

Suicidal behaviour in young people accessing mental health care

*A thesis submitted in fulfilment of the requirements
for the degree of*

Doctor of Philosophy

By

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Catherine M. McHugh

12/12/2022

Preface

The chapters of this thesis contain seven published, peer-reviewed articles. At the time of first submission, two of these manuscripts were under peer-review at scientific journals. The final published versions have been included in the final version of this thesis. This thesis has been submitted digitally in PDF format. To increase the ease of navigating between chapters for the reader, hyperlinks have been added throughout, so that clicking on the blue text will bring the reader to the relevant chapter or paper. Chapters 2, 3 and 4 each contain two articles, and Chapter 5 contains one.

Author attribution statement

Chapter 2.1 is published in *BJPsych Open*. Catherine McHugh (CM) designed the study, analysed the data, and wrote the manuscript drafts with supervision by Matthew Large (ML) and Ian Hickie (IH). All co-authors contributed intellectually to the drafts.

Chapter 2.2 is published in *Australian and New Zealand Journal of Psychiatry*. CM designed the study, analysed the data, and wrote the manuscript drafts with supervision by ML and IH. All co-authors contributed intellectually to the drafts.

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Chapter 3.2 is published in *Social Psychiatry and Psychiatric Epidemiology*. CM designed the study, analysed the data, and wrote the manuscript drafts with supervision by IH. All co-authors contributed intellectually to the drafts.

Chapter 4.1 is published in *Journal of Psychiatric Research*. CM designed the study, analysed the data, and wrote the manuscript drafts with supervision by Rico Sze Chun Lee (RL), Daniel Hermens (DH), and IH. All co-authors contributed intellectually to the drafts.

Chapter 4.2 is published in *Journal of Affective Disorders*. CM designed the study, analysed the data, and wrote the manuscript drafts with supervision by RL, DH, and IH. All co-authors contributed intellectually to the drafts.

Chapter 5 is published in *BJPsych Open*. CM designed the study, analysed the data, and wrote the manuscript drafts with supervision by IH. All co-authors contributed intellectually to the drafts.

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Dr Cate McHugh

12/12/2022

As supervisor for the candidature upon which this thesis is based, I confirm that the author attribution statements above are correct.

Professor Ian Hickie

12/12/2022

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Abstract

Suicidal behaviour is a leading cause of premature mortality and morbidity in young people. In Australia and other high-income countries, rates of suicide and suicidal behaviours in young people have increased despite increased public awareness and investment in suicide prevention. Suicide prevention can be categorised into interventions designed to operate at a population-level or targeted to specific populations or settings, such as clinical services. Whole of population interventions can also have an important role in reducing suicidal behaviour (SB) in clinical populations, for example restricting access to lethal means. Other population interventions may be expected to have less impact on reducing suicidal behaviour in high-risk groups, such as clinical populations, if they do not target the factors driving increased suicidality in these populations. The efficacy of clinical suicide prevention relies on in-depth, contemporaneous understanding of suicidal behaviour in clinical populations. Mental health system reform over the last two decades has led to the development of youth mental health (YMH) services designed to deliver early intervention care to young people to reduce the burden of disease. This has created a new clinical cohort distinct from population samples or clinical samples of adults accessing mental health services.

The overall aim of this thesis was to generate new scientific understanding of suicidal behaviour in these new clinical cohorts, which may be applied in clinical services to improve the care of young people experiencing suicidal behaviour, and ultimately reduce the impact of youth suicide. This thesis first reviews existing methodology in suicide research in **Chapter 2**, before shifting focus to novel methodologies in **Chapter 3**, which considers the application of machine learning to suicide research. In **Chapter 2** systematic review and meta-analyses of 70 years of research on suicide deaths is used to assess the predictive performance of key risk factors used to direct clinical suicide prevention.

Chapter 2.1 reports the poor sensitivity and specificity of suicidal ideation (SI) for suicide death, such that 60% of those who later die by suicide had denied suicidal ideation at a specified earlier time point. **Chapter 2.2** tests the hypothesis that suicidal behaviour (SB) is a stronger predictor of future suicide death, finding SB associated with a slightly greater odds ratio of suicide death, though the difference between the two was non-significant. Both studies conclude that the population and setting of suicide research have a significant impact on the strength of associations and outcomes reported.

