (random effect with CI)
		Generalised anxiety disorder → Frequent drinking, AUDIT, age 18 | drinking to cope (Dyer et al. 2019) [NS]	0.028 (-0.005 to 0.061)	0.006	27369.036	771.277					3110.009	87.642					
		Anxiety symptoms → Drinking related problems | drinking to cope (Armeli et al. 2008) [Sig]	0.145 (0.078 to 0.210)	0.034	841.000	122.596					678.396	98.893					
		Daily anxious mood → Daily alcohol use | drinking to cope (Grant et al. 2009) [Sig]	0.173 (0.008 to 0.328)	0.085	139.000	24.266					133.703	23.342					
		Drinking motives: drinking to cope meta-estimate					0.004	51.889	0.788	0.000			0.007	0.006	-0.006	0.019	0.007 (-0.006 to 0.019)
	Drinking motives: drinking to socialise or enhance	Daily anxious mood → Daily alcohol use | drinking to socialise (Grant et al. 2009) [Sig]	-0.230 (-0.380 to -0.068)	0.085	139.000	-32.574					133.703	-31.333					
		Daily anxious mood → Daily alcohol use | drinking to enhance (Grant et al. 2009) [NS]	0.059 (-0.107 to 0.221)	0.085	139.000	8.161					133.703	7.850					
		Drinking motives: drinking to socialise or enhance meta-estimate					-0.088	5.969	0.832	0.036			-0.088	0.061	-0.208	0.032	-0.088 (-0.208 to 0.032)
	Embarrassment	Social anxiety symptoms → Same day drinking | Embarrassing event (O'Grady et al. 2011) [NS]	0.023 (-0.067 to 0.113)	0.046	473.000	10.839					416.811	9.551					
		Social anxiety symptoms → Same evening drinking | Embarrassing event (O'Grady et al. 2011) [Sig]	-0.091 (-0.180 to -0.001)	0.046	473.000	-43.299					416.811	-38.156					
		Social anxiety symptoms → Next day drinking | Embarrassing event (O'Grady et al. 2011) [NS]	-0.011 (-0.101 to 0.079)	0.046	473.000	-5.420					416.811	-4.776					
		Social anxiety symptoms → Next evening drinking | Embarrassing event (O'Grady et al. 2011) [NS]	-0.046 (-0.135 to 0.044)	0.046	473.000	-21.672					416.811	-19.098					
		Embarrassment meta-estimate					-0.031	3.393	0.116	0.000			-0.031	0.024	-0.079	0.017	-0.031 (-0.079 to 0.017)
	Emotion dysregulation	Anxiety and withdrawal symptoms → Alcohol use disorder symptoms (binary) | Conduct disorder symptoms (Pardini et al. 2007) [NS]	-0.052 (-0.138 to 0.036)	0.008	16657.159	-861.709					2898.223	-149.931					
		Anxiety and withdrawal symptoms → Alcohol use disorder symptoms | Conduct disorder symptoms (Pardini et al. 2007) [NS]	-0.020 (-0.107 to 0.067)	0.002	208422.407	-4199.531					3450.623	-69.527					
		Anxiety and withdrawal symptoms → Alcohol abuse disorder only | Conduct disorder symptoms (Pardini et al. 2007) [NS]	0.035 (-0.052 to 0.122)	0.007	18889.403	665.741					2959.066	104.290					
		Anxiety and withdrawal symptoms → Alcohol dependence disorder only | Conduct disorder symptoms (Pardini et al. 2007) [NS]	0.015 (-0.072 to 0.102)	0.006	25198.355	372.076					3079.862	45.477					

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome* | *Moderator*	Effect Magnitude (transformed to Fisher's Z)	Fisher's Z S.E	Fixed-effect weights	Weighted effects	Mean FE z	Q	I^2	τ^2	Random weights	Random-weighted effects	Final pooled z	S.E of Pooled Estimate:	Meta LCI	Meta UCI	Meta estimate (random effect with CI)
		Emotion dysregulation meta-estimate					-0.015	98.012	0.969	0.001			-0.006	0.009	-0.023	0.012	-0.006 (-0.023 to 0.012)
	Experimental manipulation of anxiety	Social anxiety symptoms → Alcohol use initiation onset | Anticipatory anxiety (Cloutier et al. 2019) [Sig]	0.282 (0.095 to 0.450)	0.100	101.000	29.299					98.174	28.479					
		Social anxiety symptoms → Alcohol use initiation onset | Post task anxiety (Cloutier et al. 2019) [NS]	0.192 (0.000 to 0.371)	0.100	101.000	19.683					98.174	19.132					
		Experimental manipulation of anxiety meta-estimate					0.242	0.458	0.000	0.000			0.242	0.071	0.103	0.382	**0.242 (0.103 to 0.382)**
	Externalising symptoms	Generalised anxiety symptoms → Drinks per year (binary) | Externalising symptoms (Colder et al. 2017) [Sig]	-0.159 (-0.255 to -0.060)	0.051	384.000	-61.549					346.120	-55.477					
		Generalised anxiety symptoms → Drinks per year | Externalising symptoms (Colder et al. 2017) [Sig]	-0.356 (-0.440 to -0.266)	0.051	384.000	-143.066					346.120	-128.953					
		Generalised anxiety symptoms → Alcohol problems | Externalising symptoms (Colder et al. 2017) [Sig]	-0.377 (-0.459 to -0.288)	0.051	384.000	-152.146					346.120	-137.138					
		Social anxiety symptoms → Drinks per year | Externalising symptoms (Colder et al. 2017) [Sig]	-0.631 (-0.687 to -0.567)	0.051	384.000	-285.327					346.120	-257.181					
		Social anxiety symptoms → Alcohol problems | Externalising symptoms (Colder et al. 2017) [Sig]	0.101 (0.001 to 0.199)	0.051	384.000	38.973					346.120	35.128					
		Social anxiety symptoms → Weekly alcohol use | Impulsivity (Bilevicius et al. 2021) [NS]	-0.022 (-0.136 to 0.092)	0.058	294.000	-6.561					271.270	-6.054					
		Social anxiety symptoms → Alcohol related problems | Impulsivity (Bilevicius et al. 2021) [Sig]	0.190 (0.078 to 0.297)	0.058	294.000	56.517					271.270	52.147					
		Anxiety symptoms → Alcohol use | Impulsivity (Mackie et al. 2011) [NS]	-0.103 (-0.200 to -0.004)	0.051	390.000	-40.367					350.987	-36.329					
		Anxiety symptoms → Alcohol use | Sensation seeking (Mackie et al. 2011) [NS]	-0.058 (-0.156 to 0.041)	0.051	390.000	-22.575					350.987	-20.317					
		Externalising symptoms meta-estimate					-0.187	240.466	0.967	0.080			-0.186	0.018	-0.222	-0.150	**-0.186 (-0.222 to -0.150)**
	Perceptions of peer alcohol use	Social anxiety disorder → Alcohol use disorder | Perceptions of peer alcohol use (Buckner et al. 2009) [NS]	-0.069 (-0.153 to 0.015)	0.015	4227.759	-293.747					1917.411	-133.223					
		Anxiety symptoms → Alcohol related consequences | Perceptions of peer alcohol use (Pedersen et al. 2013) [NS]	-0.142 (-0.278 to -0.001)	0.073	190.000	-27.259					180.240	-25.859					

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome* | *Moderator*	Effect Magnitude (transformed to Fisher's Z)	Fisher's Z S.E	Fixed-effect weights	Weighted effects	Mean FEz	Q	I^2	τ^2	Random weights	Random-weighted effects	Final pooled z	S.E of Pooled Estimate:	Meta LCI	Meta UCI	Meta estimate (random effect with CI)
Socio-environmental		**Perceptions of peer alcohol use meta-estimate**					-0.073	0.995	0.000	0.000			-0.076	0.022	-0.119	-0.033	**-0.076 (-0.119 to -0.033)**
	Changing association over time	Social phobia symptoms → Alcohol use | Time (follow-up) (Dahne et al. 2014) [NS]	0.102 (-0.016 to 0.217)	0.001													
		Changing association over time meta-estimate															N/A
	Criminal offending related factors	--															
	Drinking context	--															
	Negative family experiences	Social anxiety disorder → Alcohol use disorder | Negative family interactions (Buckner et al. 2009) [Sig]	-0.083 (-0.166 to 0.001)	0.009													
		Negative family experiences meta-estimate															N/A
	Partner support	Social anxiety disorder → Alcohol use disorder | Partner support (Buckner et al. 2009) [NS]	0.073 (-0.011 to 0.156)	0.005													
		Partner support meta-estimate															N/A
	Peer social support	Social anxiety disorder → Alcohol use disorder | Peer social support (Buckner et al. 2009) [NS]	-0.051 (-0.135 to 0.033)	0.007													
		Peer social support meta-estimate															N/A
	Positive family experiences	Social anxiety disorder → Alcohol use disorder | Family cohesion (Buckner et al. 2009) [Sig]	-0.093 (-0.175 to -0.009)	0.009	13688.452	-1270.845					2792.835	-259.289					
		Anxiety disorder → Alcohol use disorder (binary) | Maternal support (Gorka et al. 2014) [Sig]	-0.117 (-0.184 to -0.049)	0.001	1035004.036	-1215617.040					3496.858	-410.726					
		Social anxiety disorder → Alcohol use disorder | Parent support (Buckner et al. 2009) [NS]	-0.059 (-0.142 to 0.025)	0.006	29377.676	-1729.991					3134.362	-184.576					
		Anxiety disorder → Alcohol use disorder (binary) | Paternal support (Gorka et al. 2014) [NS]	-0.054 (-0.122 to 0.014)	0.001	1176261.610	-63867.318					3498.278	-189.946					
		Positive family experiences meta-estimate					-0.084	2215.459	0.999	0.002			-0.081	0.009	-0.098	-0.064	**-0.081 (-0.098 to -0.064)**
	Socioeconomic factors	--															N/A

Meta-estimate effects <0.05 are **bolded**.

Table A18: Alcohol → anxiety relationship full meta-analytic calculations for meta-estimate results, grouped by moderator subtheme.

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome | Moderator*	Effect Magnitude (transformed to Fisher's Z)	Fisher's Z S.E	Fixed-effect weights	Weighted effects	Mean FEz	Q	I^2	τ^2	Random weights	Random-weighted effects	Final pooled z	S.E of Pooled Estimate:	Meta LCI	Meta UCI	Meta estimate (random effect with CI)
Biological	**Gender/sex**	Alcohol use → Anxiety symptoms | Gender (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	0.051													
		Gender/sex meta-estimate															N/A
	Race/ ethnicity	--															N/A
Psychological	**Alcohol outcome expectancies: positive**	Alcohol dose (placebo vs control) → Anxiety (state) | Alcohol outcome expectancies- tension reduction (Abrams et al. 2022) [NS]	0.263 (-0.008 to 0.498)	0.141	50	13.479					13.759	3.709					
		Alcohol dose (placebo vs control) → Anxiety (state) | Alcohol outcome expectancies- tension reduction (Abrams et al. 2022) [Sig]	0.305 (0.038 to 0.532)	0.141	50	15.763					10.062	3.172					
		Alcohol outcome expectancies: positive meta-estimate					0.292	0.0052	0	0			0.289	0.205	-0.113	0.69	0.289 (-0.113 to 0.690)
	Anxiety sensitivity/ Anxiety	Alcohol dose (placebo vs control) → Anxiety (state) | Anxiety sensitivity (Abrams et al. 2022) [Sig]	-0.297 (-0.525 to -0.029)	0.141	50	-15.321					10.651	-3.264					
		Alcohol use → Anxiety symptoms | Anxiety sensitivity (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	0.051	390	19.665					393.333	19.833					
		Anxiety sensitivity/ Anxiety meta-estimate					0.01	5.643	0.823	0.052			0.041	0.05	-0.057	0.139	0.041 (-0.057 to 0.139)
	Attentional processes	--															N/A
	Depression	Alcohol use → Anxiety symptoms | Hopelessness (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	0.051	390	19.665					393.333	19.833					
		Heavy episodic drinking frequency → Anxiety symptoms in adolescence | Major depressive disorder (Wojciechowski et al. 2024) [Sig]	-0.068 (-0.130 to -0.006)	0.032	998	-68.245					213.853	-14.624					
		Heavy episodic drinking frequency → Anxiety symptoms in emerging adulthood | Major depressive disorder (Wojciechowski et al. 2024) [Sig]	-0.071 (-0.132 to -0.009)	0.032	998	-71.04					197.360	-14.049					
		Depression meta-estimate					-0.05	4.7178	0.576	0.001958			-0.07	0.049	-0.166	0.027	-0.070 (-0.166 to 0.027)
	Experimental manipulation of anxiety	--															N/A
	Externalising symptoms	Alcohol use → Anxiety symptoms | Impulsivity (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	0.051	390	19.665					393.333	19.833					
		Alcohol use → Anxiety symptoms | Sensation seeking (Mackie et al. 2011) [NS]	0.050 (-0.049 to 0.149)	0.051	390	19.665					393.333	19.833					

Moderator super-ordinate theme	Moderator subtheme	Effect Label Assigned *Predictor → Outcome | Moderator*	Effect Magnitude (transformed to Fisher's Z)	Fisher's Z S.E	Fixed-effect weights	Weighted effects	Mean FE z	Q	I^2	τ^2	Random weights	Random-weighted effects	Final pooled z	S.E of Pooled Estimate:	Meta LCI	Meta UCI	Meta estimate (random effect with CI)
		Externalising symptoms meta-estimate					0.05	0	0	0			0.05	0.035654	-0.02	0.12	0.050 (-0.019 to 0.120)
Socio-environmental	**Changing association over time**	--															N/A
	Drinking context	--															N/A

Table A19: Grading of Recommendations Assessment, Development, and Evaluation (GRADE) results for moderator subthemes eligible for meta-analysis.

Moderator superordinate theme	Moderator subtheme	Number of effects (number of studies)	Number of participants	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality of evidence	Comment
Anxiety → Alcohol										
Biological	Age	2 (3)	1,369	Very serious	Very serious	Very serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	Very serious heterogeneity between studies (I^2 = 93%). Meta-estimate suggests a significant positive effect, although risk of bias is warranted for this effect.
	Gender/ sex	8 (3)	4,817	Very serious	Very serious	Serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	Very high risk of bias of included studies, very large heterogeneity (I^2 = 87.6%). Meta-estimate CIs suggest a precise, true null effect.
Psychological	Alcohol outcome expectancies: Negative	6 (1)	3,156	Very serious	Not serious- Only 1 primary study	Serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	Very high risk of bias from the single included study. Not representative sample limiting generalisability. Meta-estimate CIs suggest a precise, true null effect.
	Alcohol outcome expectancies: Positive	6 (1)	3,156	Very serious	Not serious- Only 1 primary study	Serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	Very high risk of bias from the single included study. Not representative sample limiting generalisability. Meta-estimate CIs suggest a, precise, true null effect.
	Alcohol use	4 (2)	27, 824	Not serious	Very serious	Very serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	<25% high risk of bias. Very serious inconsistency (I^2 = 99.8%) and non-generalisable context, two effects derived from pregnant sample. No concerns regarding imprecision, suggesting that we can confidently rule out a meaningful moderation effect.
	Drinking motives: Drinking to cope	12 (3)	29,588	Not serious	Very serious	Serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	High risk of bias <25% of participants. Serious heterogeneity concerns (I^2 = 78.8%). Serious limitations regarding indirectness between studies (i.e., daily diary versus longitudinal). Precise meta-estimate suggesting true, null, moderating effect.
	Drinking motives: drinking to socialise or enhance	2 (1)	284	Very serious	Not serious- Only 1 primary study	Serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	High risk of bias from the single included study and serious concerns about generalisability of the population. Meta-estimate CIs suggest a, precise, true null effect.

Moderator superordinate theme	Moderator subtheme	Number of effects (number of studies)	Number of participants	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality of evidence	Comment
Biological	Embarrassment	4 (1)	1,904	Very Serious	Not serious- Only 1 primary study	Serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	High risk of bias from the single included study and serious concerns about the generalisability of the population and setting the study was conducted in. No concerns for imprecision.
	Emotion dysregulation	4 (1)	2,024	Not serious	Not serious- Only 1 primary study	Serious	Not serious	Publication bias strongly suspected	**Moderate** ⊕⊕⊕◯	Concerns regarding the indirectness regarding the generalisability of findings derived from an all-boy sample. CI is narrow, suggesting a true null moderating effect.
	Experimental manipulation of anxiety	2 (1)	208	Very serious	Not serious- Only 1 primary study	Serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	High risk of bias from the single included study. Serious concerns with indirectness owing to the all girl sample and the less valid measure of anxiety within the experiment. Z score and CI suggests a true, moderate to large moderating effect. However, no upgrade in score owing to only a single study contributing to these effects.
	Externalising symptoms	9 (3)	3,315	Serious	Very serious	Serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	>25% high risk of bias of included participants. Very serious heterogeneity concerns (I^2 = 96.7%). Concerns regarding the comparability between sample ages from included studies and their construct measure for the moderator. Meta-estimate and CI support a small to moderate precise protective moderating effect of impulsivity.
	Perceptions of peer alcohol use	2 (2)	737	Serious	Not serious	Serious	Not serious	Publication bias strongly suspected	**Low** ⊕⊕◯◯	High risk of bias for 73% of included participants. Concerns regarding the comparability and applicability across included studies (youth in contact with court system versus clinical population). Precise estimate suggests a true, protective effect of perceptions of peer alcohol use.
	Positive family experiences	4 (2)	2,722	Very serious	Very serious	Serious	Not serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	High risk of bias for all participants included and significant inconsistency (I^2 = 99.9%). Concerns regarding the difference in indirectness between social anxiety disorder and transdiagnostic anxiety disorders. Precise estimate suggests a true, protective effect of positive family experiences.

Alcohol → Anxiety

Moderator superordinate theme	Moderator subtheme	Number of effects (number of studies)	Number of participants	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality of evidence	Comment
Psychological	Alcohol outcome expectancies	2 (1)	106	Not serious	Not serious- Only 1 primary study	Serious	Serious	Publication bias strongly suspected	**Low** ⊕⊕◯◯	Whilst an experimental context the study was in only men leading to indirectness concerns. The wide CI, no significant effect, and large effect give imprecision concerns.
	Anxiety sensitivity/ anxiety	2 (2)	446	Not serious	Very serious	Very serious	Serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	Serious concerns regarding indirectness with effects derived from male only experimental sample and longitudinal adolescent sample. The CI included both trivial and potentially meaningful moderator affects limiting the ability to rule out clinically relevant moderation, therefore imprecision was downgraded.
	Depression	3 (2)	2,395	Very serious	Serious	Very serious	Serious	Publication bias strongly suspected	**Very low** ⊕◯◯◯	Very serious concerns regarding indirectness due to the difference in depression constructs measured between the two studies. Imprecision downgraded due to very small, not significant effect with wide CI.
	Externalising symptoms	2 (1)	786	Not serious	Not serious- Only 1 primary study	Serious	Not serious	Publication bias strongly suspected	**Low** ⊕⊕◯◯	Concerns regarding the arbitrary classification of groups split into low/medium/high group for indirectness. Imprecision just falls within the bounds to not have serious concern, supports a confident conclusion that impulsivity likely has no meaningful moderating effect.

Risk of bias was assessed using the ratings from the included studies. Downgrade by 1 level (serious) if more than 25% of participants were from studies at high risk of bias. Downgrade by 2 levels (very serious) if more than 50% of participants were from high-risk studies.

Inconsistency was assessed using the I^2 statistic from the meta-estimate. Downgrade by 1 level (serious) if I^2 >50%. Downgrade by 2 levels (very serious) if I^2 >75%.

Indirectness was assessed based on whether the population, predictor, outcome, and moderator aligned well with the constructs and research question and were comparable across included studies. Downgrade by 1 level (serious) if there were concerns such as non-representative populations, poor validity of measures, non-generalisable outcome measures, context-specific cultural or policy settings, or lack of comparable methods between studies.

Imprecision was assessed based on the 95% CI around the meta-analytic estimate of the moderation effect (Fisher's Z). Values between -0.1 and +0.1 were defined as representing a trivial moderator effect, based on commonly accepted thresholds for small effect sizes (equivalent to $r \approx \pm 0.1$) (Lovakov & Agadullina, 2021). CIs crossing zero were not automatically downgraded, as the true effect may include no moderation (i.e., a null effect). Downgrade by 1 level (serious) if the CI was not narrow enough to support a confident conclusion, either ruling in or ruling out a meaningful moderator effect.

Formal assessment of **publication bias** was not possible due to an insufficient number of studies to conduct quantitative tests (e.g., funnel plot asymmetry or Egger's test) (Prasad, 2024).

Upgrading

Large and precise effect. Upgrade 1 level if the magnitude of the moderator effect is substantial and precise, with a Fisher's Z estimate well outside the trivial range (e.g., $Z > \pm 0.3$), and a narrow 95% CI that excludes the null and the trivial effect zone (± 0.1).

Consistent, gradient like differences across moderator levels. Upgrade 1 level if there is evidence of a consistent gradient or ordered pattern across levels of the moderator. Such upgrading aims to align with GRADE's does response-gradient employed in the assessment of interventions.

Highly applicable and comparable across contexts. Upgrade 1 level if the moderation effect is replicated across multiple comparable populations, settings, and measures, and is conceptually coherent.

Lovakov, A., & Agadullina, E. R. (2021). Empirically derived guidelines for effect size interpretation in social psychology. *European Journal of Social Psychology*, *51*(3), 485-504. https:/doi.org/10.1002/ejsp.2752

Prasad, M. (2024). Introduction to the GRADE tool for rating certainty in evidence and recommendations. *Clinical Epidemiology and Global Health*, *25*, 101484. https:/doi.org/10.1016/j.cegh.2023.101484

Table A20: Risk of bias assessment of studies performing mediation analysis.