Chapter 3 focuses on the application of machine learning (ML) modelling to the prediction of suicidal behaviour. **Chapter 3.1** first synthesizes the relative strengths, opportunities, and key limitations of ML applied to clinical suicide prevention. These insights are then applied in **Chapter 3.2**, a longitudinal study of young people accessing youth mental health services. Machine learning algorithms were applied to develop predictive models of suicide attempts (SA) and deliberate self-harm (DSH). Models of SA were associated with superior performance relative to those predicting

DSH. Models predicting new-onset or repeat DSH or SA performed no better than chance, however for the latter PPV remained high, indicating that all young people who present to services with DSH/SA should receive assertive clinical interventions. There was some evidence of distinct symptom profiles predicting future SA versus DSH, however there was significant cross over between these behaviours. A history of either DSH or SA was the strongest predictor of future behaviour, followed by clinical symptoms of common mental disorders.

The latter half of this thesis then considers the opportunities presented by incorporating new forms of data into future predictive modelling in suicide research. [Chapter 4](#) first explores the utility of cognition as a potential biomarker of suicidal behaviour in young people, before [Chapter 5](#) applies data linkage to assess mortality outcomes and health service use in a YMH cohort. [Chapter 4.1](#) reviews the evidence for a key proposed cognitive phenotype of suicidal behaviour in this cohort, impulsivity, finding that impulsivity is associated with a small to moderate effect on suicidal behaviour, relative to healthy controls, but not psychiatric controls. There was no evidence that sub-types of impulsivity were more useful predictors than a broader construct of impulsivity, nor that the type of self-harm or suicidal behaviour (whether associated with suicidal intent or not) was a moderator of effect. [Chapter 4.2](#) then assessed whether incorporating neurocognitive assessment into clinical care could improve prediction of suicidal behaviour at 12 months follow up. Deficits of cognitive flexibility were a key predictor of future SB. Unexpectedly, young people with SB were found to have superior cognitive functioning on a range of cognitive tests measuring executive functioning relative to clinical controls and population norms including processing speed, working memory, delayed verbal memory and visuospatial memory. This finding suggests the neurocognitive profile of young people with suicidal behaviour is unique, relative to older cohorts with suicidal behaviour.

Finally, [Chapter 5](#) presents the first study of mortality outcomes of this cohort Australia, finding that despite being earlier in the course of illness the risk of premature mortality in young people in this cohort is twice that of the general age-matched population, which increases to a five-fold increase for males. Suicide was the leading cause of death in this cohort, followed by accident and injury. Self-poisoning, whether intentional or accidental, was a primary or contributing cause in 43% of deaths. Prior emergency department presentation for any type of poisoning (whether accidental or intentional) was associated with the greatest hazard ratio for future death due to suicide or accident.

The findings of this thesis are severalfold, firstly the characteristics of suicidal behaviour in young people accessing mental health services are unique in terms of social, clinical and cognitive predictors. There is significant overlap between self-harm without suicidal intent and suicide attempts in this cohort suggesting that differentiating between types of self-harm based on intent may be less useful in than in population cohorts. The high burden of disease associated with self-harm and

suicidal behaviour suggests that all young people accessing mental health services should receive evidence-based suicide prevention interventions. Further, the high rates of adverse outcomes due to accident and injury, drug and alcohol use and emergency department presentations, highlight the importance of taking a comprehensive approach to reducing premature mortality and morbidity in this cohort. These findings suggest that developing strategies and designing interventions to address a broader construct of harm should be considered.

Leveraging the digital transformation of mental health services to develop system-wide approaches to assessment and delivery of interventions designed to reduce suicidal behaviours and associated harms presents a major opportunity in translational research and clinical service delivery. The optimal use of digital platforms and devices can increase the quality of clinical care, by improving access and consistency of interventions and capture new forms of high-quality data that can be used to further knowledge of suicidal behaviour.

Publications presented for examination

The following papers form the basis of this thesis:

McHugh, C.M., Corderoy, A., Ryan, C.J., Hickie, A., Large, M.M., 2019. Meta-analysis on sensitivity of suicidal ideation for completed suicide. *British Journal of Psychiatry Open*. 5(2) e18, 1–12. DOI: 10.1192/bjo.2018.88

Large, M.M., Corderoy, A., **McHugh, C.M.**, 2021. Is suicidal behaviour a stronger predictor of later suicide than suicidal ideation? A systematic review and meta-analysis. *Australia and New Zealand Journal of Psychiatry*. 55 (3): 254-267

McHugh, C.M., Large MM., 2020. Can machine-learning methods really help predict suicide? *Current opinion in psychiatry*. DOI: 10.1097/ycp.0000000000000609.

McHugh, C.M., Ho, N, Iorfino, F., Crouse, J.J., Nichles, A., Zmicerevska, N., Scott, E., Glozier, N., and Hickie, I.B., 2022. Predictive modelling of deliberate self-harm and suicide attempts in young people accessing primary care: An ensemble machine learning analysis of a longitudinal study. *Social Psychiatry and Psychiatric Epidemiology*. DOI: 10.1007/s00127-022-02415-7

McHugh, C.M., Lee, R.S., Hermens, D., Corderoy, A., Large, M.M., Hickie I.B., 2019. Impulsivity and Suicidal Behaviour in young people: A systematic review and meta-analysis. *Journal of Psychiatric Research*. 116 (3): 51-60

McHugh, C.M., Iorfino, F., Crouse, J.J., Tickell, A., Nichles, A., Zmicerevska, N., Ho, N., Lee, R., Hermens, D.F., Scott, E. and Hickie, I.B., 2021. Neurocognitive functioning predicts suicidal behaviour in young people with affective disorders. *Journal of Affective Disorders*, 281, pp.289-296.

McHugh, C.M., Iorfino, F., Karunaratne, N., Song, C.Y, Zmicerevska, N., Skinner, A.F, Scott, E. and Hickie, I.B., 2023. Premature mortality in young people accessing early intervention youth mental healthcare: data-linkage cohort study. *BJPsych Open*. 9, e76, 1–9. DOI: 10.1192/bjo.2023.43

Additional relevant peer-reviewed publications

A substantial contribution was also made to the following papers as part of research studies that were complementary to this thesis. The outcomes of these studies helped to inform the theoretical framework and interpretations of the data reported in this thesis.

McHugh, C.M, Song, Y. J. C., Zmicerevska, N., Crouse, J., Nichles, A., Wilson, C., ... & Hickie, I. B. (2022). Premature mortality in early-intervention mental health services: a data linkage study protocol to examine mortality and morbidity outcomes in a cohort of help-seeking young people. *BMJ open*, 12(2), e054264.

McHugh, C. Balaratnasingam. S. (2018) Impulsivity in personality disorders: current views and future directions. *Current opinion in psychiatry* 31 (1), 63-68

McHugh, C., Chapman, M., Campbell, A., Balaratnasingam. S. (2016) Increasing Indigenous self-harm and suicide rates in the Kimberley: An audit of 2005-2014 data. *Medical Journal of Australia*. 205 (1): 33.

McHugh, C., Balaratnasingam, S., Campbell, A., Chapman, M. (2016). Suicidal ideation and deliberate self-harm presentations in the Kimberley from an enhanced police - mental health service notification database. *Australasian Psychiatry*. 25(1): 35-39.

Campbell, A., Balaratnasingam, S., **McHugh, C.,** Janca, A., Chapman, M. 2016, 'Alarming increase of suicide in a remote Indigenous Australian population: an audit of data from 2005 to 2014' *World Psychiatry*. 15(3), 296-297

Campbell, A., Balaratnasingam, S., **McHugh, C.,** Chapman, M. (2016) Rising Indigenous suicide rates in Kimberley and implications for suicide prevention. *Australasian psychiatry*. 24(6), 561-564.