Study	1. Study design & selection bias							2. Confounding bias			3. Measurement bias				4. Statistical & analytical bias			5. Selection of the reported results bias			
	1.1	1.2	1.3	1.4	1.5	1.6	Decision	2.1	2.2	Decision	3.1	3.2	3.3	Decision	4.1	4.2	Decision	5.1	5.2	Decision	Overall risk
(Abrams, Matt, & and Reinertsen, 2002)	1	0	2	1	1	0	Some concerns	0	0	High	1	0	1	Some concerns	1	0	High	1	1	Low	**High**
(Bekman et al., 2010)	1	0	1	0	1	0	High	0	0	High	1	1	1	Low	1	0	High	1	1	Low	**High**
(Buckner & Turner, 2009)	1	0	1	0	2	0	High	0	1	Some concerns	1	1	1	Low	1	0	High	1	1	Low	**High**
(Collins et al., 2018)	1	0	1	1	0	0	Some concerns	0	1	Some concerns	1	1	1	Low	1	2	Some concerns	1	1	Low	**High**
(Goldstein et al., 2019)	1	0	1	0	0	0	High	1	1	Low	1	1	1	Low	1	2	Some concerns	1	1	Low	**High**
(Mackinnon et al., 2014)	1	0	1	1	0	0	Some concerns	1	1	Some concerns	1	1	1	Low	1	2	Some concerns	1	1	Low	**High**
(McCarty et al., 2023)	1	0	1	1	1	0	Some concerns	0	1	Some concerns	1	1	1	Low	1	0	High	1	1	Low	**High**
(Paulus et al., 2021)	1	0	1	1	0	0	Some concerns	0	1	Some concerns	1	1	1	Low	1	2	Some concerns	1	1	Low	**High**
(Sher et al., 2007)	1	0	2	1	0	0	Some concerns	0	1	Some concerns	1	1	1	Low	1	2	Some concerns	1	1	Low	**High**
(Wolitzky-Taylor et al., 2021)	1	0	1	1	0	0	Some concerns	0	1	Some concerns	1	1	1	Low	1	2	Some concerns	1	1	Low	**High**

*Some concerns in 3 or more domains upgraded to high risk of bias.

Table A21: Risk of bias assessment of studies performing moderation analysis.

Study	1. Study design & selection bias						2. Measurement bias				3. Statistical & analytical bias			4. Selection of the reported results bias			
	1.1	1.2	1.3	1.4	1.5	Decision	2.1	2.2	2.3	Decision	3.1	3.2	Decision	4.1	4.2	Decision	Overall Decision
(Abrams et al., 2001)	1	0	2	1	0	Some concerns	1	1	0	Some concerns	1	2	Low	1	0	Some concerns	**High**
(Abrams, Kushner, et al., 2002)	1	0	2	1	0	Some concerns	1	1	0	Some concerns	1	0	High	1	0	Some concerns	**High**
(Abrams et al., 2022)	1	0	1	1	0	Some concerns	1	1	1	Low	1	2	Low	1	1	Low	**Some concerns**
(Armeli et al., 2008)	1	0	1	0	0	High	1	1	1	Low	1	1	Some concerns	1	1	Low	**High**
(Armeli et al., 2010)	1	0	1	1	0	Some concerns	1	1	1	Low	1	0	High	1	1	Low	**High**
(Armeli, Erik, et al., 2014)	1	0	1	0	0	High	1	1	1	Low	1	1	Some concerns	1	1	Low	**High**
(Armeli, O'Hara, et al., 2014)	1	0	1	0	0	High	1	1	1	Low	1	0	High	1	1	Low	**High**
(Bilevicius et al., 2020)	1	0	1	0	0	High	1	1	1	Low	1	2	Low	1	1	Low	**High**
(Borges et al., 2018)	1	0	1	1	0	Some concerns	1	1	1	Low	1	0	High	1	1	Low	**High**
(Buckner & Turner, 2009)	1	0	1	2	0	Some concerns	1	1	1	Low	1	0	High	1	1	Low	**High**
(Carvalho et al., 2018)	1	0	1	2	0	Some concerns	1	1	0	Some concerns	1	0	High	0	0	High	**High**
(Caumiant et al., 2023)	1	0	1	0	2	High	1	1	0	Some concerns	0	0	High	1	1	Low	**High**
(Cerdá et al., 2013)	1	0	1	1	0	Some concerns	1	1	1	Low	1	2	Low	1	0	Some concerns	**Some concerns**
(Cheng et al., 2004)	1	0	1	2	1	Some concerns	1	1	0	Some concerns	1	1	Some concerns	1	1	Low	**High**
(Cloutier et al., 2019)	1	0	2	2	0	Some concerns	1	1	1	Low	1	0	High	1	1	Low	**High**
(Colder et al., 2017)	1	0	1	2	1	Some concerns	1	1	1	Low	1	2	Low	1	1	Low	**Some concerns**
(Colder et al., 2019)	1	0	1	2	0	Some concerns	1	1	0	Some concerns	0	2	High	0	0	High	**High**
(Cook et al., 2024)	1	0	1	2	0	Some concerns	1	1	1	Low	1	2	Low	0	0	High	**High**
(Dahne et al., 2014)	0	0	1	1	0	High	1	1	1	Low	1	1	Some concerns	1	0	Some concerns	**High**
(Dvorak & Simons, 2014)	1	0	1	0	0	High	1	1	1	Low	1	2	Low	1	1	Low	**High**
(Dyer et al., 2019)	1	0	1	2	0	Some concerns	1	1	1	Low	1	2	Low	1	1	Low	**Some concerns**
(Ferariu et al., 2024)	1	0	1	2	0	Some concerns	1	1	1	Low	1	2	Low	1	1	Low	**Some concerns**

Study	1. Study design & selection bias						2. Measurement bias				3. Statistical & analytical bias			4. Selection of the reported results bias			
	1.1	1.2	1.3	1.4	1.5	Decision	2.1	2.2	2.3	Decision	3.1	3.2	Decision	4.1	4.2	Decision	Overall Decision
(Gohari et al., 2023)	1	0	1	0	0	High	1	1	1	Low	0	2	High	0	0	High	**High**
(Gorka et al., 2014)	1	0	1	1	0	Some concerns	1	1	1	Low	1	0	High	1	1	Low	**High**
(Grant et al., 2009)	1	0	1	0	0	High	1	1	1	Low	1	1	Some concerns	1	1	Low	**High**
(Kaplow et al., 2001)	1	0	1	0	0	High	1	1	0	Some concerns	1	0	High	1	1	Low	**High**
(Leis et al., 2012)	0	0	1	1	0	Some concerns	1	1	1	Low	1	2	Low	1	1	Low	**Some concerns**
(Littlefield et al., 2012)	1	0	1	0	0	High	1	1	1	Low	1	1	Some concerns	1	0	Some concerns	**High**
(Mackie et al., 2011)	1	0	1	1	0	Some concerns	1	1	1	Low	1	2	Low	1	1	Low	**Some concerns**
(Marmorstein et al., 2010)	1	0	1	2	0	Some concerns	1	1	1	Low	1	0	High	1	1	Low	**High**
(Marmorstein, 2015)	1	0	1	1	0	Some concerns	1	1	1	Low	1	2	Low	1	1	Low	**Some concerns**
(Nichter & Chassin, 2015)	0	0	1	0	0	High	1	1	1	Low	0	0	High	0	0	High	**High**
(O'Grady, Cullum, Armeli, & Tennen, 2011)	1	0	1	0	0	High	0	1	1	Some concerns	1	0	High	1	1	Low	**High**
(O'Grady, Cullum, Tennen, & Armeli, 2011)	1	0	1	0	0	High	1	1	1	Low	1	1	Some concerns	1	1	Low	**High**
(Pardini et al., 2007)	1	0	1	1	0	Some concerns	1	1	1	Low	1	2	Low	1	1	Low	**Some concerns**
(Parrish et al., 2016)	0	0	1	1	0	High	1	1	0	Some concerns	0	2	High	0	0	High	**High**
(Pedersen et al., 2013)	1	0	1	2	0	Some concerns	1	1	1	Low	1	2	Low	1	1	Low	**Some concerns**
(Richton et al., 2017)	1	0	1	0	0	High	1	1	1	Low	1	0	High	1	0	Some concerns	**High**
(Sayette et al., 2001)	1	0	2	1	0	Some concerns	1	0	1	Some concerns	1	0	High	1	0	Some concerns	**High**
(Schleider et al., 2019)	1	0	1	1	0	Some concerns	1	1	1	Low	0	1	High	0	0	High	**High**
(Schmidt et al., 2007)	1	0	1	0	0	High	1	1	0	Some concerns	0	0	High	1	1	Low	**High**
(Sher et al., 2007)	1	0	2	0	0	High	1	0	1	Some concerns	1	0	High	1	1	Low	**High**
(Steele et al., 1986)	1	0	2	0	0	High	1	1	1	Low	1	0	High	0	0	High	**High**
(Steele & Josephs, 1988)	1	0	2	0	0	High	1	1	1	Low	1	0	High	1	0	Some concerns	**High**
(Stevens et al., 2014)	1	0	2	0	0	High	1	0	1	Some concerns	1	0	High	1	0	Some concerns	**High**
(Wojciechowski, 2024)	1	0	1	0	0	High	0	1	1	Some concerns	1	1	Some concerns	1	1	Low	**High**

Study	1. Study design & selection bias						2. Measurement bias				3. Statistical & analytical bias			4. Selection of the reported results bias			
	1.1	1.2	1.3	1.4	1.5	Decision	2.1	2.2	2.3	Decision	3.1	3.2	Decision	4.1	4.2	Decision	Overall Decision
(Zimmermann et al., 2003)	1	0	1	2	0	Some concerns	1	1	0	Some concerns	1	0	High	1	0	Some concerns	**High**

*Some concerns in 3 or more domains upgraded to high risk of bias.

Appendix B

Risk of bias assessment tool for mediation studies

Preface

This risk of bias assessment tool was developed as part of **Chapter 2**. This Appendix includes the development of the tool, the tool itself (Table B1), and guidance for using and scoring the tool (Table B2 to Table B7).

Development of the risk of bias tool for mediation studies

The primary purpose of this tool is to assess the risk of bias and quality of mediation studies. Mediation studies are prone to mediation-specific biases which are not adequately addressed by other risk of bias or quality assessment tools. As such this tool aims to assess mediation-specific biases and broader, general, methodological quality of mediation studies. Development of the risk of bias tool for mediation studies was guided by the overview of quality assessment practice in systematic reviews of mediation studies by (Vo et al., 2022). Additional general methodological quality assessment questions was guided by the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross Sectional Studies (Moola et al., 2020). The tool covers 5 overarching domains: i) study design and selection bias, ii) confounding bias, iii) measurement bias, iv) statistical and analytical bias, and v) selection of the reported results bias. Across the five domains there is a total of 15 signalling questions. Scores from the signalling questions are mapped to a domain-level risk of bias judgement of low risk of bias, some concerns, or high risk of bias. The domain-level judgments are then used to reach an overall judgment about risk of bias for the study. See below for the risk of bias assessment tool for mediation studies in Table B1 and mapping of signalling questions to suggested risk of bias in Table B2 to Table B7.

Risk of bias assessment tool for mediation studies.

Table B1: Risk of bias assessment tool for mediation studies

Bias domain	Signalling question	Elaboration	Response options	Maximum possible score for item
1. Study design and selection bias	1.1 Was there sufficient empirical or theoretical support for the hypothesized model(s).	Was there a theoretical rationale for investigating the mechanisms of interest. Including supporting evidence or theoretical rationale for why the intervention or exposure might have a causal relationship with the proposed mediators. Included supporting evidence or theoretical rationale for why the mediators might have a causal relationship with the outcomes.	0= No. 1= Yes.	1
	1.2 Was the planned mediation analysis preregistered?	This may include any protocols or study registrations specific to the mediation analysis.	0= No preregistration. 1= Preregistration but there were deviations from the planned research. 2= Preregistration and no deviations from the planned research.	2
	1.3 What study design was used?	Longitudinal study design may include but are not limited to retrospective cohort, prospective cohort, daily diary study, RCT, case-control design.	0= Non longitudinal design e.g., Cross-sectional design. 1= Longitudinal design without manipulation/experimentation of key variables. 2= Longitudinal design with manipulation/experimentation of key variables e.g. randomisation of exposure or mediator.	2
	1.4 Did the study design allow for temporal precedence of the exposure, mediator, and outcome to be evaluated?	Longitudinal study design will typically allow for temporal precedence, however, the timing of measures should still be assessed in a temporarily nature and this may not always be the case in a longitudinal design. i.e., if the exposure and	0= No 1= Yes	1

		outcome are both measured at the same measurement point.		
	1.5 Is the study sample representative to the population of interest?	The study should outline the source population and describe how participants were selected. Alternatively, the study has tested and reported comparisons between the sample and the population they are trying to represent.	0= No, convenience sample/ insufficient information to determine. 1= Somewhat, the study identified the source population and participants were recruited from this population but the sample who did participate were not representative of the entire population from which they were recruited. 2= Yes, the study identified the source population and participants were recruited from this population and the sample who did participate were representative of the entire population from which they were recruited. This is evidence either by discussion, reported comparisons between the sample and population, or references with additional information about samples representativeness.	2
	1.6 Did the study report a power calculation and was the study adequately powered to detect mediation?	A power calculation can be used to determine the suitability of the sample for assessing effect sizes of interest.	0= Power calculation not mentioned/insufficient power to detect a small effect size. 1= Sufficient power to detect a large effect size. 2= Sufficient power to detect a small-moderate effect size.	2
2. Confounding bias	2.1 Were confounding factors identified (or considered) for the tested models?	Confounders are "third" variables that relate to two or more variables in the mediation model which may partially explain the relationship between the exposure and outcome. Supporting theoretical rationale for a confounder may include citations for why that factor could influence the outcomes based on past evidence.	0= No. 1= Yes, potential confounding factors are explicitly outlined including supporting theoretical rationale.	1
	2.2 Did the study appropriately control for possible confounders?	Controlling for confounders may have been done via the experimental or study design itself or by appropriately accounting for potential confounders in the statistical analyses.	0= No 1= Somewhat, baseline covariates are included in the model with limited justification for inclusion. 2= Yes, identified confounders have been specifically adjusted for including mediator-outcome or mediator-mediator confounding.	2

3. Measurement bias	3.1 Was the exposure measured in a valid and reliable way?	Single or multiple exposures are all measured in valid and reliable way. Sufficient information is provided about the measure(s).	0= No/unable to determine. 1= Yes.	1
	3.2 Was the outcome measured in a valid and reliable way?	Single or multiple outcomes are all measured in valid and reliable way. Sufficient information is provided about the measure(s).	0= No/unable to determine. 1= Yes.	1
	3.3 Was the mediator measured in a valid and reliable way?	Single or multiple mediators are all measured in a valid and reliable way. Sufficient information is provided about the measure(s).	0= No/unable to determine. 1= Yes.	1
4. Statistical and analytical bias	4.1 Were statistically appropriate acceptable methods of data analysis used?	For mediation studies this may include but is not limited to product coefficient approach with bootstrapped confidence intervals, SEM, latent growth modelling and causal mediation analysis.	0= No, inappropriate methods or insufficient information to determine. 1= Yes, methods are adequate but cannot infer causal inference. E.g. Baron and Kenny, SEM. 2= Yes, methods are appropriate, are current best-practice, and can infer causal inference. E.g., potential outcomes framework.	2
	4.2 Were appropriate strategies to address incomplete data utilised?	Appropriate strategies would include but are not limited to: -Multiple imputation. -Maximum likelihood, full information maximum likelihood (FIML), Two-stage maximum likelihood (TS-ML). Inappropriate strategies would include, but are not limited to: - Listwise deletion if data not missing completely at random (MCAR) -Mean substitution. -Pairwise deletion if data not missing completely at random (MCAR).	0= No strategies used for missing data/unclear how missing data was handled. 1= Strategies used but not appropriate. 2= Appropriate strategies used OR no missing data/very little missing data. I.e. <5-10% missing.	2
5. Selection of the reported results bias	5.1 Were effect sizes reported?	Effect sizes should be reported for all mediation analyses carried out. The reporting of simply a result being significant is not sufficient.	0= No. 1= Yes, effect size reported.	1

	5.2 Were full results for all analyses/outcomes reported?	Full results should be reported for all analyses carried out, not just significant results.	0=No, only select results reported. 1= Yes, all results reported.	1
Total possible score				**22**

Reaching risk of bias judgments for each domain in the tool.

Table B1 to Table B6 present the mapping of signalling question responses to corresponding bias judgements within each of the five domains.

*Table B2: Suggested mapping of signalling questions to risk of bias judgements arising from the **study design and selection***

Signalling questions						Domain level judgement
1.1 Empirical evidence	**1.2 Preregistration**	**1.3 Study design**	**1.4 Temporal precedence**	**1.5 Sample**	**1.6 Power**	**Default risk of bias**
Both 1.1 and 1.2 are 0		1 or 2	Any response	Any response	Any response	High
Either 1.1 or 1.2 are 0		0	Any response	Any response	Any response	High
Either 1.1 or 1.2 are 0		1 or 2	0	0	Any responses	High
Either 1.1 or 1.2 are 0		1 or 2	1	1 or 2	Any responses	Some concerns
Either 1.1 or 1.2 are 0		1 or 2	0	1 or 2	Any responses	High
1.1 is 1 and 1.2 is 1 or 2		0	Any response	Any response	Any response	High
1.1 is 1 and 1.2 is 1 or 2		1	Any response	0	Any response	High
1.1 is 1 and 1.2 is 1 or 2		2	1	0	Any response	Some concerns
1.1 is 1 and 1.2 is 1 or 2		2	0	0	Any response	High
1.1 is 1 and 1.2 is 1 or 2		1 or 2	0	1 or 2	Any response	High
1.1 is 1 and 1.2 is 1 or 2		1 or 2	1	1 or 2	Any response	Some concerns
1.1 is 1 and 1.2 is 1 or 2		1 or 2	1	2	1 or 2	Low
Both 1.1 and 1.2 are 1		1 or 2	1	1 or 2	Any	Some concerns
1.1 is 1 and 1.2 is 2		1 or 2	1	1 or 2	0	Some concerns
1.1 is 1 and 1.2 is 2		2	2	2	2	Low
Both 1.1 and 1.2 are 1		1 or 2	0	1 or 2	Any	High
1.1 is 1 and 1.2 is 2		1 or 2	0	1 or 2	0	High

*Table B3: Suggested mapping of signalling questions to risk of bias judgements arising from **identification and controlling of confounding***

Signalling questions		Domain level judgement
2.1 Identification	**2.2 Controlling**	**Default risk of bias**
1	2	Low
1	1	Some
1	0	High
0	1 or 2	High
0	0	High

*Table B4: Suggested mapping of signalling questions to risk of bias judgements arising from the **measurement process**.*

Signalling questions			Domain level judgement
3.1 Exposure	**3.2 Outcome**	**3.3 Mediator**	**Default risk of bias**
1	1	1	Low
1	1	0	Some concerns
1	0	0	Some concerns
0	1	1	Some concerns
0	0	1	Some concerns
1	0	0	Some concerns
0	1	0	Some concerns
0	0	0	High

*Table B5: Suggested mapping of signalling questions to risk of bias judgements arising from the **statistical and analytical process**.*

Signalling questions		Domain level judgement
4.1 Analysis methods	**4.2 Incomplete data**	**Default risk of bias**
1 or 2	2	Low
1	1	Some
1	0	High
0	1 or 2	High
0	0	High

*Table B6: Suggested mapping of signalling questions to risk of bias judgements arising from the **selection of reported results**.*

Signalling questions		Domain level judgement
5.1 Effect sizes	**5.2 All reporting**	**Default risk of bias**
1	1	Low
1	0	Some concerns
0	1	Some concerns
0	0	High

Reaching an overall judgment about risk of bias

The algorithm for reaching on overall risk of bias judgement for a mediation study is provided in Table B7. The criteria used to determine this judgement is guided by existing Cochrane risk of bias tools (Higgins et al., 2019).

Table B7: Algorithm for reaching an overall risk of bias judgement.

Overall risk of bias judgement	**Criteria**
Low risk of bias	The study is judged to be at **low risk of bias for all domains**.
Some concerns	The study is judged to raise **some concerns in at least one domain,** but not to be at high risk of bias for any domain.
High risk of bias	The study is judged to be at **high risk of bias in at least one domain.** OR The study is judged to have **some concerns in 3 or more domains** in a way that substantially lowers confidence in the results.

References for Appendix B

Higgins, J. P. T., Savović, J., Page, M. J., Elbers, R. G., Sterne, J. A. C., Thomas, J., Page, M. J., Li, T., Higgins, J. P. T., Chandler, J., Cumpston, M., & Welch, V. A. (2019). Assessing risk of bias in a randomized trial. In (pp. 205-228). John Wiley & Sons, Ltd. https://doi.org/10.1002/9781119536604.ch8

Moola, S., Munn, Z., Tufanaru, C., Aromataris, E., Sears, K., Sfetcu, R., Currie, M., Lisy, K., Qureshi, R., Mattis, P., & Mu, P. (2020). Chapter 7: Systematic reviews of etiology and risk. In Aromataris E & M. Z (Eds.), *JBI Manual for Evidence Synthesis*. JBI. https://synthesismanual.jbi.global/

Vo, T. T., Cashin, A., Superchi, C., Tu, P. H. T., Nguyen, T. B., Boutron, I., MacKinnon, D., Vanderweele, T., Lee, H., & Vansteelandt, S. (2022). Quality assessment practice in systematic reviews of mediation studies: results from an overview of systematic reviews. *J Clin Epidemiol*, *143*, 137-148. https://doi.org/10.1016/j.jclinepi.2021.12.013

Appendix C

Risk of bias assessment tool for moderation studies

Preface

This risk of bias assessment tool was developed as part of **Chapter 2**. This Appendix includes the development of the tool, the tool itself (Table C1), and guidance for using and scoring the tool (Table C2 to Table C6).

Development of the risk of bias tool for moderation studies

The primary purpose of this tool is to assess the risk of bias and quality of moderation studies. Moderation studies are prone to moderation-specific biases which are not adequately addressed by other risk of bias or quality assessment tools. As such this tool aims to assess moderation-specific biases and broader, general, methodological quality of moderation studies. Development of the risk of bias tool for moderation studies was guided by the Editorial on moderation by Memon et al. (2019). Additional general methodological quality assessment questions was guided by the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross Sectional Studies (Moola et al., 2020). The tool covers four overarching domains: i) study design and selection bias, ii) measurement bias, iii) statistical and analytical bias, and iv) selection of the reported results bias. Across the four domains there is a total of 12 signalling questions. Scores from the signalling questions are mapped to a domain-level risk of bias judgement of low risk of bias, some concerns, or high risk of bias. The domain-level judgments are then used to reach an overall judgment about risk of bias for the study. See below for the risk of bias assessment tool for moderation studies in Table C1 and mapping of signalling questions to suggested risk of bias in Table C2 to Table C6.

Risk of bias assessment tool for moderation studies.

Table C1: *Risk of bias assessment tool for moderation studies.*

Bias domain	Signalling question	Elaboration	Response options	Maximum score for item
1. Study design and selection bias	1.1 Was there sufficient empirical or theoretical support for the hypothesized model(s)	Was there a theoretical rationale for investigating the variables of interest. Including supporting evidence or theoretical rationale for why the intervention or exposure might have a relationship with the proposed moderators. Included supporting evidence or theoretical rationale for why the moderators might have a relationship with the outcomes.	0= No. 1= Yes.	1
	1.2 Was the planned moderation analysis preregistered?	This may include any protocols or study registrations specific to the moderation analysis.	0= No preregistration. 1= Preregistration but there were deviations from the planned research. 2= Preregistration and no deviations from the planned research.	2
	1.3 What study design was used?	Longitudinal study design may include but are not limited to retrospective cohort, prospective cohort, daily diary study, RCT, case-control design.	0= Non longitudinal design e.g., Cross-sectional design. 1= Longitudinal design without manipulation/experimentation of key variables. 2= Longitudinal design with manipulation/experimentation of key variables e.g. randomisation of exposure or moderator.	2
	1.4 Is the study sample representative to the population of interest?	The study should outline the source population and describe how participants were selected. Alternatively, the study has tested and reported comparisons between the sample and the population they are trying to represent.	0= No, convenience sample/ insufficient information to determine. 1= Somewhat, the study identified the source population and participants were recruited from this population but the sample who did participate were not representative of the entire population from which they were recruited. 2= Yes, the study identified the source population and participants were recruited from this population and the sample who did participate were representative of the entire population from which they were recruited. This is evidence	2

			either by discussion, reported comparisons between the sample and population, or references with additional information about samples representativeness.	
	1.5 Did the study report a power calculation and was the study adequately powered to detect moderation?	A power calculation can be used to determine the suitability of the sample for assessing effect sizes of interest.	0= Power calculation not mentioned/insufficient power to detect a small effect size 1= Sufficient power to detect a large effect size. 2= Sufficient power to detect a small-moderate effect size.	2
2. Measurement bias	2.1 Was the exposure measured in a valid and reliable way?	Single or multiple exposures are all measured in valid and reliable way. Sufficient information is provided about the measure(s).	0= No/unable to determine. 1= Yes.	1
	2.2 Was the outcome measured in a valid and reliable way?	Single or multiple outcomes are all measured in valid and reliable way. Sufficient information is provided about the measure(s).	0= No/unable to determine. 1= Yes.	1
	2.3 Was the moderator measure in a valid and reliable way?	Single or multiple moderators are all measured in valid and reliable way. Sufficient information is provided about the measure(s).	0= No/unable to determine. 1= Yes.	1
3. Statistical and analytical bias	3.1 Were statistically appropriate acceptable methods of data analysis used?	For moderation studies this will typically be the inclusion of an interaction term in a model. Sufficient information should be provided about the statistical methods used.	0= No/unable to determine. 1= Yes.	1
	3.2 Were appropriate strategies to address incomplete data utilised?	Appropriate strategies would include but are not limited to: -Multiple imputation. -Maximum likelihood, full information maximum likelihood (FIML), Two-stage maximum likelihood (TS-ML). Inappropriate strategies would include, but are not limited to: - Listwise deletion if data not missing completely at random (MCAR) -Mean substitution. -Pairwise deletion if data not missing completely at random (MCAR).	0= No strategies used for missing data/unclear how missing data was handled. 1= Strategies used but not appropriate. 2= Appropriate strategies used OR no missing data/very little missing data. I.e. <5-10% missing.	2

4. Selection of the reported results bias	4.1 Were effect sizes reported?	Effect sizes should be reported for all moderation analyses carried out. The reporting of simply a result being significant is not sufficient.	0= No. 1= Yes, effect size reported.	1
	4.2. Were full results for all analyses/outcomes reported?	Full results should be reported for all analyses carried out, not just significant results.	0=No, only select results reported. 1= Yes, all results reported.	1
Total possible score				**17**

Reaching risk of bias judgments for each domain in the tool.

Table C2 to Table C5 present the mapping of signalling question responses to corresponding bias judgements within each of the four domains.

*Table C2: Suggested mapping of signalling questions to risk of bias judgements arising from the **study design and selection**.*

Signalling questions					Domain level judgement
1.1 Empirical evidence	**1.2 Preregistration**	**1.3 Study design**	**1.4 Sample**	**1.5 Power**	**Default risk of bias**
Both 1.1 and 1.2 are 0		1 or 2	Any response	Any response	High
Either 1.1 or 1.2 are 0		0	Any response	Any response	High
Either 1.1 or 1.2 are 0		1 or 2	0	Any responses	High
Either 1.1 or 1.2 are 0		1 or 2	1 or 2	Any responses	Some concerns
1.1 is 1 and 1.2 is 1 or 2		0	Any response	Any response	High
1.1 is 1 and 1.2 is 1 or 2		1	0	Any response	High
1.1 is 1 and 1.2 is 1 or 2		2	0	Any response	Some concerns
1.1 is 1 and 1.2 is 1 or 2		1 or 2	1 or 2	Any response	Some concerns
1.1 is 1 and 1.2 is 1 or 2		1 or 2	2	1 or 2	Low
Both 1.1 and 1.2 are 1		1 or 2	1 or 2	Any	Some concerns
1.1 is 1 and 1.2 is 2		1 or 2	1 or 2	0	Some concerns

*Table C3: Suggested mapping of signalling questions to risk of bias judgements arising from the **measurement process**.*

Signalling questions			Domain level judgement
2.1 Exposure	**2.2 Outcome**	**2.3 Moderator**	**Default risk of bias**
1	1	1	Low
1	1	0	Some concerns
1	0	0	Some concerns
0	1	1	Some concerns
0	0	1	Some concerns
1	0	0	Some concerns
0	1	0	Some concerns
0	0	0	High

*Table C4: Suggested mapping of signalling questions to risk of bias judgements arising from the **statistical and analytical process**.*

Signalling questions		Domain level judgement
3.1 Analysis methods	**3.2 Incomplete data**	**Default risk of bias**
1	2	Low
1	1	Some
1	0	High
0	1 or 2	High
0	0	High

*Table C5: Suggested mapping of signalling questions to risk of bias judgements arising from the **selection of reported results**.*

Signalling questions		Domain level judgement
4.1 Effect sizes	**4.2 All reporting**	**Default risk of bias**
1	1	Low
1	0	Some concerns
0	1	Some concerns
0	0	High

Reaching an overall judgment about risk of bias

The algorithm for reaching on overall risk of bias judgement for a moderation study is provided in Table C6. The criteria used to determine this judgement is guided by existing Cochrane risk of bias tools (Higgins et al., 2019).

Table C6: Algorithm for reaching an overall risk of bias judgement.

Overall risk of bias judgement	**Criteria**
Low risk of bias	The study is judged to be at **low risk of bias for all domains**.
Some concerns	The study is judged to raise **some concerns in at least one domain,** but not to be at high risk of bias for any domain.
High risk of bias	The study is judged to be at **high risk of bias in at least one domain.** OR The study is judged to have **some concerns in 3 or more domains** in a way that substantially lowers confidence in the results.

References for Appendix C

Higgins, J. P. T., Savović, J., Page, M. J., Elbers, R. G., Sterne, J. A. C., Thomas, J., Page, M. J., Li, T., Higgins, J. P. T., Chandler, J., Cumpston, M., & Welch, V. A. (2019). Assessing risk of bias in a randomized trial. In *Cochrane Handbook for Systematic Reviews of Interventions, Second Edition* (pp. 205-228). John Wiley & Sons, Ltd. https://doi.org/10.1002/9781119536604.ch8

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Appendix D

Protocol paper for Chapter 2

Preface

This systematic review protocol has been published as:

Gückel, T., Prior, K., Newton, N. C., & Stapinski, L. A. (2023). Mediators and moderators in the co-occurring anxiety and alcohol use relationship: protocol for a systematic review and meta-analysis. *JMIR Research Protocols*, *12*, e48875. https://doi.org/10.2196/48875.

TG conceptualised the study with support from KP, NCN and LAS. TG wrote the original manuscript. All authors critically revised the manuscript and approved the final versions.

Protocol

Mediators and Moderators in the Co-Occurring Anxiety and Alcohol Use Relationship: Protocol for a Systematic Review and Meta-Analysis

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Abstract

Background: Anxiety and alcohol use commonly co-occur. Previous research has demonstrated the bidirectional and mutually reinforcing nature of this relationship, with an increasing body of research investigating the mediating and moderating mechanisms driving this association. Within the existing mediation and moderation research, however, there have been contrasting findings and, at times, null results among some population groups.

Objective: This protocol outlines a systematic review and meta-analysis aiming to synthesize and clarify mediators and moderators in the anxiety-alcohol and alcohol-anxiety relationships.

Methods: Systematic searches will be conducted in the electronic databases Medline, PsycINFO, Embase, Cochrane Central Register of Controlled Trials, Scopus, and Web of Science to identify studies that investigated mediators and moderators of the relationship between anxiety and alcohol use, including clinical and subclinical levels. Studies that look at the relationship between anxiety and alcohol use outcomes, as well as alcohol use and anxiety outcomes, will be included in order to capture an in-depth understanding of the mechanisms driving the association in either direction. No limits will be placed on study year or study language. Included study designs will be observational studies, including cohort, cross-sectional, and longitudinal studies, and secondary analyses of randomized controlled trials reporting quantitative results. Selected studies will also have their reference lists hand-searched for other relevant papers. Study quality will be assessed with the Joanna Briggs Institute Checklists for Analytical Cross-Sectional Studies and Cohort Studies. Mediators and moderators will be narratively synthesized in line with the biopsychosocial framework, where results will be grouped into biological, psychological, and social or environmental factors. If the data are sufficiently homogeneous, a meta-analysis will be conducted with mediation and moderation analyses synthesized separately. The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework will also be used to assess the strength of cumulative evidence.

Results: Electronic database searches were conducted in September 2022. After duplicates were removed, a total of 7330 titles and abstracts were screened. Full-text reviewing is currently under way, with the results expected to be available by the end of 2023.

Conclusions: Given the significant individual and societal impacts of co-occurring anxiety and alcohol use, this review will help clarify mechanisms linking these two concerns. Identified mechanisms, where possible, can then be targeted in prevention, early intervention, and treatment approaches to improve the outcomes for individuals experiencing co-occurring anxiety and alcohol use.

Trial Registration: PROSPERO CRD42023358402; https://tinyurl.com/2m2e3enp

International Registered Report Identifier (IRRID): DERR1-10.2196/48875

(JMIR Res Protoc 2023;12:e48875) doi: 10.2196/48875

KEYWORDS

alcohol use; alcohol; anxiety; comorbidity; drinking; electronic databases; mediator; meta-analysis; moderator; prevention; systematic review

Introduction

Globally, anxiety disorders are the most common psychiatric disorders, with an estimated 301 million individuals experiencing one or more anxiety disorders in their lifetime [1]. Alcohol use is also highly prevalent, with an estimated 32.5% of people aged 15 years or older globally being current drinkers [2]. Among drinkers, high rates of risky drinking and alcohol use disorders are seen. A large nationally representative survey of 36,309 adults in the United States found 12.9% of individuals drink at high-risk levels, defined as 4+ standard drinks for women and 5+ standard drinks for men, at least weekly [3]. Additionally, among those who drink, 17.5% experienced an alcohol use disorder in the past year [3]. Comorbidity between mental health and substance use concerns is common, most notably between anxiety and alcohol use. Indeed, among individuals with an anxiety disorder, it is estimated that 20%-40% will also experience an alcohol use disorder in their lifetime [4]. When anxiety and alcohol use co-occur, symptom severity can be worse, and treatment adherence and outcomes are typically poorer compared to individuals with an anxiety or alcohol disorder alone [5,6].

Several theories have been proposed to explain the comorbid, bidirectional relationship between anxiety and alcohol use. Arguably, the most common is the self-medication model [7,8] which suggests individuals drink alcohol to alleviate symptoms of anxiety or general negative affect, in turn leading to a reliance on alcohol over time and the development of a subsequent alcohol use disorder. The use of alcohol for self-medication also aligns with other theories, including the tension-reduction theory [9] and the stress response dampening model [10]. Conversely, there is the opposite causal explanation that alcohol misuse and alcohol use disorders promote anxiety disorders, known as the substance-induced anxiety model or kindling or stress hypothesis [6,11,12]. Following prolonged periods of heavy alcohol consumption, withdrawal or cessation can lead to adaptations in the brain and wider nervous system, which can induce or worsen anxiety [6,11]. In addition to evidence of causal, bidirectional pathways between anxiety and alcohol, there is also support for a mutual-maintenance model also referred to as the “vicious cycle of comorbidity” [13]. This model demonstrates how the biopsychosocial outcomes of one disorder (eg, anxiety) will often serve to maintain or exacerbate the other disorder (eg, alcohol use disorder). An example of such a relationship can be seen when an individual with social anxiety who is self-medicating with alcohol develops a reliance on alcohol and over time experiences alcohol-related consequences like decreased productivity, interpersonal issues, and anxiety-induced withdrawal. These consequences exacerbate the initial anxiety and result in further drinking, thus maintaining the problematic feed-forward cycle [6,13]. Together, these theoretical frameworks suggest a complex bidirectional relationship between anxiety and alcohol use, with longitudinal and prospective studies confirming that experiencing an anxiety disorder or an alcohol use disorder can increase the risk of developing the other [14,15].

Previous critical and systematic reviews have established a strong body of evidence for a relationship between anxiety and alcohol use [12,16]. These reviews have typically focused on the temporal sequencing of the anxiety-alcohol relationship [16,17]; comorbidity between a specific anxiety disorder, for example, social anxiety disorder, and alcohol use [5,18-21]; the treatment of comorbid anxiety and alcohol use disorders [22-25]; or all of the above [12,26]. Yet, despite substantial existing research, the specific mechanisms driving anxiety and alcohol comorbidity are still poorly understood. The proposed systematic review will be the first to synthesize and clarify the specific mediators and moderators driving the relationship between anxiety and alcohol use.

Given the bidirectional nature of comorbid anxiety and alcohol use, the planned review will investigate the relationship in both directions. Figures 1 and 2 are path diagrams visually demonstrating the relationships that will be examined. Figure 1 illustrates anxiety as the exposure/predictor variable (X) and alcohol use as the outcome variable (Y), while Figure 2 illustrates the relationship in the opposite direction, where alcohol use is the exposure/predictor (X) and anxiety is the outcome (Y). As illustrated in Figures 1 and 2, a mediator or moderator is a third variable that affects the relationship between the exposure and outcome of interest [27]. Investigating mediators is warranted to better understand causal mechanisms that account for a relationship between X and Y [28]. In short, by identifying mediators, the proposed review will highlight factors explaining *how* or *why* the association between anxiety and alcohol, or alcohol and anxiety, occurs. If modifiable, these mediators can then be targeted in prevention, early intervention, and treatment approaches. To get a complete understanding of the anxiety and alcohol relationship, investigating the role of moderating variables is also necessary. The synthesis of moderators will highlight factors that affect the direction or strength of the relationship between X and Y [27]. As such, moderators can help understand *when* the relationship between anxiety and alcohol or alcohol and anxiety will occur. Given the breadth of possible mediating and moderating mechanisms studies can investigate, the review may identify mechanisms that can act as both a mediator and a moderator in the anxiety-alcohol relationship. An example of such a factor is positive alcohol use expectancies, with previous research identifying it as both a mediator and moderator in the relationships of interest [29-31].

Figure 1. Diagram demonstrating the possible mediator (Me) and moderator (Mo) pathways between the exposure variable anxiety (X) and outcome variable alcohol (Y).

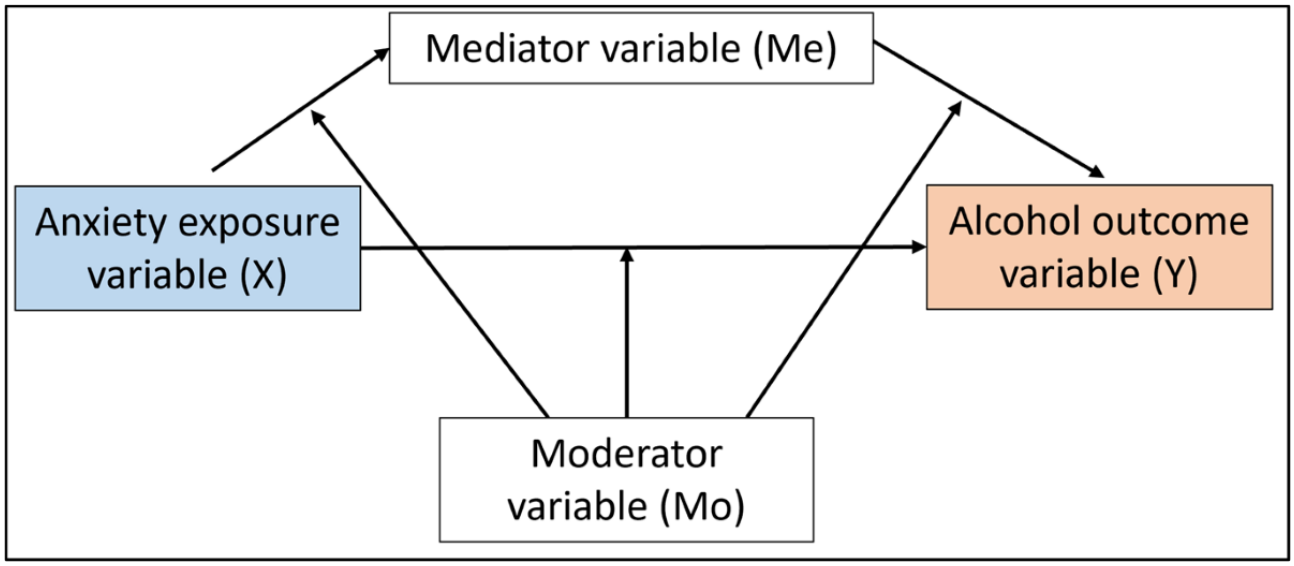
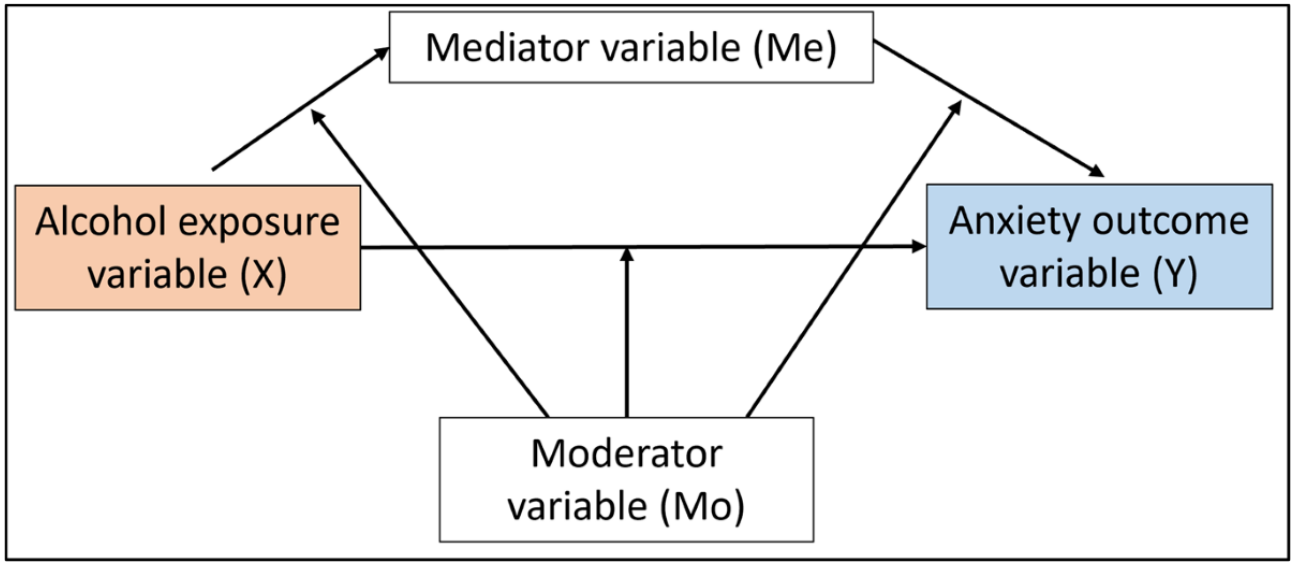


Figure 2. Diagram demonstrating the possible mediator (Me) and moderator (Mo) pathways between the exposure variable alcohol (X) and outcome variable anxiety (Y).