Conference presentations

- 2022 Royal Australia New Zealand College of Psychiatrists Section on Youth Mental Health Conference. Alice Springs.
Oral presentation, 'Integrated care models in youth mental health'
- 2020 Centre for Research Excellence YouthE: Healthcare system reform for youth suicide prevention. Sydney.
Oral presentation, 'Neurocognitive predictors of Suicidal Behaviour in young people accessing mental healthcare'
- 2018 RANZCP Neuropsychiatry Section Conference. Melbourne.
Oral presentation, 'Neurocognition in Anorexia Nervosa'
- 2017 Society for Mental Health Research. Canberra.
Oral presentation, 'Sensitivity and specificity of suicidal ideation for completed suicide'
Oral presentation, 'Suicidal Behaviour and Deliberate Self-Harm in Help-Seeking Young People: A Cross-Sectional Exploration of Demographic and Clinical Associations'
- 2017 International Association of Suicide Research Summit. Nevada, United States. *Upcoming*
Oral presentation accepted, 'Suicidal Behaviour and Deliberate Self-Harm in Help-Seeking Young People: A Cross-Sectional Exploration of Demographic and Clinical Associations'

Poster presentation accepted, 'Sensitivity of Assessment for Suicidal Ideation to Detect Later Completed Suicide in Mental Health Services'
- 2017 Royal Australia New Zealand College of Psychiatrists Congress. Adelaide.
Oral presentation, 'Impulsivity and suicidal behaviour in young people'
- 2016 Royal Australia New Zealand College of Psychiatrists Congress. Hong Kong.
Oral presentation, 'Deliberate self-harm and suicidality in the Kimberley'

List of common abbreviations

AI: Artificial intelligence

DSH: Deliberate-self harm

MI: Mental illness

ML: Machine learning

SA: Suicide attempt

SB: Suicidal behaviour

SI: Suicidal ideation

YMH: Youth mental health

Chapter 1: Introduction

1.1 Suicide in young people

Suicide is a leading cause of death in young people, and associated suicidal behaviours are a major cause of morbidity. In Australia, suicide rates have increased amongst young people aged 15-19 (from 8.0 in 2010 to 11.5 suicides per 100,000 in 2019), as well as those aged 20-24 (11.8 in 2010 to 16.4 suicides per 100,000 in 2019), such that suicide is the leading cause of death amongst those aged 15-35 years (1). Suicide rates amongst young men are twice that of young women, such that 75% of suicide deaths occur in men (2). First nations communities are also disproportionately impacted by youth suicide (3). Other demographic groups at greatly elevated risk of suicide, include those identifying as LGBTIQI, military veterans, people living with mental illness and rural and remote populations (4-6). Australia's increasing youth suicide rates are not unique, and other high-income countries, such as the United States and the United Kingdom report similar trends (7-9). In low- and middle-income countries, where 80% of global suicide deaths occur, data on suicide mortality rates are less readily available (10).

The impact of suicide on families and communities is profound, and those who lose a loved one to suicide are impacted over a lifetime. Exposure to suicide is also known to increase the risk of suicide amongst family, peers and other community members. The risk of contagion may be particularly acute in communities already at increased risk, and exposed to poverty, trauma and discrimination, such as in First Nations communities or amongst LGBTIQI young people (11). Although suicide is a leading cause of death in young people, crude suicide rates per 100,000 are generally lower in young people than in older age groups, which reflects the lower mortality rates from other causes in this group (12). However, the societal costs of youth suicide are immense due to the years of life lost. From a health economic perspective youth suicide in Australia is estimated to cost up to \$22 billion per year via lost productivity, bereavement and health system costs (13).

Rates of suicidal behaviour, including suicide attempts and non-suicidal deliberate self-harm, have also been increasing in young people (14, 15). This is of particular concern given suicidal behaviour and self-harm are key predictors of future suicidal behaviour and suicide death (16). Independent from its relation to suicide death, self-harm is a major cause of morbidity in adolescents and young adults, and the leading cause of Disability Adjusted Life Years (17).

1.2 Theoretical models of suicidal behaviour

The complex and multifaceted nature of suicide and self-harm has given rise to a range of theoretical models grounded in different disciplines. Early sociological theories of suicide emphasized the role of social integration, where an individual's connection to, and identification with a group has a protective effect against suicidal ideation and behaviour. These theories propose that the social ties an individual has to the group give life meaning and also bring social support, validation and companionship (18). Conversely, the disruptions to these connections, that may occur with relationship breakdown or loss of employment, or through structural social inequities, discrimination, and major disruptions to social bonds, such as that experienced by first nations communities in post-colonial societies, act to increase risk of suicide.

Theories grounded in clinical sciences, such as psychology or psychiatry, have focused on the strong association between suicide and mental illness. These theories examine the suicidal process at the level of the individual, rather than at a group or population level. Psychological and cognitive theories look to the role of cognitions such as hopelessness and worthlessness, or psychological traits, such as perfectionism and cognitive inflexibility in driving suicidal ideation and behaviour (16). Biological theories have used a range of modalities, such as neuroimaging, molecular science and genetics, to identify structural and functional brain or systemic changes associated with suicidal behaviour (19). Many theories recognise the importance of both static and dynamic risk factors in the expression of suicidal behaviour. For example, Mann's stress-diathesis model of suicidal behaviour, proposes an individual has a diathesis, or trait-like, static disposition towards a particular response when under conditions of stress, leading to emergence of the suicidal state (20).

In recent decades there has been a convergence of theories of suicide, under the 'ideation-to-action framework' of suicidal behaviour, which aim to differentiate those who develop suicidal ideation from those who engage in suicidal behaviour (21). Ideation-to-action frameworks include influential theories of suicidal behaviour such as the Interpersonal-psychological theory (IPT) of suicidal behaviour (22) and the Integrated Motivational-Volitional (IMV) theory (23). The Interpersonal-psychological theory, for example, considers suicide to be a result of the interplay between three key factors; the first two, perceived burdensomeness and thwarted belongingness are necessary for suicidal ideation, while the third, acquired capability for suicide, describes the factors necessary for suicidal action. Though influential, many theoretical models are difficult to test empirically, and the relative weighting of different contributing factors is unclear. There is also some evidence that leading theoretical models, such as the IPT model, may be less valid in young people (24-26). For example, Barzilay et al (2017) found that the association between acquired capability and suicidal behaviour was independent of

perceived burdensomeness/thwarted belongingness in adolescents, and that any effect of the latter two constructs on suicidal behaviour was largely mediated by depressive symptoms.

Critics have also highlighted the failure of many leading theories, including ideation-to-action frameworks, to integrate with developments within the neurosciences (27) or with frameworks such as the Research Domain Criteria (28, 29). These limitations are considered important constraints on improving research translation and impact of suicide research, with focus now shifting to the development of formal models that can inform computational modelling (30).

1.3 Differentiating between population and clinical suicide prevention

Given the major impact of suicide on society, suicide prevention has been a key priority for national governments, as well as international bodies, such as the World Health Organisation (WHO) for decades. In general, suicide prevention is taken to mean interventions that aim to prevent suicide deaths, and may also target suicidal ideation and behaviours, including deliberate self-harm. The development of national suicide prevention plans has been central to these efforts. In 1995, Australia became one of the first nations with a national strategy published as the National Youth Suicide Prevention Strategy (NYSPS), which ran from 1995-1999 (31). Other high-income countries soon followed, with the United States developing its first national strategy in 2001 (32), and the United Kingdom in 2012 (33). While there have been many goals and interventions common to different national strategies, the emphasis on particular approaches to suicide prevention may be influenced by the development of new theoretical frameworks, new empirical evidence, as well as health-system and political factors. National level suicide prevention strategies typically include goals and interventions that combine universal, whole of population approaches and interventions targeting high-risk groups, such as clinical populations. (34). Interventions may occur across the spectrum of prevention, including primary prevention, as well as secondary and tertiary prevention measures, such as aftercare and postvention. Whole of population programs include interventions that aim to increase community awareness of suicidality and help-seeking, for example mental health first aid or gatekeeper training (35), or public policy measures, such as those that aim to reduce access to means of suicidal behaviour, by reducing the availability of pharmaceutical medicines or pesticides (36) or monitoring so-called suicide hot spots (37). On the other hand, many population strategies that target sub-groups or settings associated with increased risk of suicide, include school-based programs for children and adolescents, or programs specific to military veterans or rural populations.