To our knowledge, this will be the first study to systematically identify and synthesize research on mediators and moderators of the comorbid anxiety and alcohol relationship. The outcomes of the review will specifically answer the following questions:

- What mediates the relationship between anxiety and alcohol use?
- What moderates the relationship between anxiety and alcohol use?

Methods

Guidelines and Registration

This protocol was written in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines [32]. The systematic review has been registered in PROSPERO, the International Prospective Register of Systematic Reviews (CRD42023358402).

Eligibility Criteria

Guided by the population, exposure, outcome (PEO) framework for conducting systematic reviews of association (etiology) [33], the below criteria will be used to determine eligible studies and structure the search strategy.

Population

All human populations are of interest for the proposed systematic review, and as such, no limits will be placed on the study population or participant type. Animal studies will be excluded.

Exposure and Outcome

Given the bidirectional nature of anxiety and alcohol comorbidity, the proposed systematic review will include studies investigating these concerns in either direction. Therefore, studies where anxiety is the exposure and alcohol use is the outcome, as well as studies where alcohol use is the exposure and anxiety is the outcome, will be included.

A broad classification will be used to define the anxiety exposure and outcome in this review. Anxiety will be conceptualized in line with the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5), where anxiety disorders are differentiated from obsessive compulsive and related disorders, and trauma and related-stressor disorders [34]. Per the DSM-5, anxiety disorders include generalized anxiety, social anxiety (social phobia), separation anxiety, selective mutism, specific phobia, agoraphobia, and panic disorder. Both studies that assess disorder-level measures or subclinical symptom measures will be included in the review. In addition to these definitions of anxiety, studies reporting broad symptoms of anxiety or anxious traits, such as anxiety sensitivity (eg, Anxiety Sensitivity Index-3), will also be included.

Like anxiety, a broad classification will be used to define the alcohol use exposure or outcome. This review is interested in the full spectrum of alcohol use and related difficulties and will include, but is not limited to, studies reporting frequency or quantity of alcohol consumption; hazardous, binge, or risky drinking; and alcohol use disorders.

Only studies where both the exposure and outcome are measured in the same individual will be included in this review. Studies looking at mediators or moderators between parents and offspring will be excluded.

Study Characteristics

Observational studies including cohort, cross-sectional, and longitudinal studies, and secondary analyses of randomized controlled trials reporting quantitative results will be included. Studies only evaluating intervention or treatment outcomes, including mediators or moderators of an intervention, will be excluded. Additionally, studies only reporting prevalence data will be excluded. Studies must be published in a peer-reviewed journal, with reviews, meta-analyses, and information in books, reports, letters, or conference abstracts being excluded from this systematic review. No limits will be placed on publication year or study language.

Information Sources and Search Strategy

Searches will be conducted in the electronic databases Medline (Ovid), PsycINFO (Ovid), Embase (Ovid), Cochrane Central Register of Controlled Trials (Ovid), Scopus, and Web of Science. Search strategies will be tailored to each database and use a combination of keywords and subject headings or medical subject headings (MeSH) where appropriate. A total of 3 overarching themes of anxiety, alcohol, and mediator or moderator will be used to structure the search, with search terms combined using the Boolean operators “AND” and “OR.” No year or language limits will be imposed on any of the searches. The reference lists of eligible studies will also be hand-searched to find additional studies not picked up in the electronic database searches. Full search strategies for each database are presented in Multimedia Appendix 1.

Study Selection and Extraction

All identified studies will be imported into the web-based systematic review software Covidence [35], where duplicates will automatically be removed. All titles and abstracts will be screened by a primary reviewer, with a random sample of 50% screened independently by a second reviewer. The full text of potentially eligible studies, identified through screening, will then be reviewed and assessed against the eligibility criteria by both reviewers. Disagreement between reviewers at both stages will be resolved through consultation, and if required, a third reviewer. Cohen κ will be calculated at the screening and full-text stage to determine the interrater agreement between reviewers, with a κ statistic of 0.8 considered a strong level of agreement [36]. The results of the screening and study selection process will be summarized with a PRISMA flow diagram in the final systematic review.

Data will be independently extracted by a primary reviewer using a data extraction spreadsheet in Excel (Microsoft Corp). A second reviewer will check and confirm all extracted data, with any disagreements reconciled through discussion. The following information will be extracted, and, if needed, the corresponding authors of included studies will be contacted for missing information:

- Publication details, including study authors and publication year
- Study characteristics, including study design, location, and sample size
- Sample population characteristics; for example, age, sex, ethnicity, socioeconomic status, and education
- Characteristics of anxiety exposure or outcome; for example, type of anxiety or anxiety disorder (if applicable), measure to assess anxiety, and age of onset
- Characteristics of alcohol use exposure or outcome; for example, frequency or quantity of use, age of initiation, hazardous or binge drinking, and alcohol use disorder
- Relevant information on the mediators and moderators examined, including the statistical analysis approach used; for example, mediator or moderator classification, assessment of mediator or moderator, single or multiple mediators or moderators assessed, whether confounders were controlled for, and overall strength of effect

Risk of Bias

Studies deemed eligible for inclusion in the systematic review will have their quality and risk of bias assessed independently by 2 reviewers. Disagreements between reviewers will be resolved through discussion and consultation with a third reviewer if required. Appraisal will be done using the Joanna Briggs Institute Critical Appraisal Tools [37]. Both the Checklist for Analytical Cross-Sectional Studies and the Checklist for Cohort Studies will be used to accommodate the different research designs of the included studies. These checklists evaluate the study sample, measurement of exposure and outcome variables, confounding, appropriateness of statistical analysis, and follow-up reporting (cohort checklist only) across 11 questions in the cohort studies checklist and 8 questions in the cross-sectional studies checklist.

Data Synthesis

Overview

A narrative synthesis of individual mediators and moderators from the included studies will be performed, with results

grouped in line with the biopsychosocial model [38]. This model encompasses biological factors like sex and age, psychological factors including cognitive and behavioral facets, and social factors, which encompass an individual's broader environment and the society in which they live. Furthermore, it is likely the relationships between anxiety and alcohol use will change between different groups; therefore, subgroup synthesis is planned for age subgroups (as defined by the World Health Organization), anxiety subgroups (as defined by the DSM-5), alcohol use sub groups broken down by severity (eg, mild, moderate, severe alcohol use disorder), and lastly, population types (eg, college students, veterans, specific cultural groups, etc). The inclusion of these subgroups will be reliant on data within the included studies, and if other key groupings emerge, further sub-group analyses may be conducted. Other information extracted, including publication details, study characteristics, sample population characteristics, and exposure and outcome characteristics, will also be narratively synthesized.

Given the broad inclusion criteria, it is anticipated that there will be high heterogeneity across studies. However, if the available data within the included studies is sufficiently homogenous, a meta-analysis will be conducted, with mediation and moderation analyses synthesized separately. Studies with comparable exposure and outcome measures and comparable mediator and moderator variables will be included in the meta-analysis. The indirect effects of mediation models will be synthesized using the methods defined in Cheung [39]. The synthesis of moderating variables will be dependent on the statistical analysis within individual studies but will include pooled estimates of coefficients.

Confidence in Cumulative Evidence

The cumulative strength of evidence from included studies will be assessed using the GRADE framework [40]. This framework enables a conclusion to be drawn on whether there is high, moderate, low, or very low confidence in the findings.

Results

This systematic review is currently underway. In September 2022, initial database searches identified 7330 unique studies for title and abstract screening. It is anticipated that the review, including data extraction and synthesis, will be completed by December 2023. Upon completion, results will be reported in line with PRISMA and disseminated in a peer-reviewed journal. Before submission, searches will be rerun to capture any additional articles that have been published since the initial database searches.

Discussion

This paper summarizes the protocol for a systematic review and prospective meta-analysis on mediators and moderators in the co-occurring anxiety and alcohol relationship. The review will incorporate studies from a wide spectrum of anxiety and alcohol classifications, including from anxiety symptoms to anxiety disorders and from alcohol use to alcohol use disorders. The biopsychosocial model will be used to synthesize identified factors to determine the distinct roles of biological, psychological, and social mechanisms.

Existing studies often examine a single mediator or moderator, despite evidence of multiple mechanisms contributing to the alcohol and anxiety relationship [12]. In light of this, this review will be the first to consolidate the literature to date on mediators and moderators driving this common comorbidity. Identified mediators and moderators can then be used as targets to develop and refine prevention, early intervention, and treatment approaches for comorbid anxiety and alcohol use concerns. In some cases, the identified mediating and moderating factors may not be modifiable in interventions; nonetheless, synthesizing this evidence will help advance the theoretical basis underlying this common comorbidity. As this review will focus on both the pathway from anxiety to alcohol use and the pathway from alcohol use to anxiety, findings may suggest different prevention and intervention approaches are needed depending on the temporal sequencing of the two disorders. One limitation, however, of the planned review is the inclusion of cohort and cross-sectional studies, which will limit the ability to draw causal conclusions for all results. The inclusion of these study designs is warranted nonetheless, as preliminary searches indicated most mediation and moderation studies for anxiety and alcohol were not longitudinal.

The findings of this review will offer critical insights into the conceptualization of comorbid anxiety and alcohol use, providing a foundation for researchers, clinicians, and policy makers to enhance outcomes in addressing this complex clinical manifestation. These results have the potential to drive advancements in understanding, prevention, and treatment strategies, thereby positively impacting individuals experiencing anxiety and alcohol use concerns.

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Data Availability

Data sharing is not applicable to this article as no data sets were generated or analyzed during this study.

Authors' Contributions

All authors (TG, KP, NCN, and LAS) conceived the initial idea for the systematic review. TG drafted the manuscript, and KP, NCN, and LAS provided critical insights. All authors contributed to the revision of the manuscript and approved the final version.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Electronic database searches.
[DOCX File , 24 KB-Multimedia Appendix 1]

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Abbreviations

DSM-5: Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition
GRADE: Grading of Recommendations, Assessment, Development, and Evaluations
MeSH: medical subject headings
PEO: population, exposure, outcome
PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols

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Appendix E

Supplementary materials for Chapter 3

Preface

This Appendix includes supplementary material for **Chapter 3**. Supplementary materials include: confounder and key study variable correlations (Table E1), data availability breakdown for key variables (Table E2), results from complete case models (Table E3 to Table E6), p-value corrections (Table E7 to Table E10) and observed versus imputed means for key study variables (Table E11).

Table E1: Correlations between confounders and key study variables at baseline.

		Wave 1 BSI anxiety symptoms		**Wave 1 hazardous alcohol use**	
ANOVA		F	*p*	F	*p*
	Country of birth	0.641	.527	0.01	.99
	Average school grades	1.353	.241	9.754	**<.001**
t- test		t	*p*	t	*p*
	Sex	-2.17	**.031**	1.1	.273

Table E2: Breakdown of available data for key study variables at each follow-up timepoint.

	Wave 1 Baseline	**Wave 2 6-month follow-up**	**Wave 3 1-year follow-up**	**Wave 4 2-year follow-up**	**Wave 5 3-year follow-up**	**Wave 6 5-year follow-up**	**Wave 7 7-year follow-up**
Sex	418, 100%	N/A†	N/A†	N/A†	N/A†	N/A†	N/A†
Age (years)	417, 99.8%	N/A†	N/A†	N/A†	N/A†	N/A†	N/A†
Anxiety symptoms (BSI)	418, 100%	341, 81.6%	366, 87.6%	345, 82.5%	302, 72.2%	222, 53.1%	193, 46.2%
Hazardous alcohol use (AUDIT-C)	418, 100%	357, 85.4%	376, 90.0%	358, 85.6%	316, 75.6%	219, 52.4%	188, 45.0%
Depression symptoms (BSI)	418, 100%	341, 81.6%	366, 87.6%	345, 82.5%	302, 72.2%	222, 53.1%	193, 46.2%
Impulsivity (SURPS)	418, 100%	358, 85.6%	379, 85.6%	358, 85.6%	321, 76.8%	220, 52.6%	187, 44.7%
Sensation seeking (SURPS)	418, 100%	358, 85.6%	379, 85.6%	358, 85.6%	321, 76.8%	220, 52.6%	187, 44.7%
Coping-anxiety drinking motives (Modified DMQ-R)	N/A#	353, 84.4%	374, 89.5%	356, 85.2%	316, 75.6%	217, 51.9%	185, 44.3%
Conformity drinking motives (Modified DMQ-R)	N/A#	353, 84.4%	374, 89.5%	356, 85.2%	316, 75.6%	217, 51.9%	185, 44.3%
Enhancement drinking motives (Modified DMQ-R)	N/A#	353, 84.4%	374, 89.5%	356, 85.2%	316, 75.6%	217, 51.9%	185, 44.3%
Social drinking motives (Modified DMQ-R)	N/A#	353, 84.4%	374, 89.5%	356, 85.2%	316, 75.6%	217, 51.9%	185, 44.3%

Was not measured at that time point.
† Only baseline measure of this variable used in analyses.

Table E3: Complete case linear regression examining the cross-sectional associations between anxiety symptoms (predictor) and hazardous alcohol use (outcome) at each study wave.

		Unadjusted model				**Adjusted model†**			
	n	B	95% Confidence Interval		*p*	B	95% Confidence Interval		*p*
			LL	UL			LL	UL	
Wave 1, 13.4 years	418	0.046	0.016	0.077	**.003**	0.041	0.011	0.07	**.007**
Wave 2, 14.0 years	341	0.162	0.119	0.205	**<.001**	0.165	0.122	0.209	**<.001**
Wave 3, 14.5 years	366	0.092	0.049	0.135	**<.001**	0.096	0.052	0.14	**<.001**
Wave 4, 15.4 years	344	0.093	0.027	0.159	**.006**	0.107	0.04	0.174	**.002**
Wave 5, 16.4 years	301	0.128	0.037	0.22	**.006**	0.143	0.05	0.236	**.003**
Wave 6, 19.0 years	215	0.089	-0.015	0.192	.092	0.125	0.026	0.225	**.014**
Wave 7, 20.5 years	184	-0.026	-0.143	0.09	.654	-0.013	-0.129	0.104	.832

†Adjusted models include sex, country of birth, and average school grades at wave 1.
P values <0.05 are **bolded**.
LL: Lower limit; UL: Upper limit

Table E4: Complete case linear regression of the longitudinal, lagged, associations between anxiety symptoms (predictor) and hazardous alcohol use (outcome).

Wave, mean age	*n*	**Unadjusted model**				**Adjusted model†**			
		B	95% Confidence Interval		*p*	B	95% Confidence Interval		*p*
			LL	UL			LL		LL
Anxiety Wave 1, 13.4 years to Alcohol Wave 2, 14 years	357	0.032	-.028	.093	.298	0.031	-.031	.093	.326
Anxiety Wave 2, 14 years to Alcohol Wave 3, 14.5 years	315	0.035	-.008	.077	.113	0.033	-.011	.077	.136
Anxiety Wave 3, 14.5 years to Alcohol Wave 4, 15.4 years	335	0.096	.020	.171	**.013**	0.109	.034	.185	**.005**
Anxiety Wave 4, 15.4 years to Alcohol Wave 5, 16.4 years	286	0.04	-.056	.136	.412	0.051	-.046	.148	.300
Anxiety Wave 5, 16.4 years to Alcohol Wave 6, 19 years	186	-0.049	-.154	.055	.353	-0.013	-.116	.09	.809
Anxiety Wave 6, 19 years to Alcohol Wave 7, 20.5 years	170	0.009	-.116	.134	.886	0.023	-.102	.148	.72

†Adjusted models include sex, country of birth, and average school grades at wave 1.
P values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

Table E5: Complete case linear regressions examining the potential moderating effect of factors on the association between anxiety and hazardous alcohol use cross-sectionally across seven separate ages†.

Wave, mean age	Moderator[#]	*n*	Unstandardised Beta for interaction term	95% Confidence Interval		*p*
				LL	UL	
Wave 1, 13.4 years						
	Sex (reference male)	418	0.063	-0.014	0.14	.107
	Depression	418	0.001	-0.003	0.005	.6
	Impulsivity	418	0.018	0.01	0.026	**<.001**
	Sensation seeking	418	0.017	0.008	0.026	**<.001**
Wave 2, 14.0 years						
	Sex (reference male)	341	-0.229	-0.345	-0.113	**<.001**
	Depression	341	0.017	0.011	0.022	**<.001**
	Impulsivity	341	0.055	0.044	0.065	**<.001**
	Sensation seeking	341	0.041	0.032	0.05	**<.001**
	Conformity drinking motives	341	0.047	0.04	0.053	**<.001**
	Coping-anxiety drinking motives	341	0.046	0.039	0.053	**<.001**
	Enhancement drinking motives	341	0.029	0.024	0.034	**<.001**
	Social drinking motives	341	0.029	0.024	0.035	**<.001**
Wave 3, 14.5 years						
	Sex (reference male)	366	-0.261	-0.377	-0.145	**<.001**
	Depression	366	0.011	0.005	0.016	**<.001**
	Impulsivity	366	0.038	0.023	0.052	**<.001**
	Sensation seeking	366	0.03	0.02	0.04	**<.001**
	Conformity drinking motives	366	0.018	0.01	0.026	**<.001**
	Coping-anxiety drinking motives	366	0.015	0.005	0.025	**.004**
	Enhancement drinking motives	366	0.01	0.004	0.016	**.002**
	Social drinking motives	366	0.015	0.008	0.022	**<.001**
Wave 4, 15.4 years						
	Sex (reference male)	344	0.044	-0.119	0.207	.596
	Depression	344	0.013	0.004	0.023	**.005**
	Impulsivity	343	0.012	-0.006	0.031	.193
	Sensation seeking	343	0.007	-0.009	0.023	.418
	Conformity drinking motives	344	0.007	-0.006	0.021	.277
	Coping-anxiety drinking motives	344	0.011	-0.001	0.023	.061
	Enhancement drinking motives	344	0.002	-0.006	0.01	.616
	Social drinking motives	344	-0.012	-0.019	-0.005	**.001**
Wave 5, 16.4 years						
	Sex (reference male)	301	0.282	0.034	0.529	**.026**
	Depression	301	0.007	-0.007	0.021	.314
	Impulsivity	300	0.007	-0.018	0.031	.594
	Sensation seeking	300	-0.01	-0.029	0.009	.315
	Conformity drinking motives	301	0.008	-0.007	0.022	.290
	Coping-anxiety drinking motives	301	0.011	-0.005	0.026	.167
	Enhancement drinking motives	301	0.007	-0.002	0.017	.109
	Social drinking motives	301	0.014	0.004	0.024	**.008**
Wave 6, 19.0 years						
	Sex (reference male)	215	-0.066	-0.303	0.17	.12
	Depression	215	-0.003	-0.019	0.014	.756
	Impulsivity	213	0.015	-0.015	0.044	.325
	Sensation seeking	213	-0.0002	-0.026	0.025	.984
	Conformity drinking motives	215	-0.001	-0.024	0.022	.921
	Coping-anxiety drinking motives	215	0.004	-0.015	0.024	.659
	Enhancement drinking motives	215	0.003	-0.011	0.016	.698
	Social drinking motives	215	0.004	-0.013	0.021	.625
Wave 7, 20.5 years						
	Sex (reference male)	184	0.219	-0.166	0.604	.263
	Depression	184	0.002	-0.019	0.023	.878
	Impulsivity	178	0.016	-0.027	0.059	.473
	Sensation seeking	178	-0.008	-0.04	0.023	.600

	Conformity drinking motives	184	0.01	-0.02	0.041	.514
	Coping-anxiety drinking motives	184	-0.014	-0.046	0.018	.375
	Enhancement drinking motives	184	-0.007	-0.024	0.011	.462
	Social drinking motives	184	-0.0001	-0.025	0.024	.990

†Adjusted models include sex, country of birth, and average school grades at wave 1.
#Each moderator was tested in a separate model; interaction terms reflect results from individual analyses.
P values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

Table E6: Complete case linear regressions examining the potential moderating effect of factors on the association between anxiety and hazardous alcohol use longitudinally across adolescence and young adulthood†.