Clinical suicide prevention is generally used to refer to interventions that occur within the context of the health system. Historically, the models of suicidal behaviour influential in clinical services have focused on the strong association with mental illness. As a result, clinical services have primarily

focused on treating mental health symptoms, such as depression, as a means of reducing suicidal ideation and behaviour. Criticisms of this approach have highlighted that this trajectory is only one of many possible, and that such an approach may assume a linearity in the association between suicidal ideation and suicide deaths, where planning and episodes of suicidal behaviour are intermediate steps indicating increased intent and lethality (34). Use of structured risk assessment tools became common in many clinical services before concerns became widespread about the limitations of such tools and the potential harms associated with their use to inform clinical decision making, particularly where clinical interventions may involve hospitalization against the individuals will (34). The limitations of risk assessment used in clinical practice are grounded in their low positive predictive value, which is inherent for health outcomes associated with low prevalence, such as suicide deaths. In recent decades, clinical suicide prevention strategies have included a broader range of measures, including use of structured risk assessment tools, brief interventions such as safety planning (38) and means restriction counselling, as well as interventions such as suicide-specific psychotherapies and aftercare following an episode of suicidal crisis. Implementation frameworks, such as the Zero suicide program, have been used to guide clinical services into taking a systematic approach to improving the quality of care for suicidal ideation and behaviours (39).

Australia's current strategy, the National Mental Health and Suicide Prevention Plan, 2007-2022 (40), outlines a whole of government approach, that emphasizes the importance of addressing the social determinants of suicide and increasing community awareness and engagement in suicide prevention. The plan describes a commitment to early intervention by identifying individuals experiencing distress in a broad range of settings, such as community services or workplaces, and supporting access to care. The strategy has been used to direct significant government investment in mental health and suicide prevention in Australia, with total funding said to have increased by 90% since 2012-13 (41).

1.4 Early intervention services and suicide prevention

As with theoretical models of suicidal behaviour, suicide prevention strategies must consider context when applied to specific populations, such as young people accessing mental health services. Over the last two decades, there has been increasing focus on youth-specific mental health services designed to deliver early intervention care with the goal of preventing progression and chronicity of mental illness (42). Early intervention services were initially developed for young people experiencing psychosis and aimed to reduce the development of chronic mental illness and the associated social and functional impairment associated with psychosis (43, 44). Given the success of early intervention for psychosis, the paradigm was then applied to a broader range of mental health presentations and clinical stages. Despite these services being well received by young people, their families or carers and the wider community (45), there has been criticism of the model. Critics have questioned the clinical and cost-effectiveness of early intervention clinical services for young people and suggested

funding should be re-directed to existing public mental health services designed to treat adults with moderate to severe mental illness (46). Regardless of these criticisms, demand for youth mental health services have continued to grow. In Australia, and a number of other high-income countries there has been an increase in presentations of young people with self-harm to hospitals and mental health services (47, 48). The increased demand has contributed to strain on health systems already stretched to capacity by the COVID-19 pandemic, and renewed efforts to develop effective and cost-effective interventions.

The increase in self-harm and suicidal behaviour in young people has occurred despite significant investments in various suicide prevention programs. Such increases are not easily explained by existing theoretical models of suicide, although a number of studies have reported the detrimental impact of the societal disruption of the COVID-19 pandemic on the mental health of young people (49). Perhaps of the bigger question facing health funders and clinical services, is how the existing national and state-level suicide prevention strategies, and the interventions they support, should be applied to prevent or reduce the suicidal behaviour of young people. Of concern, many current strategies, such as Australia's, were developed prior to the paradigm shift towards early intervention mental health care had been realised. Thus, the unique characteristics of these new clinical cohorts were not understood, which may not impact the efficacy of whole of population measures but is a crucial element of effective clinical suicide prevention. This thesis does not aim to summarise or test suicide prevention interventions, but rather consider the limitations of existing methodologies, the opportunities of novel methodological approaches, and the implications for clinical suicide prevention in youth mental health services.

1.5 Aims of this thesis

The overall aim of this thesis was to generate new scientific understanding of suicidal behaviour in young people accessing mental health services, which may be applied in clinical services in order to reduce the impact of suicidal behaviour.

The first aim of this thesis was to assess the utility of key clinical risk factors in predicting suicide deaths. Specifically, the role of suicidal ideation and behaviour, two common risk factors used to direct suicide prevention interventions in clinical services. To achieve this, systematic review and meta-analysis are used to summarise over 70 years of research on the association between suicide death and suicidal ideation or behaviour, as well as potential moderators of effect.

The second aim of this thesis was to explore the application of machine learning modelling to clinical suicide prevention in youth mental health services. To achieve this, a narrative review of initial research in the field synthesises the opportunities and limitations of this novel analytic approach. These insights are then applied to a longitudinal study of young people accessing youth mental health services to assess the performance of predictive modelling using machine learning and consider the utility of such models in clinical services.

The third aim of this thesis was to explore potential biomarkers of suicidal behaviour in young people, specifically cognition, and assess whether cognition remains a useful predictor of suicidal behaviour in the developing brain. The impact of enhanced clinical assessment, which incorporates cognitive testing, on suicide prevention in youth mental health services is then considered.

The final aim of this thesis was to characterise premature mortality risk in young people accessing early intervention youth mental health services, including all-cause and cause-specific (suicide and accident-related), as well as health service use predictors of mortality. In doing so, this aim seeks to identify new directions, or the re-prioritising of existing approaches, which may increase the impact of clinical suicide prevention strategies.

1.6 Methodology

i) Sample and setting

While this thesis primarily focuses on the suicidal behaviour of young people (12-30 years old) accessing mental health services, at times a broader range of ages and settings are included in order to identify characteristics that may differentiate youth clinical cohorts from the wider population.

Chapters that include systematic review and meta-analysis ([Chapter 2](#), [Chapter 3.1](#)) included studies with adults of any age. These studies, as well as [Chapter 4.1](#), also include studies that sampled outside of clinical settings, for example population settings or with the inclusion of healthy controls.

From [Chapter 3.2](#) the thesis narrows to focus exclusively on young people, which includes adolescents (12-18) and young adults (up to the age of 30). [Chapter 5](#) tracks outcomes up to 12 years after a young person's initial presentation to an early intervention youth mental health service, thus outcomes in adults over the age of 30 are described.

[Chapters 3.2](#), [4.2](#) and [5](#) focus on young people accessing early intervention, youth mental health care at the Brain and Mind Centre (BMC) youth clinics in Sydney, Australia. The clinics are primarily based at the Brain and Mind Centre, in Camperdown in central Sydney, with an additional clinic in Campbelltown in South Western Sydney. These clinics include a mix of early intervention, youth mental health services that consist of primary mental health care (*headspace*) as well as more specialised early intervention mental health services, including psychiatrists, psychologists and other allied health professionals. These clinics are accessed by young people aged 12-30 years old with presentations ranging from early clinical stages, characterised by non-specific symptoms, through to full-threshold psychiatric disorders.

Young people accessing the BMC youth clinics were invited to participate in the Brain and Mind Research Register (BPRR), a longitudinal cohort study of 7081 young people presenting to the Brain and Mind Centre's (BMC) youth mental health clinics in the Sydney suburbs between October 2008 and October 2021 (50).

Inclusion criteria of the BPRR cohort study were:

- 1) Age between 12 and 30 years at first presentation to the service
- 2) Attendance of at least one visit to the service.

Exclusion criteria of the BPRR cohort study were:

- 1) Medical instability or lack of capacity to give informed consent (as determined by a psychiatrist)
- 2) History of neurological disease (e.g., tumour, head trauma, epilepsy)
- 3) Medical illness known to impact cognitive and brain function (e.g., cancer, electroconvulsive therapy in last 3 months)
- 4) Clinically evident intellectual disability
- 5) Insufficient English to participate in the research protocol.

The BPRR records basic social and demographic details, as well as the date of first visit. Sub-cohorts of the BPRR contain rich longitudinal clinical assessment (n= 2767) (50) and additional neurocognitive or neurobiological assessments (n=1003) (51). The sampled studied in [Chapter 4.2](#) included 830 young people from the latter cohort who participated in neurocognitive assessment, of which 195 were excluded due to primary diagnosis of schizophrenia spectrum disorder.