Wave, mean age	Moderator[#]	*n*	Unstandardised Beta for interaction term	95% Confidence Interval		*p*
				LL	UL	
Anxiety Wave 1, 13.4 years to Alcohol Wave 2, 14 years						
	Sex (reference male)	357	0.158	-0.033	0.349	.104
	Depression	357	0.011	0.001	0.022	**.03**
	Impulsivity	357	0.022	-0.001	0.045	.061
	Sensation seeking	357	0.011	-0.01	0.031	.307
Anxiety Wave 2, 14 years to Alcohol Wave 3, 14.5 years						
	Sex (reference male)	315	-0.031	-0.156	0.093	.621
	Depression	315	0.009	0.003	0.014	**.003**
	Impulsivity	315	0.001	-0.01	0.013	.839
	Sensation seeking	315	0.006	-0.004	0.016	.24
	Conformity drinking motives	315	0.007	-0.003	0.017	.142
	Coping-anxiety drinking motives	315	-0.0005	-0.013	0.012	.942
	Enhancement drinking motives	315	-0.011	-0.018	-0.003	**.006**
	Social drinking motives	315	-0.009	-0.016	-0.001	**.03**
Anxiety Wave 3, 14.5 years to Alcohol Wave 4, 15.4 years						
	Sex (reference male)	335	-0.133	-0.336	0.069	.195
	Depression	335	0.015	0.006	0.025	**.001**
	Impulsivity	335	0.027	0.0003	0.054	**.047**
	Sensation seeking	335	0.021	0.003	0.038	**.022**
	Conformity drinking motives	335	0.008	-0.007	0.023	.28
	Coping-anxiety drinking motives	335	0.006	-0.012	0.025	.51
	Enhancement drinking motives	335	-0.0002	-0.014	0.014	.979
	Social drinking motives	335	0.009	-0.004	0.023	.18
Anxiety Wave 4, 15.4 years to Alcohol Wave 5, 16.4 years						
	Sex (reference male)	286	0.221	-0.004	0.447	.054
	Depression	286	0.016	0.003	0.029	**.019**
	Impulsivity	285	0.002	-0.024	0.029	.871
	Sensation seeking	285	-0.01	-0.032	0.013	.4
	Conformity drinking motives	286	0.009	-0.011	0.029	.38
	Coping-anxiety drinking motives	286	0.015	-0.005	0.035	.147
	Enhancement drinking motives	286	0.003	-0.011	0.016	.703
	Social drinking motives	286	-0.005	-0.017	0.007	.417
Anxiety Wave 5, 16.4 years to Alcohol Wave 6, 19 years						
	Sex (reference male)	186	0.135	-0.124	0.395	.304
	Depression	186	-0.003	-0.017	0.012	.722
	Impulsivity	186	-0.021	-0.048	0.007	.141
	Sensation seeking	186	-0.017	-0.038	0.004	.106
	Conformity drinking motives	186	-0.009	-0.025	0.008	.298
	Coping-anxiety drinking motives	186	0.002	-0.019	0.023	.86
	Enhancement drinking motives	186	-0.002	-0.016	0.012	.766
	Social drinking motives	186	-0.003	-0.019	0.012	.677
Anxiety Wave 6, 19 years to Alcohol Wave 7, 20.5 years						
	Sex (reference male)	170	-0.058	-0.406	0.291	.745
	Depression	170	-0.008	-0.029	0.013	.445
	Impulsivity	170	-0.019	-0.062	0.023	.376

	Sensation seeking	170	-0.012	-0.044	0.02	.458
	Conformity drinking motives	170	-0.01	-0.036	0.015	.43
	Coping-anxiety drinking motives	170	-0.009	-0.038	0.02	.546
	Enhancement drinking motives	170	-0.008	-0.026	0.01	.401
	Social drinking motives	170	-0.006	-0.028	0.017	.626

†Adjusted models include sex, country of birth, and average school grades at wave 1.
#Each moderator was tested in a separate model; interaction terms reflect results from individual analyses.
P values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

Table E7: Raw and adjusted P-values for linear regression examining the cross-sectional associations between anxiety symptoms (predictor) and hazardous alcohol use (outcome) at each study wave.

Wave, mean age	**Adjusted model†**				
	B	95% Confidence Interval		Raw *p-value*	Benjamini-Hochberg Procedure *p-value*
		LL	UL		
Wave 1, 13.4 years	0.041	0.011	0.070	**.007**	**.012**
Wave 2, 14.0 years	0.158	0.115	0.202	**<.001**	**.004**
Wave 3, 14.5 years	0.1	0.056	0.144	**<.001**	**.004**
Wave 4, 15.4 years	0.085	0.021	0.149	**.01**	**.014**
Wave 5, 16.4 years	0.141	0.051	0.232	**.002**	**.005**
Wave 6, 19.0 years	0.109	-0.004	0.221	.059	.069
Wave 7, 20.5 years	0.028	-0.093	0.149	.645	.645

†Adjusted models include sex, country of birth, and average school grades at Wave 1.
P values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

Table E8: Raw and adjusted P-values for linear regression of the longitudinal, lagged associations between anxiety symptoms (predictor) and hazardous alcohol use (outcome).

Wave, mean age	**Adjusted model†**				
	B	95% Confidence Interval		Raw *p-value*	Benjamini-Hochberg Procedure *p-value*
		LL	UL		
Anxiety Wave 1, 13.4 years to Alcohol Wave 2, 14 years	0.034	-0.023	0.091	.244	.325
Anxiety Wave 2, 14 years to Alcohol Wave 3, 14.5 years	0.043	-0.006	0.091	.086	.258
Anxiety Wave 3, 14.5 years to Alcohol Wave 4, 15.4 years	0.091	0.017	0.165	**.016**	.096
Anxiety Wave 4, 15.4 years to Alcohol Wave 5, 16.4 years	0.049	-0.039	0.137	.271	.325
Anxiety Wave 5, 16.4 years to Alcohol Wave 6, 19 years	0.024	-0.077	0.126	.634	.634
Anxiety Wave 6, 19 years to Alcohol Wave 7, 20.5 years	0.067	-0.052	0.185	.266	.325

†Adjusted models include sex, country of birth, and average school grades at Wave 1.
P values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

Table E9: Raw and adjusted P-values for linear regressions examining the potential moderating effect of factors on the association between anxiety and hazardous alcohol use cross-sectionally across seven separate ages†.

Wave, mean age	Moderator[#]	Unstandardised Beta for interaction term	95% Confidence Interval		Raw p-value	**Benjamini-Hochberg Procedure *p-value***
			LL	UL		
Wave 1, 13.4 years						
	Sex (reference male)	0.063	-0.014	0.140	.107	.058
	Depressive symptoms	0.001	-0.003	0.005	.600	.884
	Impulsivity	0.018	0.010	0.026	<.001	.003
	Sensation seeking	0.017	0.008	0.026	<.001	.003
Wave 2, 14.0 years						
	Sex (reference male)	-0.163	-0.300	-0.027	.020	.058
	Depressive symptoms	0.014	0.008	0.019	<.001	.003
	Impulsivity	0.049	0.036	0.062	<.001	.003
	Sensation seeking	0.049	0.027	0.046	<.001	.003
	Conformity drinking motives	0.043	0.034	0.053	<.001	.003
	Coping-anxiety drinking motives	0.043	0.034	0.052	<.001	.003
	Enhancement drinking motives	0.027	0.021	0.033	<.001	.003
	Social drinking motives	0.027	0.021	0.033	<.001	.003
Wave 3, 14.5 years						
	Sex (reference male)	-0.211	-0.335	-0.088	<.001	.003
	Depressive symptoms	0.009	0.003	0.014	.001	.003
	Impulsivity	0.033	0.017	0.048	<.001	.003
	Sensation seeking	0.027	0.016	0.038	<.001	.003
	Conformity drinking motives	0.016	0.008	0.025	<.001	.003
	Coping-anxiety drinking motives	0.013	0.002	0.024	.019	.058
	Enhancement drinking motives	0.008	0.0004	0.015	.040	.104
	Social drinking motives	0.012	0.005	0.020	.001	.003
Wave 4, 15.4 years						
	Sex (reference male)	0.019	-0.136	0.173	.814	.917
	Depressive symptoms	0.01	0.001	0.019	.032	.088
	Impulsivity	0.008	-0.011	0.027	.408	.786
	Sensation seeking	0.006	-0.010	0.021	.478	.802
	Conformity drinking motives	-0.0003	-0.015	0.015	.967	.984
	Coping-anxiety drinking motives	0.007	-0.006	0.020	.300	.650
	Enhancement drinking motives	-0.001	-0.009	0.007	.771	.908
	Social drinking motives	-0.012	-0.020	-0.004	.002	.007
Wave 5, 16.4 years						
	Sex (reference male)	0.188	-0.046	0.422	.115	.260
	Depressive symptoms	0.004	-0.009	0.017	.501	.807
	Impulsivity	0.005	-0.018	0.029	.650	.884
	Sensation seeking	-0.009	-0.028	0.009	.326	.652
	Conformity drinking motives	0.006	-0.010	0.021	.460	.802
	Coping-anxiety drinking motives	0.006	-0.010	0.022	.473	.802
	Enhancement drinking motives	0.005	-0.005	0.015	.321	.652
	Social drinking motives	0.01	0.000	0.020	.044	.109
Wave 6, 19.0 years						
	Sex (reference male)	0.012	-0.183	0.208	.900	.955
	Depressive symptoms	0.0003	-0.014	0.015	.970	.984
	Impulsivity	0.006	-0.020	0.032	.652	.884
	Sensation seeking	-0.006	-0.029	0.017	.596	.884
	Conformity drinking motives	-0.004	-0.023	0.016	.696	.905

Coping-anxiety drinking motives	0.0002	-0.019	0.019	.984	.984
Enhancement drinking motives	-0.002	-0.016	0.013	.829	.917
Social drinking motives	-0.002	-0.019	0.014	.786	.908
Wave 7, 20.5 years					
Sex (reference male)	0.038	-0.189	0.264	.744	.906
Depressive symptoms	0.002	-0.015	0.018	.854	.925
Impulsivity	0.005	-0.026	0.035	.749	.906
Sensation seeking	-0.004	-0.026	0.018	725	.906
Conformity drinking motives	0.006	-0.019	0.030	.648	.884
Coping-anxiety drinking motives	-0.006	-0.032	0.021	.663	.884
Enhancement drinking motives	-0.006	-0.022	0.010	.467	.802
Social drinking motives	-0.006	-0.024	0.012	.512	.807

†Adjusted models include sex, country of birth, and average school grades at Wave 1.
#Each moderator was tested in a separate model; interaction terms reflect results from individual analyses.
P values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

Table E10: Raw and adjusted P-values for linear regressions examining the potential moderating effect of factors on the association between anxiety and hazardous alcohol use longitudinally across adolescence and young adulthood†.

Wave, age	Moderator[#]	Unstandardised Beta for interaction term	95% Confidence Interval		Raw *p-value*	Benjamini-Hochberg Procedure *p-value*
			LL	UL		
Anxiety Wave 1, 13.4 years to Alcohol Wave 2, 14 years						
	Sex (reference male)	0.121	-0.034	0.276	.126	.748
	Depressive symptoms	0.007	-0.002	0.015	.137	.748
	Impulsivity	0.014	-0.006	0.033	.170	.748
	Sensation seeking	0.011	-0.006	0.033	.262	.790
Anxiety Wave 2, 14 years to Alcohol Wave 3, 14.5 years						
	Sex (reference male)	-0.052	-0.178	0.074	.414	.790
	Depressive symptoms	0.004	-0.001	0.010	.14	.748
	Impulsivity	0.003	-0.009	0.015	.587	.833
	Sensation seeking	0.007	-0.003	0.016	.174	.748
	Conformity drinking motives	0.006	-0.004	0.016	.215	.788
	Coping-anxiety drinking motives	0.002	-0.010	0.014	.693	.897
	Enhancement drinking motives	-0.05	-0.013	0.003	.187	.748
	Social drinking motives	-0.004	-0.012	0.004	.367	.790
Anxiety Wave 3, 14.5 years to Alcohol Wave 4, 15.4 years						
	Sex (reference male)	-0.101	-0.310	0.107	.341	.790
	Depressive symptoms	0.01	0.001	0.020	**.030**	.748
	Impulsivity	0.021	-0.005	0.046	.113	.748
	Sensation seeking	0.016	-0.002	0.034	.077	.748
	Conformity drinking motives	0.006	-0.009	0.021	.431	.790
	Coping-anxiety drinking motives	0.003	-0.016	0.022	.749	.915
	Enhancement drinking motives	-0.0009	-0.015	0.014	.906	.949
	Social drinking motives	0.006	-0.008	0.021	.406	.790
Anxiety Wave 4, 15.4 years to Alcohol Wave 5, 16.4 years						
	Sex (reference male)	0.169	-0.041	0.379	.114	.748
	Depressive symptoms	0.01	-0.002	0.023	.100	.748
	Impulsivity	0.003	-0.022	0.028	.815	.936
	Sensation seeking	-0.009	-0.030	0.012	.420	.790
	Conformity drinking motives	0.003	-0.016	0.023	.737	.915
	Coping-anxiety drinking motives	0.01	-0.010	0.031	.324	.790
	Enhancement drinking motives	-0.001	-0.015	0.012	.851	.936
	Social drinking motives	-0.006	-0.018	0.005	.287	.790
Anxiety Wave 5, 16.4 years to Alcohol Wave 6, 19 years						

Sex (reference male)	0.077	-0.137	0.291	.481	.823
Depressive symptoms	-0.003	-0.016	0.010	.66	.880
Impulsivity	-0.01	-0.034	0.014	.419	.790
Sensation seeking	-0.008	-0.026	0.010	.364	.790
Conformity drinking motives	-0.005	-0.020	0.010	.495	.823
Coping-anxiety drinking motives	-0.0003	-0.018	0.018	.97	.970
Enhancement drinking motives	-0.001	-0.014	0.011	.848	.936
Social drinking motives	-0.002	-0.015	0.012	.804	.936
Anxiety Wave 6, 19 years to Alcohol Wave 7, 20.5 years					
Sex (reference male)	-0.01	-0.218	0.200	.932	.954
Depressive symptoms	-0.005	-0.021	0.011	.561	.823
Impulsivity	-0.002	-0.033	0.028	.874	.938
Sensation seeking	-0.008	-0.035	0.018	.531	.823
Conformity drinking motives	-0.007	-0.028	0.015	.544	.823
Coping-anxiety drinking motives	-0.005	-0.026	0.015	.621	.854
Enhancement drinking motives	-0.008	-0.024	0.008	.317	.790
Social drinking motives	-0.005	-0.023	0.012	.546	.823

†Adjusted models include sex, country of birth, and average school grades at Wave 1.
#Each moderator was tested in a separate model; interaction terms reflect results from individual analyses.
P values <.05 are **bolded**.
LL: Lower limit; UL: Upper limit

Table E11: Observed versus imputed means for key study characteristics.

Variable, *M (SD)*		**Wave 1 Baseline**	**Wave 2 6-month follow-up**	**Wave 3 1-year follow-up**	**Wave 4 2-year follow-up**	**Wave 5 3-year follow-up**	**Wave 6 5-year follow-up**	**Wave 7 7-year follow-up**
		418	341	366	343	300	213	177
Age (years)	Complete Case	13.38 (0.44)	13.97 (0.42)	14.47 (0.37)	15.42 (0.36)	16.41 (0.35)	19.03 (0.41)	20.45 (0.4)
	Imputed	-	N/A	N/A	N/A	N/A	N/A	N/A
Anxiety symptoms (BSI)	Complete Case	1.94 (2.57)	2.15 (3.26)	1.99 (2.98)	2.58 (3.5)	2.68 (3.51)	3.11 (3.47)	3.22 (3.24)
	Imputed	-	2.25 (3.34)	2.10 (3.08)	2.62 (3.53)	2.72 (3.47)	3.18 (3.47)	3.66 (3.58)
Hazardous alcohol use (AUDIT-C)	Complete Case	0.25 (0.82)	0.4 (1.41)	0.43 (1.28)	1.32 (2.21)	2.51 (2.86)	6.13 (2.67)	5.92 (2.69)
	Imputed	-	0.43 (1.39)	0.47 (1.30)	1.32 (2.18)	2.58 (2.86)	6.18 (2.73)	6.10 (2.79)
Depression symptoms (BSI)	Complete Case	3.55 (4.34)	3.73 (4.7)	3.89 (5.01)	4.62 (5.47)	4.4 (5.2)	6.03 (5.18)	5.68 (4.89)
	Imputed	-	3.87 (4.74)	3.96 (5.09)	4.63 (5.44)	4.48 (5.21)	6.15 (5.30)	6.17 (5.13)
Impulsivity (SURPS)	Complete Case	10.96 (2.56)	11.06 (2.83)	10.93 (2.67)	11.07 (2.84)	10.9 (3.4)	10.08 (2.72)	9.50 (2.51)
	Imputed	-	11.12 (2.83)	11.05 (2.67)	11.16 (2.86)	11.04 (3.07)	10.20 (2.94)	9.96 (2.79)
Sensation seeking (SURPS)	Complete Case	15.66 (3.21)	15.64 (3.42)	15.70 (3.41)	15.85 (3.6)	16.24 (3.8)	15.94 (3.52)	15.75 (3.72)
	Imputed	-	15.78 (3.45)	15.74 (3.40)	15.88 (3.56)	16.24 (3.84)	16.00 (3.74)	15.78 (3.90)
Coping-anxiety drinking motives (Modified DMQ-R)	Complete Case	N/A	4.38 (1.84)	4.37 (1.77)	5.10 (2.66)	5.88 (3.39)	7 (3.48)	7.36 (3.25)
	Imputed	N/A	4.36 (1.72)	4.38 (1.74)	5.17 (2.75)	5.97 (3.41)	7.39 (3.73)	7.76 (3.59)
Conformity drinking motives (Modified DMQ-R)	Complete Case	N/A	5.5 (2.34)	5.38 (2.07)	5.71 (2.4)	6.56 (3.98)	6.44 (3.09)	6.50 (2.96)
	Imputed	N/A	5.49 (2.22)	5.40 (2.07)	5.84 (2.66)	6.60 (3.96)	6.79 (3.31)	7.05 (3.40)
Enhancement drinking motives (Modified DMQ-R)	Complete Case	N/A	5.74 (2.84)	5.76 (2.6)	7.22 (4.4)	9.18 (5.65)	12.04 (5.6)	11.90 (5.2)
	Imputed	N/A	5.71 (2.70)	5.84 (2.71)	7.31 (4.51)	9.21 (5.63)	12.19 (5.61)	11.82 (5.27)
Social drinking motives (Modified DMQ-R)	Complete Case	N/A	5.91 (2.89)	5.98 (2.66)	7.69 (4.61)	9.91 (5.46)	15.00 (4.94)	15.78 (4.6)
	Imputed	N/A	5.92 (2.78)	6.06 (2.75)	7.89 (4.82)	10.12 (5.46)	15.17 (5.23)	15.85 (4.91)

Appendix F

Supplementary materials for Chapter 4

Preface

This Appendix includes supplementary material for **Chapter 4**. Supplementary materials include mediation equations (Supplementary material F1), complete case models (Table F1) and additional supplementary analyses (Table F2 and Table F3).

Supplementary material F1: Equations for the effects of interest.

See (VanderWeele & Vansteelandt, 2014) for full details.

Total effect

The total effect (TE) is the effect of *X* on *Y* and equals the sum of the TNDE and the PNIE or, equivalently, the sum of the PNDE and the TNIE:

$$Y_a - Y_a* = Y_{aMa} - Y_{a*M*} = (Y_{aMa} - Y_{aMa*}) + (Y_{aMa*} - Y_{a*Ma*})$$

Pure natural direct effect

The pure natural direct effect (PNDE) is the effect of *X* on *Y*, while fixing each individual's mediator to the value that would naturally have been observed had the individual been in the control group:

$$\begin{aligned} &E[Y_{aM_{a^*}} - Y_{a^*M_{a^*}}|c] \\ &\quad = \theta_0 + \theta_1 a + \sum_{i=1}^{K} \theta_2^{(i)} E[M^{(i)}|c,a^*] + \sum_{i=1}^{K} \theta_3^{(i)} a E[M^{(i)}|c,a^*] \\ &\quad + \sum_{i=1,j=1}^{K,K} \tau^{(ij)} E[M^{(i)}M^{(j)}|c,a^*] + \theta_4{}'c - [\theta_0 + \theta_1 a^* + \sum_{i=1}^{K} \theta_2^{(i)} E[M^{(i)}|c,a^*] \\ &\quad + \sum_{i=1}^{K} \theta_3^{(i)} a^* E[M^{(i)}|c,a^*] + \sum_{i=1,j=1}^{K,K} \tau^{(ij)} E[M^{(i)}M^{(j)}|c,a^*] + \theta_4{}'c] \\ &\quad = \{\theta_1 + \sum_{i=1}^{K} \theta_3^{(i)} E[M^{(i)}|c,a^*]\}(a - a^*) \end{aligned}$$

If $M^{(i)}$ is continuous, E[M(i)||c,a*]=β(i)0+β(i)1a+β(i)'2c

Total natural indirect effect

The total natural indirect effect (TNIE) is the effect of *X* on *Y* through *M*, when the direct effect is held constant at the treatment-group level.

$$
\begin{aligned}
&E[Y_{aM_a} - Y_{aM_{a^*}}|c] \\
&\quad = \theta_0 + \theta_1 a + \sum_{i=1}^{K} \theta_2^{(i)} E[M^{(i)}|c,a] + \sum_{i=1}^{K} \theta_3^{(i)} a E[M^{(i)}|c,a] \\
&\quad + \sum_{i=1,j=1}^{K,K} \tau^{(ij)} E[M^{(i)}M^{(j)}|c,a] + \theta_4{}'c - \{\theta_0 + \theta_1 a + \sum_{i=1}^{K} \theta_2^{(i)} E[M^{(i)}|c,a^*] \\
&\quad + \sum_{i=1}^{K} \theta_3^{(i)} a E[M^{(i)}|c,a^*] + \sum_{i=1,j=1}^{K,K} \tau^{(ij)} E[M^{(i)}M^{(j)}|c,a^*] + \theta_4{}'c\} \\
&\quad = \sum_{i=1}^{K} \{\theta_2^{(i)} + \theta_3^{(i)} a\}\{E[M^{(i)}|c,a] - E[M^{(i)}|c,a^*]\} \\
&\quad + \sum_{i=1,j=1}^{K,K} \tau^{(ij)}\{E[M^{(i)}M^{(j)}|c,a] - E[M^{(i)}M^{(j)}|c,a^*]\}.
\end{aligned}
$$

If $M^{(i)}$ is continuous, E[M(i)||c,a]−E[M(i)||c,a*]=β(i)1(a−a*).

VanderWeele, T. J., & Vansteelandt, S. (2014). Mediation Analysis with Multiple Mediators. *Epidemiologic methods*, *2*(1), 95-115. https://doi.org/10.1515/em-2012-0010

Table F1: Complete cases estimate of causal multiple mediation effects of the Inroads intervention on alcohol use and social anxiety outcomes at 6 months post baseline (n = 80).

	Total Effect (TE)				**Pure Natural Direct Effect (PNDE)**				**Total Natural Indirect Effect (TNIE)**			
	Estimate	***p***	**95% Confidence Interval**		**Estimate**	***p***	**95% Confidence Interval**		**Estimate**	***p***	**95% Confidence Interval**	
Social anxiety symptoms outcome	-4.721	**0.004**	-1.861	-8.564	-5.403	**0.008**	-1.939	-9.878	0.682	0.516	4.296	-1.015
Mean standard drinks per day outcome	-1.048	**0.004**	-0.282	-1.565	-0.636	0.136	0.125	-1.277	-0.412	0.072	-0.009	-0.966

Estimates are reported on the mean difference scale with effects with p values <0.05 bolded. Models include age, sex, and the respective outcome at baseline as confounders.

Table F2: Estimates of causal multiple mediation short-term effects of the Inroads intervention on alcohol use and social anxiety outcomes with both the mediators and outcomes measured at 2-months post baseline.

	Total Effect (TE)				**Pure Natural Direct Effect (PNDE)**				**Total Natural Indirect Effect (TNIE)**			
	Estimate	***p***	**95% Confidence Interval**		**Estimate**	***p***	**95% Confidence Interval**		**Estimate**	***p***	**95% Confidence Interval**	
Imputed models (n = 123)												
Social anxiety symptoms outcome	-3.397	**<0.001**	-1.013	-6.154	-3.067	**<0.001**	-1.328	-6.611	0.211	0.392	1.074	-0.393
Mean standard drinks per day outcome	-0.228	0.228	0.160	-0.622	-0.209	0.280	0.190	-0.712	-0.019	0.984	0.255	-0.280
Complete case models (n = 80)												
Social anxiety symptoms outcome	-3.869	**<0.001**	-1.012	-7.828	-4.680	**0.016**	-1.161	-9.321	0.810	0.352	4.219	-0.739
Mean standard drinks per day outcome	-0.673	0.116	0.132	-1.138	-0.267	0.696	0.578	-1.087	-0.405	0.188	0.126	-0.930

Estimates are reported on the mean difference scale with effects with p values <0.05 bolded. Models include age and sex at baseline as confounders.

Table F3: Estimates of causal multiple mediation effects of the Inroads intervention on alcohol use and social anxiety outcomes with the inclusion of the outcome at time 2 as a mediator-outcome confounder.

	Total Effect (TE)				**randomized analogue of Pure Natural Direct Effect (R PNDE)**				**Randomized analogue of Total Natural Indirect Effect (R TNIE)**			
	Estimate	***p***	**95% Confidence Interval**		**Estimate**	***p* value**	**95% Confidence Interval**		**Estimate**	***p***	**95% Confidence Interval**	
Imputed models (n = 123)												
Social anxiety symptoms outcome	-3.709	**0.008**	-1.481	-6.17	-3.714	**0.008**	-1.589	-6.273	0.005	0.644	0.831	-0.425
Mean standard drinks per day outcome	-0.601	**0.004**	-0.160	-1.038	-0.530	**0.012**	-0.109	-0.999	-0.071	0.748	0.226	-0.230
Complete case models (n = 80)												
Social anxiety symptoms outcome	-7.486	**<0.001**	-3.695	-11.499	-7.774	**<0.001**	-3.300	-11.878	0.288	0.824	3.464	-1.332
Mean standard drinks per day outcome	-0.902	**<0.001**	-0.323	-1.566	-0.604	0.068	0.074	-1.396	-0.297	0.156	0.113	-0.862

Estimates are reported as randomised analogues with effects with p values <0.05 bolded.

Models include age, sex, and the respective outcome at baseline as confounders.

Appendix G

Psychological mechanisms of change in reducing co-occurring social anxiety and alcohol use: A causal mediation analysis of the online Inroads intervention

Preface

This causal mediation analysis has been published as:

Gückel, T., Prior, K., Newton, N. C., Baillie, A. J., Teesson, M., & Stapinski, L. A. (2025). Psychological mechanisms of change in reducing co-occurring social anxiety and alcohol use: A causal mediation analysis of the online Inroads intervention. *Behaviour Research and Therapy*, *191*, 104766. https://doi.org/10.1016/j.brat.2025.104766

TG led the development of the study using data from the Inroads RCT. TG, KP, NCN and LAS conceptualised the study. NCN, AB, MT and LAS secured funding for the Inroads RCT. KP and LAS were responsible for ethics and governance of overall trial administration. TG developed the methodology and conducted the formal analysis. TG wrote the original manuscript. All authors critically revised the manuscript and approved the final version.

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Psychological mechanisms of change in reducing co-occurring social anxiety and alcohol use: A causal mediation analysis of the online Inroads intervention☆,☆☆

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ABSTRACT

Background: Research has documented the prevalence and treatment of co-occurring anxiety and alcohol use, but the mechanisms underlying treatment efficacy, especially in online interventions, remain unclear. This study investigated the potential behavioral, cognitive, and motivational mechanisms mediating the effectiveness of 'Inroads,' the first online early intervention for co-occurring anxiety and hazardous alcohol use in young adults.
Methods: Data from an Australian randomized controlled trial with 123 participants aged 17–24 (M = 21.6) was used. Causal multiple mediation analysis tested whether improvements in social anxiety symptoms could jointly be attributable to reductions in maladaptive emotion regulation and alcohol use, and whether reductions in alcohol use (mean drinks per day) could jointly be attributable to reductions in maladaptive emotion regulation, alcohol motives (drinking to cope with anxiety and for enhancement), and alcohol outcome expectancies (tension reduction and social lubrication).
Results: The results did not support a joint mediated effect for the hypothesized mechanisms in the social anxiety or alcohol use model.
Conclusions: Additional research is required to further understand the specific mechanisms, driving reductions in social anxiety and alcohol use within integrated treatments. This is especially true for social anxiety where, there was no evidence to suggest that the hypothesized mediators contributed to change in social anxiety symptoms.

1. Introduction

1.1. Background and rationale

The expansion of online interventions and treatments for psychological disorders provides great promise for improving accessibility and equitability to mental health care. Online treatments have the potential to circumvent barriers to traditional face-to-face care which can include, but are not limited to, stigma, cost, privacy concerns, and difficulty accessing evidence-based treatment at a convenient time or location (Lattie et al., 2022). Several reviews have established the efficacy of online treatments for a number of psychological disorders including depression (Ahern et al., 2018; Linardon et al., 2019), anxiety and emotional disorders (Linardon et al., 2019; Taylor et al., 2021), eating disorders (Taylor et al., 2021), and substance use disorders (Taylor et al., 2021). Furthermore, evidence has also emerged which shows comparable clinical effects between face-to-face and online cognitive behavior therapy (CBT) for depression and anxiety disorders (Esfandiari et al., 2021; Kambeitz-Ilankovic et al., 2022). Despite the indicated advantages of online treatments, they are not without limitations. Low adherence persists as a significant challenge for the field; with studies often reporting poor engagement and completion of online mental health interventions or tools (Leung et al., 2022). Supported or guided online treatments, however, have been found to improve adherence and outcomes for individuals (Andersson & Titov, 2014; Leung et al., 2022). Another limitation of online interventions is the limited research on

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their suitability for individuals with comorbid mental health and substance use conditions (Andersson & Titov, 2014; Boumparis et al., 2019). While studies and trials of online interventions have predominately focused on disorder-specific treatments, few have explored intervention effectiveness in individuals with multiple conditions. Given the frequent overlap of mental health and substance use concerns, further research is necessary to understand how online interventions may benefit those with co-occurring conditions (Kingston et al., 2017; Lai et al., 2015).

Two prevalent psychological disorders which frequently co-occur are anxiety and alcohol use disorders (AUD) (Glantz et al., 2020; Lai et al., 2015). Research suggests that one in four individuals (25.9 %) with social anxiety disorder (SAD) also experience an AUD, a rate significantly higher than that observed in the general population (Glantz et al., 2020). Treatment-seeking populations exhibit even higher rates of co-occurrence, with as many as one in three individuals receiving treatment, for either AUD or SAD, experiencing both conditions concurrently (Bakken et al., 2005). The co-occurrence of these two disorders can be complex, as each disorder can reinforce and intensify the other in a feed-forward or mutual maintenance pattern (Smith & Randall, 2012). Unsurprisingly, single-disorder treatments targeting anxiety or AUD in isolation are less effective for people with these co-occurring concerns (Kelly & Daley, 2013; Smith & Randall, 2012; Stapinski et al., 2024; Wolitzky-Taylor, 2023). Instead, integrated treatments, which target the mechanisms driving the interrelation between the two concerns, are advantageous in improving treatment outcomes (Stapinski et al., 2024). Differing from single-disorder or dual-focused treatments, integrated treatments harness effective components from both anxiety and AUD treatments, offering explicit guidance on managing behaviors that reinforce the inter-relationship between these two disorders (Stapinski et al., 2015). To date, few integrated treatments simultaneously addressing both anxiety disorders and AUD have been developed, and these treatments have primarily been tested among adults in traditional face-to-face settings (Kushner et al., 2013; Morley et al., 2016; Stapinski, Sannibale, et al., 2021; Wolitzky-Taylor et al., 2022). The efficacy of these face-to-face treatments has been established in reducing social anxiety symptoms (Stapinski, Sannibale, et al., 2021; Wolitzky-Taylor et al., 2022) and improving alcohol-related outcomes (Kushner et al., 2013; Morley et al., 2016), although the benefits for transdiagnostic anxiety-related outcomes have been less pronounced. Given that 75 % of mental health disorders emerge before age 24, and young adulthood is also the time when alcohol use and anxiety disorders typically peak and symptoms escalate (de Lijster et al., 2017; McEvoy et al., 2011; Teesson et al., 2010), early interventions are needed during this critical period. Building upon the efficacy of integrated anxiety-alcohol treatments among adults, interventions addressing these concerns among young adults offer the potential to prevent the progression and escalation to chronic, life-long anxiety and alcohol use disorders. Furthermore, online interventions have the potential for significant benefit among this age group, with two-thirds of young people reporting they would access online interventions for their mental health (Sweeney et al., 2019). Previous research has also shown the efficacy of online cognitive behavioral therapy for depression and anxiety in this population (Kessler et al., 2005). Therefore, the online integrated *Inroads* program for anxiety and alcohol was developed specifically for young adults.

The *Inroads* program is the first online, integrated, intervention for young adults that targets anxiety symptoms, hazardous alcohol use, and the interconnections between both concerns (Stapinski et al., 2019). Early interventions which target hazardous or risky drinking (defined as a score of 8 or more on the Alcohol Disorder Identification Test (AUDIT) (Babor et al., 2001)) are advantageous among young adults as consumption at hazardous levels is common and predicts progression to AUD (Harrison et al., 2008; Kranzler & Soyka, 2018). Comprising of five online modules delivered over five weeks, combined with psychologist support via email or phone, the *Inroads* program's content is underpinned by CBT and motivational enhancement therapy to, in an integrated delivery, target symptoms of generalized and/or social anxiety and hazardous alcohol use concurrently. The program was co-developed with the target population, drawing on components of effective face-to-face anxiety-alcohol treatments (Stapinski et al., 2015), with input from clinicians who work with youth.

In a randomized controlled trial (RCT) of the program among Australians aged 17–24, the integrated *Inroads* intervention group (n = 62) saw significant improvement across anxiety and alcohol outcomes compared to an alcohol assessment plus alcohol information control group (n = 61). While the control condition provided psychoeducation for alcohol use only, it was chosen to establish a baseline from which to measure the incremental benefits of the integrated treatment for both anxiety and alcohol use. This approach demonstrated the added value of addressing both conditions simultaneously, setting the stage for future comparisons with more comprehensive, disorder-specific treatments.

During the trial, both groups reduced their drinking across primary and secondary alcohol use outcomes. At the post-intervention 2-month follow-up participants in both groups had reduced on the primary outcome of mean standard drinks per day in the past month and secondary outcomes of hazardous alcohol use (AUDIT total score) and binge drinking (≥5 standard drinks on a single occasion). However, by the 6-month follow-up, significant group differences emerged for mean daily alcohol use and hazardous alcohol use, suggesting a rebound effect in the control group's drinking, whilst the *Inroads* group saw sustained effects (Stapinski, Prior, et al., 2021). In regard to anxiety outcomes, social anxiety symptoms significantly improved in the *Inroads* group, with between group differences sustained at the 6-month follow-up. Participants in the control group did not significantly improve their social anxiety. Superior reductions in generalized anxiety, in the *Inroads* group, were only observed post-intervention. By the 6-month follow-up the control group achieved comparable reductions in generalized anxiety symptoms to the intervention group. The current study is a secondary analysis of this RCT to explore potential mediators of these alcohol and social anxiety outcomes. The anxiety outcomes observed align with findings from face-to-face treatments, where superior benefits are often found for social anxiety treatments over generalized or transdiagnostic anxiety treatments which are integrated with alcohol treatments (Kushner et al., 2013; Morley et al., 2016; Stapinski et al., 2024; Stapinski, Sannibale, et al., 2021; Wolitzky-Taylor et al., 2022). This may be due to the greater chronicity and natural fluctuations in the course of generalized anxiety compared to social anxiety. Unlike social anxiety, which tends to show more stable treatment gains, generalized anxiety is often influenced by external life stressors and has a more variable long-term course, with periods of remission and relapse even after treatment (Keller, 2002; Rowa et al., 2017).

1.2. Mechanisms of change in co-occurring anxiety and alcohol use treatment

Integrated treatment for anxiety and alcohol use is underpinned by a CBT framework, with the aim of treatment to address the motivational, cognitive, and behavioral processes that drive and maintain each condition and the interactions between them (Stapinski et al., 2015; Wolitzky-Taylor et al., 2022). For effective treatment of co-occurring anxiety and alcohol use problems, it is important to promote the ability to adaptively regulate emotional responses to internal and external stressors. Furthermore, in view of the mutually reinforcing relationship between anxiety and alcohol use, it is also important to address this interconnection and challenge inaccurate and unhelpful cognitions or expectations regarding the positive effects of alcohol on anxiety (e.g., improved social performance) (Kushner et al., 2013; Stapinski et al., 2015). Despite a strong theoretical basis for the co-occurrence and treatment of these two conditions, to date, specific mechanisms driving treatment efficacy have not been tested. Given the efficacy of the online *Inroads* anxiety-alcohol intervention on reducing social anxiety

symptoms and mean daily alcohol use (Stapinski, Prior, et al., 2021), understanding *how* the program is able to reduce these outcomes is important. This will be done by testing hypothesized mechanisms of change, i.e. mediating factors. Knowing explicitly *how* interventions work is vital for advancing the effectiveness of co-occurring anxiety and alcohol interventions, particularly in the context of online intervention delivery given their potential for low-cost, widespread dissemination. Given the limited trials on integrated treatments for co-occurring social anxiety and alcohol use, the underlying mechanisms thought to drive treatment efficacy are yet to be tested. As such the hypothesized mediators for this study are guided by the clinical, theoretical, and cross-sectional research on co-occurring anxiety and alcohol use.

1.2.1. Mediators for social anxiety treatment in the context of comorbid alcohol use

For social anxiety, the key mechanisms theorized to underlie integrated interventions are reductions in both maladaptive emotion regulation behaviors and alcohol use, which are hypothesized mechanisms to drive improvements in social anxiety symptoms (Stapinski et al., 2015). Underlying cognitions in social anxiety tend to be dominated by fear of negative evaluation and an inflated likelihood of negative consequences (Hofmann, 2007; Rapee & Heimberg, 1997). Within the *Inroads* program, CBT aims to target these cognitions and behaviors by helping individuals identify and reappraise threat cognitions to determine their realistic probability and potential outcomes, a process referred to as 'emotion surfing'. During this process, two maladaptive emotion regulation processes are targeted; cognitive reappraisal and expressive suppression (Stapinski et al., 2015). Cognitive reappraisal is defined as the attempt to reinterpret emotion-eliciting situations in a way which alters its meaning and emotional impact (Lazarus & Alfert, 1964), while expressive suppression is a form of response modulation which attempts to reduce or conceal outward emotional expressions (Gross, 1998). Targeting maladaptive or negative cognitions is not unique to integrated treatment however, with increases in reappraisal and decreases in negative cognitions also found to mediate treatment outcomes for SAD in single-disorder CBT treatments (Goldin et al., 2012; Kivity et al., 2021). A hypothesized mechanism unique to integrated treatment, however, is the reduction of alcohol use. Due to alcohol's demonstrated rebound effects, both pharmacologically and physiologically, on anxiety symptoms, reducing alcohol consumption is thought to mediate reductions in social anxiety symptoms (Kushner et al., 2000; Stapinski et al., 2015). Whilst individuals may see short-term benefits to anxiety symptoms from drinking, over the long-term intoxication or withdrawal from alcohol may exacerbate anxiety symptoms via directly inducing symptoms of trait, generalized, or panic anxiety, generating additional psychosocial stressors (Kushner et al., 2000). Furthermore, a reliance on alcohol within social settings prevents disconfirmation of threat expectancies and reduces confidence to manage these situations without alcohol (Stapinski et al., 2015).

1.2.2. Mediators for alcohol use treatment in the context of comorbid social anxiety

Notably, the mechanisms hypothesized to change and reduce alcohol use in the context of co-occurring anxiety-alcohol use extend beyond simply reducing anxiety symptoms. Instead, they involve challenging positive drinking motives and positive alcohol expectancies. Drinking motives are conceptualized as an individual's reasons for choosing to drink (Cooper, 1994), while alcohol expectancies refer to the beliefs an individual holds about the physical or social outcomes that will occur from drinking (Jones et al., 2001). While both motives and expectancies are associated with alcohol use, an individual's expectation about a particular effect of alcohol, does not necessarily mean they will drink for that related motive (Cox & Klinger, 1988). Within the current context, the *motivation* for individuals to drink typically stems from a belief that alcohol will have potential anxiety-reducing effects (Anker & Kushner, 2019; Stapinski et al., 2015). Within the four-factor drinking motive framework, both enhancement and coping motives have consistently been related to heavier drinking and alcohol-related problems (Cooper, 1994). Enhancement motives are characterized as an internally generated, positive motive to drink to enhance positive mood or wellbeing (Cooper, 1994). Prior research has found enhancement motives mediate the relationship between social anxiety and alcohol-related problems (Buckner et al., 2006). Whilst some studies have found evidence for other drinking motives, such as social and conformity motives, influencing drinking behaviors (Boyle et al., 2022; Sheehan et al., 2013) this evidence has been inconsistent, particularly among younger age groups (Rowicka, 2021; Sheehan et al., 2013; Sjodin et al., 2021). A newer five-factor model for measuring drinking motive constructs has been developed, however, which separates motives for coping with anxiety versus coping with depression drinking (Grant et al., 2007). Despite a significant body of work on the role of drinking motives in the context of anxiety concerns, much of this work has been in cross-sectional or non-treatment contexts. This empirical evidence points to coping-anxiety drinking motives and enhancement drinking motives as theoretically hypothesized mediators in anxiety-alcohol treatment. Alcohol outcome *expectancies* also contribute to the motivations and maintenance of alcohol use. Individuals with anxiety hold optimistic and positive expectancies about alcohol's effects including its potential to aid social situations, i.e. tension reduction expectancies and social lubricant expectancies (Moss & Albery, 2009; Stapinski et al., 2015). Thus, hypothesized mechanisms underlying co-occurring anxiety-alcohol problems are the expectancy that alcohol will act as a relaxant (tension-reduction) and the motive to use alcohol to cope with their anxiety. Within integrated treatments, like *Inroads,* motives for drinking and the tension reduction and social lubricant alcohol expectancies are explicitly identified and targeted through motivational, cognitive, and behavioral strategies (Grant et al., 2007; Kushner et al., 1994). This includes experimental designs which help individuals identify and challenge alcohol-related motivation and expectancy cognitions, i.e. "drinking thinking". Doing so helps individuals evaluate the realistic evidence about what happens when they drink, i.e. expectation versus reality, with the aim of eliciting corrective evidence of the true cost of drinking. Interventions challenging alcohol expectancies, outside the co-occurring anxiety and alcohol context, have been found to significantly reduce alcohol use and related outcomes (Scott-Sheldon et al., 2012). In addition to challenging the positive beliefs about alcohol, reducing maladaptive emotion regulation is also a hypothesized mechanism of change for alcohol use reduction (Stapinski et al., 2015). Similar to social anxiety, CBT strategies for alcohol use reduction aim to help individuals more adaptively regulate their emotional responses, by increasing cognitive reappraisal and decreasing expressive suppression (Kushner et al., 2009; Stapinski et al., 2015). Previous research, in the context of interventions for alcohol use alone, have also shown these cognitive processes to be influential factors in improving alcohol related treatment outcomes (Petit et al., 2015; Rodriguez et al., 2019). Whilst factors such as self-efficacy, social support, and craving have been identified as mediators in alcohol and other drug treatment, research has not established these as core to integrated treatments and as such were not included in the current models (Maisto et al., 2024).

1.3. The current study objectives

This is the first study to investigate joint mediators of an efficacious, online, integrated treatment aimed at reducing anxiety and hazardous alcohol use among young adults. The study's objectives are to assess the hypothesized causal pathways that underpin the effectiveness of an online anxiety-alcohol intervention among young adults, using a causal inference framework. To establish temporal precedence among exposure, mediators, and outcomes (Kazdin, 2007), the study analyzes mediating variables at time 2 (post-treatment, 2 months post-baseline, follow-up 1) and significant outcome variables at time 3 (6 months post-baseline, follow-up 2). In the randomized controlled trial of the

primary study the anxiety-alcohol intervention group exhibited superior improvements in social anxiety but not general anxiety symptoms at time 3 (6 months post-baseline), thus this study focuses on identifying mediators related to social anxiety treatment efficacy. As outlined earlier, significant improvements were observed across various alcohol-related outcomes including reductions in mean drinks per day, hazardous alcohol use (per the AUDIT), and frequency of binge drinking. Thus, to align with the primary alcohol outcome of the original trial we focused on mean drinks per day in this study. Building upon theoretical foundations in anxiety, alcohol use, and their co-occurrence, it is hypothesized that.

- Decreases in maladaptive emotion regulation (cognitive reappraisal and expressive suppression) and alcohol use at 2-months post baseline will jointly mediate the effects of the *Inroads* program on reducing social anxiety symptoms at 6 months, with the combined influence of these mediators resulting in significant mediation.
- Decreases in maladaptive emotion regulation (cognitive reappraisal and expressive suppression), alcohol motives (drinking to cope with anxiety and enhancement), and alcohol outcome expectancies (tension reduction and social lubricant) 2-months post baseline will jointly mediate the effects of the *Inroads* program on reducing mean drinks per day at 6 months, with the combined influence of these mediators resulting in significant mediation.

2. Methods

2.1. Study design and source of data

This study was designed and written in accordance with the guidelines for reporting mediation analyses (AGReMA) (Lee et al., 2021). Data for the current study were derived from a parallel RCT conducted online, nationally, across Australia. The design and protocol for the original study can be found in (Stapinski et al., 2019). The current study was not registered alongside the original RCT protocol and thus should be considered exploratory. Eligible participants were randomized to either the *Inroads* intervention condition or an alcohol information and safe drinking guidelines control condition.

2.2. Participants

Recruitment to the original study ran from December 2017 to September 2018. The target population were 17–24-year-olds in Australia reporting hazardous alcohol use and at least mild generalized or social anxiety symptoms. These thresholds were aligned with the nature of the treatment which is an early intervention designed to provide an intervention to individuals experiencing sub-threshold symptoms, to prevent the exacerbation to a more chronic disorder. Hazardous alcohol use was determined by scores $\geq$8 on the Alcohol Use Disorder Identification test (AUDIT) (Babor et al., 2001). Scores $\geq$20 on the AUDIT were used to determine probable alcohol dependence in this population (Babor et al., 2001; O'Brien et al., 2020). Mild anxiety was determined by a score of $\geq$5 on the Generalized Anxiety Disorder-7 (GAD-7) Questionnaire (Spitzer et al., 2006) or a score $\geq$6 on the Mini-Social Phobia Inventory (Mini-SPIN) (Seeley-Wait et al., 2009). Although the Mini-SPIN focusses on anxiety symptoms consistent with social anxiety disorder, the GAD-7 has been found to index symptoms across multiple disorders and is sensitive to GAD, panic, and social anxiety disorder, facilitating screening of young people with a range of anxiety presentations. Total scores on the GAD-7 range from 0 to 21, with scores of $\geq$5, $\geq$10, and $\geq$15 representing cut points for mild, moderate, and severe anxiety, respectively (Kroenke et al., 2007). Individuals currently receiving ongoing psychological treatment or requiring more intensive or specialized support (e.g., with current active suicidal ideation) were excluded from the study. No further eligibility requirements were dictated for participants to be included in the mediation analysis. From 547 participants screened for eligibility, a total of 123 were eligible and randomized to either *Inroads* (n = 62) or control (n = 61). The 123 eligible participants had a mean age of 21.6 years (SD = 2.2) and comprised of 32 % male, 67 % female, and 1 % transgender or non-binary individuals. The majority of participants were born in Australia (82 %), resided in a major city (89 %), were heterosexual (73 %), and were employed full time (40 %) or part time/casually (27 %). Full exclusion criteria, participant flow through the trial, and demographic data are reported in the main outcomes paper (Stapinski, Prior, et al., 2021).

2.3. Effects of interest

In the current study, the pure natural direct effect (PNDE), total natural indirect effect (TNIE), and total effect (TE) were estimated for each causal mediation model (Robins & Greenland, 1992). These estimates are part of the 'counterfactual causal framework or 'potential outcomes framework' which is unique to causal mediation (Rubin, 1978). Causal mediation analysis defines the difference between two potential outcomes and is advantageous over traditional mediation analysis because it allows for a more precise understanding of the causal pathways by isolating the direct effects of an intervention from its indirect effects through mediators (Pearl, 2001; VanderWeele, 2015). This method provides clearer insights into how and why an intervention works, offering a more detailed breakdown of the mechanisms at play. In the current study, the PNDE represents the direct effect of the exposure variable (*Inroads* versus control) on the outcome of interest (either anxiety or alcohol), whilst hypothetically holding the mediator's constant at typical or average values that would be observed in the control group. This helps assess the independent contribution of the intervention (exposure) on outcomes, separate from any mediated effects through the mediators. The TNIE represents the indirect intervention effect on the outcome of interest through the multiple mediators. Within the potential outcomes framework, this TNIE represents a hypothetical scenario in which the *Inroads* intervention is implemented, causing the mediators to take on the values they would have had if participants moved from the control group to the intervention group. Lastly, the TE is calculated as the intervention's effects on the outcomes that come from both the direct (PNDE) and indirect (TNIE) effects of the mediators, i.e., TE = PNDE + TNIE.

2.4. Assumed causal models

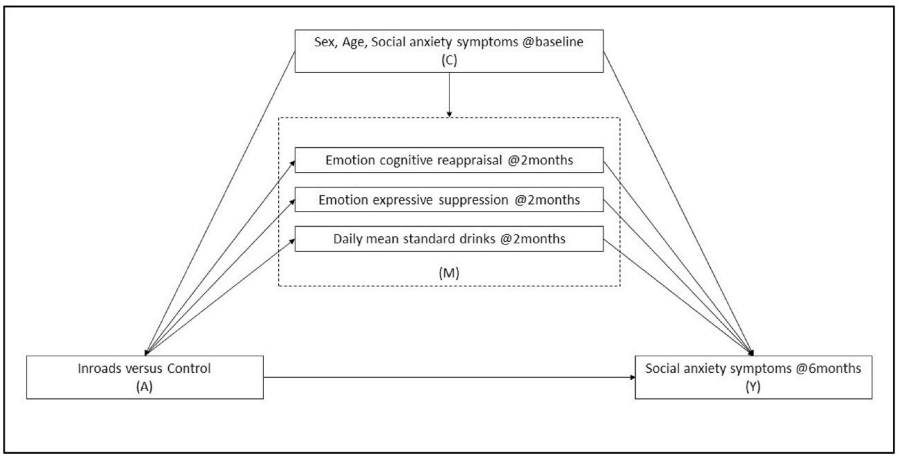
In line with the study objectives and the effects of interest, Figs. 1 and 2 depict the assumed causal models we tested. Across both models the exposure(A) is the intervention group (*Inroads* versus control), and the outcome(Y) is either social anxiety symptoms as seen in Fig. 1 or daily mean standard drinks as seen in Fig. 2.

2.5. Causal assumptions

To draw causal inference several assumptions must be met to estimate direct and indirect effects (VanderWeele & Vansteelandt, 2014), these include.

1. No unmeasured confounding on the intervention-outcome relationship.
2. No unmeasured confounding on the intervention-mediator relationship.
3. No unmeasured confounding on the mediator-outcome relationship.
4. No mediator-outcome confounder influenced by the intervention.
5. No mediator-mediator interactions that influence the outcome.

It can be expected that treatment randomization to either the intervention or control will hold assumptions 1 and 2 true (VanderWeele & Vansteelandt, 2014). To increase the plausibility of no unmeasured



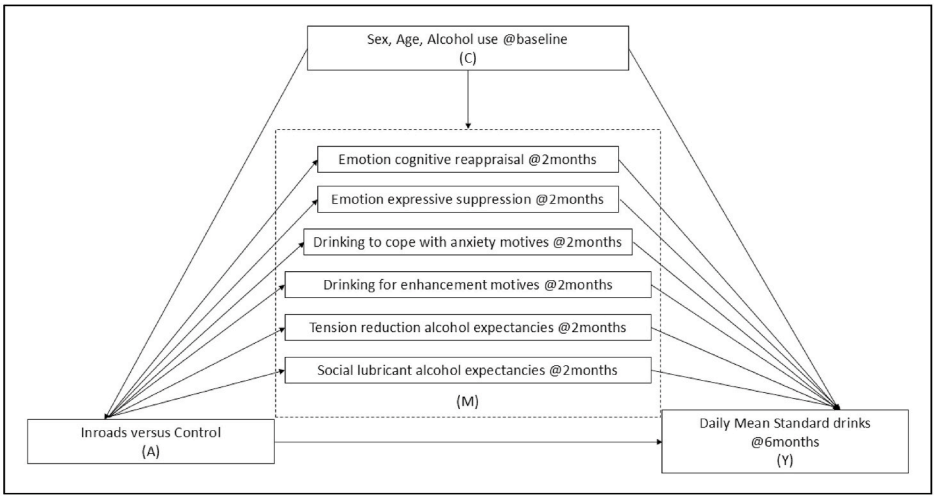
A (exposure): Inroads versus control.

M (mediators): Emotion cognitive reappraisal, emotion expressive suppression, daily mean standard drinks.

Y (outcome): social anxiety symptoms.

C (confounders not affected by the exposure): Sex, age, and social anxiety symptoms at baseline.

Fig. 1. Directed Acyclic Graph illustrating the causal model of interest for social anxiety symptom outcome.



A (exposure): Inroads versus control.

M (mediators): Emotion cognitive reappraisal, emotion expressive suppression, drinking to cope with anxiety motives, drinking for enhancement motives, tension reduction alcohol expectancies, social lubricant alcohol expectancies.

Y (outcome): Daily mean standard drinks.

C (confounders not affected by the exposure): Sex, age, daily mean standard drinks at baseline.

Fig. 2. Directed Acyclic Graph illustrating the causal model of interest for daily mean standard drinks outcome.

confounding, multiple baseline covariates were accounted for in the models and sensitivity analyses for unmeasured confounding were conducted. The covariates included age, sex, and either anxiety symptoms or daily alcohol use at baseline.

2.6. Measurement

All measures were collected via self-report surveys, administered via the study website. The data used for mediation analyses were all individual-level data collected within the eligibility and baseline (time 1), 2-months post baseline follow-up (time 2), and 6-months post baseline follow-up (time 3) surveys.

2.6.1. Exposure

Intervention: The exposure of interest was assignment to either the online *Inroads* anxiety-alcohol intervention group or control group (time

1). Following consent and completion of the online eligibility and baseline surveys, participants were randomized via the trial website using a computer-generated sequence which the research team were blinded to. Individuals randomized to the anxiety-alcohol intervention were given access to the five, online self-guided *Inroads* program modules. The modules are designed to be completed sequentially and consist of the following content: 1) Understanding alcohol use motives and inter-relationship with anxiety; 2) Cognitive therapy for anxious thoughts; 3) Strategies for sticking to drinking limits and addressing positive alcohol beliefs; 4) Facing fears through behavioral experiments; 5) Social support, goal-setting, and relapse prevention (Stapinski et al., 2019). Within the modules, there is a combination of static information, videos, case vignettes, quizzes, and open-ended questions for participants to use as reflection points. In addition to the online content, participants received support from a clinical psychologist via personalized weekly feedback emails and a 30-min telephone or text chat session following modules 1 and 4. Although the intervention was designed to be completed over 5 weeks, participants were given flexibility and allowed to finish the modules up until the first study follow-up (time 2), which occurred 2 months after the baseline assessment. Further details of the intervention and its theoretical underpinnings are provided elsewhere (Stapinski et al., 2019).

Control: Individuals randomized to the control group received a pamphlet containing information about the effects and harms of alcohol use, national Australian safe drinking guidelines, and links to national telephone helplines and information websites. This information was provided on screen immediately following randomization and was also emailed to participants.

2.6.2. Mediators

2.6.2.1. Maladaptive emotion regulation behaviors. The Emotion Regulation Questionnaire for Children and Adolescents (ERQ-CA) was used to assess expressive suppression (i.e., the forced attempt to not express discomfort) and cognitive reappraisal (i.e., the attempt to acknowledge and reinterpret emotions) at 2-months post-baseline (time 2, follow-up 1) (Gullone & Taffe, 2012). The child and adolescent version of the ERQ was developed in an Australian sample and was based on the original model of emotion regulation developed by Gross et al. which has demonstrated construct validity for measuring expressive suppression and cognitive reappraisal (Gross & John, 2003). Four questions were used to assess expressive suppression such as "I control my feelings by not showing them." Scores on this scale ranged from 4 to 20, with higher scores corresponding to greater expressive suppression. Six questions were used to assess cognitive reappraisal such as "I control my feelings about things by changing the way I think about them". Scores on this scale ranged from 6 to 30, with higher scores reflecting more positive emotion regulation via cognitive reappraisal (Robins & Greenland, 1992). Within the study's sample, the scores from these scales had acceptable internal consistency at baseline with a Cronbach's Alpha of $\alpha = 0.69$ for the expressive suppression scale and $\alpha = 0.85$ for the cognitive reappraisal scale.

2.6.2.2. Drinking motives. The five-factor Modified Drinking Motives Questionnaire Revised (DMQ-R) was used to measure drinking motives 2-months post-baseline (time 2, follow-up 1) (Grant et al., 2007). Across twenty-eight questions, participants indicated their motivation for alcohol consumption based on specific reasons using a 5-point Likert scale, ranging from 1 ('almost never'/'never') to 5 ('almost always'/'always'). Higher scores on each scale indicated a greater inclination to drink alcohol for those reasons. Of the five-factors measured, coping-anxiety motives and enhancement motives were considered potential mediators in the current study. Within the current study's sample good internal consistency at baseline was seen for both subscale scores, with $\alpha = 0.73$ for coping-anxiety motives and $\alpha = 0.8$ for enhancement motive measures.

2.6.2.3. Alcohol outcome expectancies. Tension reduction and social lubricant alcohol outcome expectancies 2-months post-baseline (time 2, follow-up 1) were measured with the Alcohol Outcome Expectancies questionnaire developed by Kushner et al., 1994; Kushner et al., 1994). Nine questions such as "drinking helps me to forget my worries" were used to assess tension reduction alcohol expectancies and eight questions such as "drinking makes me feel less shy" were used for social lubricant alcohol expectancies. Within the current study, there was good internal consistency of these measures at baseline, with $\alpha = 0.85$ for tension reduction alcohol expectancies and $\alpha = 0.88$ for social lubricant alcohol expectancies. Questions were answered on a 5-point Likert scale ranging from 0 (not at all) to 4 (a lot) with higher scores indicating a greater expectancy for the respective alcohol outcome.

2.6.2.4. Alcohol use-mean drinks per day. For the anxiety outcome model, alcohol use 2-months post-baseline (time 2, follow-up 1) was considered a mediator. This was assessed by mean standard drinks consumed per day over the past month, collected via an online version of the Timeline Followback (TLFB) procedure (Hareskov Jensen et al., 2023). A standard drink was defined as 10g (12.5 ml) of pure alcohol.

2.6.3. Outcomes

2.6.3.1. Anxiety outcome. Social anxiety symptoms at 6-months post-baseline (time 3, follow-up 2) were assessed with the shortened forms of the Social Interaction Anxiety Scale (SIAS-6) and Social Phobia Scale (SPS-6) developed by (Peters et al., 2012). The SIAS-6/SPS-6 includes 12 items which are scored on a 5-point Likert scale from 0 "Not at all characteristic or true of me" to 4 "Extremely characteristic or true of me". Total possible scores can range from 0 to 48, with higher scores indicative of greater social anxiety, and a score ≥ 7 on the SIAS-6 indicative of a probable social anxiety diagnosis (Peters et al., 2012). Excellent internal consistency was seen at baseline within this samples' SIAS-6/SPS-6 scores ($\alpha = 0.88$) and previous research has demonstrated its utility in clinical and undergraduate samples (Carleton et al., 2014; Peters et al., 2012).

2.6.3.2. Alcohol mean drinks per day outcome. Alcohol use 6-months post-baseline (time 3, follow-up 2) was assessed by mean standard drinks consumed per day over the past month, collected via an online version of the TLFB procedure (Hareskov Jensen et al., 2023). A standard drink was defined as 10g (12.5 ml) of pure alcohol.

All mediators and outcome measures were kept as continuous variables to draw meaningful clinical conclusions to treatment outcomes that would otherwise be lost with dichotomizing the covariates of interest (Altman & Royston, 2006).

2.6.4. Confounders

The following baseline (time 1) measures were included as confounders in both models: age in years, sex, and either the anxiety or alcohol outcome of interest at time 1.

2.7. Statistical methods

2.7.1. Causal multiple mediation analysis

Causal multiple mediation analysis under the counterfactual framework using the potential outcomes approach was conducted to infer causal inference. Two separate models investigated the effects associated with the anxiety and alcohol outcomes of interest. Models used the linear regression-based approach as outlined in VanderWeele & Vansteelandt, 2014 to estimate direct and indirect effects of interest. See supplementary material or VanderWeele & Vansteelandt, 2014, p. 108 for the equations for the PNDE, TNIE, and TE. This approach is suitable

for models with a continuous outcome and multiple continuous mediators. All analyses were done with R studio version 4.3.2, with the "cmest" function in the "CMAverse" R package (Shi et al., 2021) used to estimate causal effects, with results reported on the mean difference scale. Bias-corrected and accelerated bootstrapping with 500 samples were used to calculate standard errors and 95 % confidence intervals for estimated effects. Primary analyses were two separate multiple mediation models developed for the two outcomes of interest as seen in Figs. 1 and 2. Both models accounted for baseline confounders unaffected by the exposure, including sex, age, and baseline levels of the outcome measure.

2.7.2. Data imputation

Missing data were handled using multivariate imputation by chained equations (MICE) (Azur et al., 2011). Of the 123 participants, 80 (65 %) provided complete data for *both* the 2- and 6-month follow-up variables of interest, and 96 (78 %) provided data for *at least one* of the 2- or 6-month follow-up assessments. Individuals with incomplete data or loss to follow-up at 2 and/or 6 months did not differ significantly at baseline in sociodemographic or outcome variables from those who completed assessments. All 123 participants had complete baseline data and participants who did not have follow-up data for both 2 and 6month follow-up variables (43, 35 %) were included in analysis with their follow-up data handled with MICE, under the assumption of Missing at Random (MAR). To ensure the MAR assumption (i.e. missingness is assumed to be independent of unobserved variables) was reasonable, our imputation models included key study variables and covariates (i.e. baseline measures of outcome variables, sex, age) predictive of attrition or missing responses. Imputation of missing values was done by predictive mean matching informed by variables included within the respective models (i.e., exposure, mediators, outcome, and confounders). This was done with the "args_mice" argument of the cmest function within the CMAverse R package. Eighty imputed datasets run for twenty cycles were utilized for each model, to improve the stability of estimates and reduce power falloff (Graham et al., 2007). Imputed models are reported for all analyses with complete case models reported in Supplementary Material Table 1.

2.7.3. Sensitivity analyses

To test robustness of the mediation analyses, extrapolation of unmeasured mediator-outcome confounding was calculated. E-values were calculated using the "cmsens" function from the CMAverse package (Shi et al., 2021) and are reported for the pure natural direct effect (PNDE) and total natural indirect effect (TNIE) for the two causal models of interest. As the causal estimates were for continuous outcomes on the difference scale, E-values were transformed into risk ratios using the transformation as described by VanderWeele & Ding, 2017. E-values closer to 1 indicate the results may be more sensitive to potential unmeasured confounding.

Furthermore, in addition to the two primary multiple mediation models, two additional sensitivity analyses were conducted to examine i). whether treatment effects immediately post-treatment (2-months) were mediated by changes in mediators at the same time point and ii). potential confounding in the mediator-outcome relationship. Both imputed and complete case analyses were conducted for these models.

The first set of models assessed whether post-treatment (2-month) mediators explained short-term (2-month) treatment effects on outcomes (i.e. cross-sectional multiple mediation analyses), rather than longer-term (6-month) effects. This analysis aimed to determine whether changes in mediators observed at 2 months played a direct role in shaping outcomes at the same timepoint. This informs questions about whether a short time-lag between the mediator and the outcome might be more sensitive to mediated effects than the 4-month time-lag within the primary models. One model included 2-month social anxiety mediators predicting 2-month social anxiety outcomes, and another model included 2-month alcohol mediators predicting 2-month alcohol outcomes. Otherwise, the same mediators and covariates as the primary analyses were included (see Figs. 1 and 2) and a linear regression-based approach was used.

The second set of models explored potential confounding in the mediator-outcome relationship by including 2-month outcome measures as an additional covariate. This analysis aimed to account for the possibility that changes in the outcome variable (e.g. social anxiety or alcohol use) occurred alongside changes in the mediators, rather than being temporally separated and caused by them. One model included 2-month social anxiety mediators predicting 6-month social anxiety outcomes, adjusting for the 2-month social anxiety symptom measure as a mediator-outcome confounder (L variable). Similarly, the second model included 2-month daily alcohol use mediators predicting the 6-month daily alcohol use outcome, adjusting for the 2-month alcohol use measure as a mediator-outcome confounder (L variable). The inclusion of a continuous measure as mediator-outcome confounder warranted the use of the g-formula approach for these models (Robins, 1986).

2.8. Power considerations

The primary RCT was designed with 80 % power to detect a moderate main treatment effect of 0.5 on efficacy of outcomes (Stapinski et al., 2019). As the current study is an ad-hoc analysis, the trial was not designed to be powered to detect specific mediation effects. More recent methods have been developed for determining power for causal mediation analyses, however, these have not been extended to multiple mediation or longitudinal causal mediation study designs (Qin, 2024). Using the methods for single mediation, a sample size of 123 would yield 84 % power to detect a small total indirect effect of 0.2, from small-medium standardized path coefficients of 0.3 for paths X→M, M→Y, and X→Y (Qin, 2024).

2.9. Ethical approval

Ethical approval was granted by the University of New South Wales (HC17185) and University of Sydney (2018/877) Human Research Ethics Committees, and the trial was prospectively registered with the Australian New Zealand Clinical Trials Registry (ACTRN12617001609347). All participants provided informed consent via the *Inroads* study website.

3. Results

3.1. Participants

At baseline, anxiety symptoms were high with 72 % reporting moderate (score >10) to severe (>15) generalized anxiety per the GAD-7, and 75 % meeting criteria for a probable social anxiety disorder per the SIAS-6 (score ≥7). High levels of alcohol use were also seen across the sample with participants consuming an average of 3.5 standard drinks per day (SD = 3.1) or 104 standard drinks in the past month, and 60 % reporting alcohol use behaviors, per the AUDIT, indicative of alcohol dependence (score ≥20). Additional participant characteristics are reported in the primary outcomes paper (Stapinski, Prior, et al., 2021). No significant differences were seen at baseline between the intervention and control group on any symptom, sociodemographic, or outcome variable of interest for this study.

3.2. Effects of intervention on anxiety outcome

Results for the causal multiple mediation for both the anxiety and alcohol models can be seen in Table 1.

Based on the potential outcomes framework, a significant total effect was observed for the anxiety model, indicating a five-point decrease (95 % CI = −1.509 to −8.191) in social anxiety symptom scores for individuals in the *Inroads* condition compared to the control group. The

Table 1
Estimates of causal multiple mediation effects of the Inroads intervention on social anxiety and alcohol outcomes.

	Total Effect (TE)				Pure Natural Direct Effect (PNDE)				Total Natural Indirect Effect (TNIE)			
	Estimate	P value	95 % Confidence Interval		Estimate	P value	95 % Confidence Interval		Estimate	P value	95 % Confidence Interval	
Social anxiety symptoms outcome	−4.907	**<0.001**	−1.509	−8.191	−4.967	**<0.001**	−1.337	−8.137	0.060	0.908	1.701	−1.024
Mean standard drinks per day outcome	−0.807	**<0.001**	−0.415	−1.271	−0.515	**0.032**	−0.050	−1.116	−0.292	0.068	0.009	−0.551

Estimates are reported on the mean difference scale with effects with p values < 0.05 bolded. Models include age, sex, and the respective outcome at baseline as confounders.

significant total effect in the model was primarily driven by the Pure Natural Direct Effect (PNDE). Specifically, the *Inroads* intervention had a direct effect of reducing social anxiety symptoms by five points (95 % CI = −1.337 to −8.137), independent of any indirect effects mediated through increases in cognitive reappraisal and decreases in suppressive emotion regulation and alcohol use. No significant TNIE was observed via the hypothesized mediators.

3.3. Effects of intervention on alcohol outcome

A significant total effect was observed for the alcohol model, indicating that individuals in the *Inroads* condition consumed, on average, one standard drink per day less than those in the control group. Within this total effect, the Pure Natural Direct Effect (PNDE) but not the Total Natural Indirect Effect (TNIE) were found to be significant. Specifically, the *Inroads* intervention had a significant direct effect of decreasing individuals' alcohol use by 0.5 standard drinks per day (95 % CI = −0.050 to −1.116). The TNIE indicated a non-significant decrease of 0.3 standard drinks per day (95 % CI = 0.009 to −0.551) for *Inroads* individuals compared to controls. Since the 95 % confidence interval for the TNIE includes zero, there was insufficient evidence of a mediated effect through the combined increase in cognitive reappraisal and decrease in suppressive emotion regulation, drinking to cope with anxiety motives, drinking for enhancement motives, tension reduction alcohol expectancies, and social lubricant alcohol expectancies.

3.4. Sensitivity analyses

The E-values for unmeasured confounding in both models are presented in Table 2. The PNDE E-values for the anxiety and alcohol models were 2.6 and 2.0, respectively. Given the inclusion of theoretically supported covariates in each model, it is unlikely that unmeasured confounders of this magnitude would fully explain the observed associations. However, the TNIE E-values for both models are close to one, suggesting reduced confidence in the adequacy of the models to account for all potential confounders. Specifically, the E-value of 1.1 for the anxiety model suggests that an unmeasured confounder with a weak association with the multiple mediators and outcome could have explained away the TNIE. In contrast, the E-value of 1.6 for the alcohol model suggests an unmeasured confounder with a moderate association with the multiple mediators and drinking outcome would be needed to have explained away the TNIE.

Table 2
E-values for unmeasured confounding and 95 % Confidence Intervals associated with the anxiety and alcohol models.

	Pure Natural Direct Effect (PNDE)			Total Natural Indirect Effect (TNIE)		
	E-value	95 % Confidence Interval		E-value	95 % Confidence Interval	
Social anxiety symptoms outcome	2.572	1.634	1.0	1.081	1.0	1.0
Mean standard drinks per day outcome	1.992	1.101	1.0	1.630	1.075	1.0

E-values are reported on the risk ratio scale.

Results of the sensitivity analysis exploring potential mediation of short-term treatment effects or mediator-outcome confounding can be seen in Supplementary Tables 2 and 3 respectively. In these analyses, the significant effects ($P < 0.005$) for the anxiety model remained across both sensitivity analyses, although the observed estimates were slightly smaller. For the alcohol models, the mediator-outcome confounding sensitivity analyses also showed slightly smaller estimates, but the pattern of significance remained consistent with the primary analyses. However, in the sensitivity analyses examining mediators of short-term (2-month) alcohol reductions, there was no evidence of a significant PNDE or a significant total effect (Supplementary Table 2). The lack of significant PNDE and total effect in the supplementary model predicting short term (2-month) alcohol outcomes is consistent with the main RCT findings, where intervention versus control effects on drinking were only observed at the 6-month follow-up.

4. Discussion

This study aimed to examine whether hypothesized behavioral, cognitive, and motivational mechanisms jointly mediate the effectiveness of the *Inroads* intervention in reducing anxiety and daily alcohol use among young adults. As the first online intervention designed to promote coping skills for managing anxiety, hazardous alcohol use, and their interconnections, it is important to test the potential mechanisms driving these effects. The findings of this current study demonstrated evidence of a total effect of the *Inroads* program on reducing social anxiety symptoms and mean daily alcohol use at six months post-intervention, even when accounting for mediating factors. Contrary to hypotheses though, no significant mediated indirect effect was found based on measured values of mediators at time 2 and social anxiety or alcohol outcomes at time 3 whilst accounting for baseline covariates.

The *Inroads* anxiety-alcohol treatment did not appear to reduce social anxiety symptoms via the hypothesized mediators, notably one of which was reducing alcohol use. This is at odds with current theoretical models of co-occurring anxiety and alcohol use, where a reduction in alcohol use would in turn be presumed to also reduce anxiety symptoms (Smith & Randall, 2012). Alcohol has been shown to exacerbate anxiety by triggering symptoms, creating additional psychosocial stressors, and/or reinforcing threat expectancies, leading to the "vicious cycle of comorbidity", with both disorders reinforcing one another (Baillie & Sannibale, 2007). As the current study looked at joint causal mediation, further research is needed to elucidate the causal role of specific mediators, like alcohol use, in reducing anxiety symptoms. Furthermore, whilst there wasn't evidence for the hypothesized mediators of symptom change, it is possible that the detection of mediation effects was limited by the delay between assessment of mediators at 2 months post baseline and outcomes at 6 months. The four-month lag between the measurement of mediators and the social anxiety outcome may not have appropriately captured how changes in the proposed mechanisms subsequently account for reductions in social anxiety seen among

intervention participants. In the context of intervention participants also observing the greatest reductions in social anxiety symptoms from baseline to 2-months post intervention, additional measurement time points, throughout the 2-month treatment duration, could further elucidate the role of mediator timing on treatment outcomes. Given the current study did not find significant effects, however, for the hypothesized mediators at the measured timepoints, the question regarding what is driving the efficacy of the *Inroads* intervention on reducing social anxiety symptoms remains. Outside of online interventions, perceived social self-efficacy, estimated social cost, and avoidance have been identified as mediators in SAD treatments (Hedman et al., 2013; Rukmini et al., 2021). Future research is needed to determine the role these psychological mechanisms may play in the role of online anxiety-alcohol treatments.

There was not statistical evidence in the current study that reductions in drinking, within the context of co-occurring anxiety and hazardous alcohol use, were mediated by the hypothesized mechanisms of positive expectancies and motives about the effects alcohol, and maladaptive emotion regulation. While the joint mediation estimate of the total natural indirect effect did not reach statistical significance (b = −0.292, CI: 0.009 to −0.551, P = 0.068), the current study had only 84 % power to detect the small-medium effects. Future research, with greater statistical power, may help identify potential small indirect effects through these hypothesized mediators. Further work is needed to clarify whether significant mediation effects would be observed if mediators and outcomes were measured closer (rather than with a 4-month lag), or whether it is additional mechanisms entirely that contribute to the intervention's overall impact on alcohol use. This is particularly important given the significant pure natural direct effect observed (b = −0.515, CI: 0.050 to −1.116, P = 0.032). As with the anxiety model, joint causal mediation analysis limits the ability to identify the specific effects of individual mediators, suggesting the presence of additional pathways influencing the observed reductions. When compared to other studies investigating mechanisms of change among alcohol-only online interventions, similar (i.e., null, or weak) effects are seen. An online alcohol education course for college students found no mediating effect of positive alcohol expectancies on drinking behaviors (Paschall et al., 2014). Similarly, a personalized feedback alcohol intervention for 18–25 year olds found no effect of decreases in drinking to cope motives mediating reduced alcohol use (Lau-Barraco et al., 2018). These education courses, however, were preventative interventions which may not be directly comparable to treatment and intervention mechanisms of change. Additionally, other psychological mechanisms, such as self-efficacy, confidence, and knowledge of how to change, have been found to mediate outcomes in online and telehealth alcohol treatments (Bendtsen et al., 2023; Brincks et al., 2024). Although not considered the key mechanistic drivers in the motivation and maintenance of co-occurring anxiety and alcohol use specifically, further research is needed to understand whether these are also potential mechanistic targets for *integrated* anxiety-alcohol treatments.

The current study has several strengths including its use of modern causal mediation methods, and longitudinal study design allowing for temporal precedence and causality to be inferred. There are, however, several limitations which must be considered. Firstly, is the likelihood of residual or unmeasured confounding. Despite including sex, age, and baseline outcome measures as potential confounders in each model, the observed E-values suggests effects could still be influenced by other unmeasured covariates. Further research is needed to elucidate the robustness of the observed causal relationships and whether there are additional confounding factors, on the mediator-outcome relationship, which should be considered in the context of integrated anxiety-alcohol treatments, and other psychological treatments more broadly. Specifically, this may also include mediator-outcome confounders which are affected by the exposure, like post-treatment levels of alcohol use. Sustained changes in alcohol use are highly correlated with alcohol use reduction immediately post treatment, and these early alcohol reductions could also influence the hypothesized mediators. For example, reduced alcohol use at post intervention might lead to reduced coping-motives for drinking. This possibility of a reverse causation relationship means that levels of anxiety/alcohol use at 2 months may confound the observed association between the mediators and outcomes at 6 months. We conducted sensitivity analyses to estimate mediation effects controlling for this potential mediator-outcome confounding, which suggested a slight reduction in effects sizes but no substantiative change to the study conclusions. Secondly, despite being the first online intervention targeting co-occurring anxiety and hazardous alcohol use in young adults, the modest trial sample size (n = 123) and subsequent attrition at follow-up assessments may have introduced bias to the estimated effects. This, attrition, however was mitigated in the current study through gold standard missing data imputation approaches. Future evaluation of the *Inroads* program will address potential sample size and attrition bias through a RCT with a larger sample. This trial aims to recruit a sample of n = 500, which will be powered to detect between-group differences when comparing the *Inroads* integrated alcohol-anxiety program (plus telehealth and email support from a non-specialist support person) to a brief alcohol-feedback control program, with an effect size of d = 0.3 and 0.9 power (Prior et al., 2024). Lastly, there are potential limitations, as alluded to earlier in this discussion, related to the measurement of the mediating variables, both in terms of their theoretical basis and timing of measurement. Whilst the measures chosen were well validated, there is the possibility that they did not adequately capture the psychological and behavioral constructs which were hypothesized to be mechanisms of change. Additionally, the mediating variables were measured 2-months post-baseline and the outcomes 6-months post-baseline. The length of time between the measurement of mediating mechanisms and outcomes may not have been appropriate to capture these psychological and behavioral factors. Measuring the hypothesized mediators immediately post treatment and at additional timepoints throughout treatment, combined with an earlier follow-up measurement of outcomes, may provide greater insight into how the anxiety-alcohol treatment was efficacious. Finally, given the lack of evidence for the hypothesized mediators in the social anxiety and alcohol use models, unmeasured or incorrectly measured mediators remain a limitation in the current study. Additional studies would benefit from testing refined measures which more accurately capture the constructs pertaining to the mechanisms of change for anxiety and alcohol treatments.

5. Conclusion

The aim of this study was to identify the mechanistic drivers of an efficacious treatment for co-occurring anxiety and alcohol use in young people. Whilst there was evidence of an overall effect of treatment on the anxiety and alcohol use outcomes, the study did not find sufficient evidence that these effects were jointly mediated by the hypothesized processes of maladaptive emotion regulation and alcohol use for social anxiety reductions, or maladaptive emotion regulation, positive alcohol expectancies, and coping or enhancement alcohol use motives for reductions in alcohol use. Like other treatment and intervention mediation studies (Greenberg et al., 2023; Moskowitz et al., 2023; Sunderland et al., 2024), this reflects the challenge of delineating the psychological processes that underlie effective treatment. Our results may reflect that the hypothesized mediators were inadequately captured by the study measures, or alternatively that there are different psychological processes driving treatment effects. Further research is needed to better understand *how* integrated anxiety-alcohol treatments, like *Inroads*, achieve their effects so these mechanisms can continue to be refined and built upon in future online interventions.

CRediT authorship contribution statement

Tara Gückel: Writing – review & editing, Writing – original draft,

Methodology, Investigation, Formal analysis, Conceptualization. **Katrina Prior:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **Nicola C. Newton:** Writing – review & editing, Supervision, Funding acquisition. **Andrew J. Baillie:** Writing – review & editing, Funding acquisition. **Maree Teesson:** Writing – review & editing, Funding acquisition. **Lexine A. Stapinski:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2025.104766.

Data availability

The authors do not have permission to share data.

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Appendix H

Supplementary materials for Chapter 5

Preface

This Appendix includes supplementary material for **Chapter 5**. Supplementary materials include an overview on Inroads module content (Table H1), barriers and enablers survey measures (Supplementary material H1 and Supplementary material H2), and the semi-structured interview guide (Supplementary material H3).

Table H1: Overview of content and skills introduced in each module of the Inroads program.

Modules	Skills learned
Module 1	Normative feedback about alcohol use; understanding motives for change and the interrelationship between anxiety and alcohol use; psychoeducation regarding the cognitive, physiological, and behavioural aspects of anxiety and alcohol use; goal setting and drinking limits; and emotion surfing to ride out cravings and uncomfortable feelings
Module 2	Understanding the ABC model and cognitive therapy targeting anxious thoughts
Module 3	Cognitive behavioural therapy strategies for sticking to drinking limits, cognitive therapy targeting positive alcohol expectancies (i.e.. 'drinking thinking'), assertiveness, and handling group dynamics
Module 4	Understanding avoidance and anxiety and graded behavioural experiments
Module 5	Enhancing social support, longer-term goal setting, and relapse prevention

Supplementary material H1:Program enablers survey question

How much do you agree with the following statements about things that **helped you engage** with/complete the Inroads program.

Individual/ user enablers
I noticed improvements in my anxiety or alcohol use which motivated me to continue with the program.
There were practical skills that I could apply directly to help with my anxiety.
Program enablers
The program felt well suited to my circumstances which helped me engage.
The new module available email and SMS reminders helped me engage.
The weekly progress summary emails and goal reminders helped me engage.
The videos helped me engage with the program.
The 'real life examples' helped me engage with the program.
Technology and environment enablers
It helped that the program was online.
The program was user friendly which helped me to engage with it.

Items are ranked on a 5-point Likert scale from 'fully disagree' to 'fully agree'

Supplementary material H2: Program barriers survey question.

How much do you agree with the following statements about things that **got in the way of engaging** with/completing the Inroads program.

Individual/ user barriers
I forgot about the program.
I could not spare the time for the program.
Too many things were going on in my life so I could not make the program a priority.
I realised I'm not ready to make changes to help my anxiety or drinking so didn't want to do the program.
I did not feel motivated to engage with/complete the program.
Program barriers
I felt the need to talk to someone in person, rather than doing this program.
I did not feel the program was tailored enough for me specific circumstances.
The skills in the program were too hard to apply.
There was too much content in the program.
Technology and environment barriers
I did not feel sure that my responses were anonymous.
I had technical difficulties with the program.

Items are ranked on a 5-point Likert scale from 'fully disagree' to 'fully agree'

Supplementary material H3: Semi-structured interview guide

Introduction

Hi,

Thanks very much for taking the time for this phone call today. My name is [name] and I'm a Researcher based at the Matilda Centre for Research in Mental Health and Substance Use at the University of Sydney.

The purpose of this interview is for you to provide feedback on your experience with the Inroads program and study. Based on the feedback we receive in these phone interviews and in the follow-up surveys we're running, we hope to make updates and adaptions to the program to ensure we are developing effective and engaging online programs for people with anxiety and alcohol use concerns. There are no right or wrong answers today, and myself and the research team are very open to all feedback, so please feel free to be as honest as possible.

The interview will take up to 60 minutes. We're audio recording the session but anything you say will be de-identified so any comments you make cannot be linked back to you. Can I please confirm you are okay with the interview being audio recorded?

Do you have any questions at this point? If not, let's get started.

Heard about Inroads/motivation for enrolling

- To start off, can you tell me how you first heard about the Inroads program or the Inroads trial.
  If they don't remember
    - We did some social media advertising, did you see an ad online? We also did some TV and radio interviews, so you may have heard about us through that?
    - That's okay, it's been a while now since you would have first signed up to the program!
- Do you remember why you registered for the program in the first place?
    - Can you talk me through a bit more why you decided to register for the program.
    - What specifically were you hoping the Inroads program would help with?
    - What specifically were you hoping to get out of the Inroads program?
- In your own words can you describe who the Inroads program was for and what it aimed to help with?
  Probing question

- What did being in the Inroads study involve?
- Did the Inroads program end up being what you thought it would be?
- Was it different or similar to what you think it would be?
- Did you mainly access the program on your phone or a laptop/desktop computer?

Experience with the program

I'll now ask some questions about your experience with the Inroads program. It doesn't matter how much, if any, of the program you completed, we're interested in hearing about everyone's experiences and feedback.

- To start off with do you want to tell me a bit about your general experience with the Inroads program. For example, did you go and complete module 1 straight after finishing the initial surveys?
  Probing question
  - Can you remember how many of the modules you completed?
  - Did you do all of module 1 in one sitting?
  - Did you read or listen to the character stories?
  - What was your first impression of the program?
  - Did the program align with your specific issues and did you feel it could help?
  - After completing the modules did you put in place any of the ideas?
  - Did you receive and read the weekly therapist emails?
    - What was your impression of the emails?
    - What did you think of the feedback in the emails?

- Now after talking through those things and thinking about your time in the Inroads study, were there any factors that got in the way of you engaging with the program? These can be either personal factors or program related factors.
  Probing question
  - Was there anything specific that made it hard to engage with the program?
  - Do you have any ideas for how we could update the program to improve that?

- Were there any factors that helped you engage with the program?
  Probing question
  - Was there anything specific that helped you engage with and work through the program?
  - Do you think the emails and text messages helped?
  - Would you recommend we keep doing/including that in the program?
  - Are there any ways we could tweak XX to be even better?

- When it comes to online programs, would you prefer an online program that is fully self-guided (by that I mean you work through it on your own, with no guidance or support) or would you prefer to have some phone calls or email conversations with someone from our research team in addition to having access to the online program?
  Probing question
    - Can you expand a bit more on why you'd prefer that format?
    - If the program wasn't self-guided, what additional support would you like? Some options of additional support might be:
        - Technical support with using the program
        - A welcome phone call from the research team explaining the program and letting you know the additional support available.
        - Check-ins with a psychologist/therapist. How often would you like these to be.
    - If the program was to provide additional support in addition to the online modules, would you rather it be via phone calls or chatting with someone back-and-forth via email or text messages?
    - Would you like the option of scheduling a psychologist or technical support person you could call if needed.

Magic wand question

- Now thinking broadly, if you could design your ideal online program for anxiety and alcohol use, what would it look like?
  Probing questions
    - What technological features would you like the program to have?
    - Is there anything the program definitely **shouldn't** have?
    - Would you be more likely to access a program that's a website or via an app?

Closing questions

- I know we've already covered a lot of ground today but is there anything else you'd like to add, or think is important for me to know?
  Probing questions
    - Is there anything you expected us to talk about that we haven't covered?
    - Any other comments about the Inroads programs or ideas for how we can improve it?
    - Any ideas for how we can better communicate what the Inroads study involves?

Final remarks

Thank you very much, the feedback and suggestions you've provided are really valuable to our research team and I appreciate the time you've taken to have this phone call.

If anything we've discussed today has brought up feelings of anxiety or you're wanting more help, you can log back into the Inroads program at any time or on the Inroads website we have a list of mental health and substance use support services. I'll also send through an email with this list of services which Lifeline, a 24/7 service you can call on 13 11 14.

Thank you again, I'll send through your $70 reimbursement very soon, so please check your email. In the meantime, feel free to get in contact via email if you have any follow-up questions.