[Chapter 3.2](#) studies a cohort of 801 young people drawn from the Sydney BMC youth clinics and two headspace clinics in urban Melbourne. This cohort study, known as the ‘Transitions’ study, was designed to investigate outcomes of common presentations to youth mental health services (52).

In [Chapter 5](#) the entire BPRR cohort (n= 7081) Was linked to three external databases held by the Centre for Health Record Linkage (CHeReL) in New South Wales (NSW), Australia (53, 54). These databases were the Register of Births, Deaths and Marriages (RBDM), the Australian Coordinating Registry (ACR) Cause of Death- Unit Record File (CoD-URF), the Emergency Department Data Collection (EDDC) and the Admitted Patient Data Collection (APDC).

Young people included on the BPRR (n=7081) gave consent for the collection of basic sociodemographic information and to be contacted about future research studies. For young people who participated in BPRR sub-cohorts including the longitudinal study of clinical and neurobiological outcomes and the Transitions study, written informed consent to use of their routinely collected clinical data for research purposes was provided by participants and/or their guardians.

For [Chapter 5](#), which required linking the existing BPRR database to external datasets a waiver of consent was granted by the NSW Population and Health Services Research Ethics Committee (PHSREC) according to the criteria required for a waiver of consent outlined in the National Statement on Ethical Conduct in Human Research (2007). These criteria were (1) that the purposes of the study could not be met without temporary re-identification; (2) contacting participants for reconsent was not practicable, given the large number of participants and that the key outcome of interest was death; and (3) that there was no reason to believe participants would not have consented to the use of their routinely collected data for this study, given they had previously consented to more sensitive information being accessed, such as their individual medical record.

ii) Outcomes of interest

This thesis considers suicidal behaviour and non-suicidal self-harm in clinical populations of young people as occurring along a spectrum of intent and lethality, in keeping with previous definitions by Hawton et al. (55). While suicidal behaviour is the focus of this thesis, non-suicidal self-harm is also included as an outcome of interest in a number of studies. Definitions used in each study are described in detail in the methods section of each study. In general studies where self-harm associated with suicidal intent, and self-harm without suicidal intent, are both a focus of analysis ([Chapter 3.2](#), [Chapter 5](#)) the terms suicidal behaviour (for the former) and non-suicidal self-harm (for the latter) are used. In [Chapter 4.2](#), however, suicidal behaviour was defined as any intentional self-injurious behaviour that may result in serious harm or potentially death. This included behaviours regardless of whether intent to die was present, given the often-ambiguous nature of intent, particularly in young people. Thus, the term is inclusive of behaviours associated with intent to die (suicide attempts) or with no intent to die (often termed deliberate self-harm or non-suicidal self-injury). In review papers, such as [Chapter 4.1](#), the terms and definitions used in the original research studies are used.

Chapter 2: Predictive modelling of suicidal behaviour

2.1 Suicidal ideation as a predictor of completed suicide

McHugh, C.M., Corderoy, A., Ryan, C.J., Hickie, I.B., Large, M.M., 2019. Meta-analysis on sensitivity of suicidal ideation for completed suicide. *British Journal of Psychiatry Open*. 5(2). DOI: [10.1192/bjo.2018.88](https://doi.org/10.1192/bjo.2018.88)

2.1.1 Abstract

Background

The expression of suicidal ideation is considered to be an important warning sign for suicide. However, the predictive properties of suicidal ideation as a test of later suicide are unclear.

Objective

Our objective was to assess the strength of the association between suicidal ideation and later suicide measured by effect size, sensitivity and specificity and positive predictive value.

Method

We located English language studies indexed in PubMed that reported the expression or non-expression of suicidal ideation among people who later died by suicide or did not. A random effects meta-analysis was used to assess the pooled Odds Ratio (OR), Sensitivity, Specificity and Positive Predictive Value (PPV) of suicidal ideation for later suicide among groups of people from psychiatric and non-psychiatric settings.

Results

There was a moderately strong but highly heterogeneous association between suicidal ideation and later suicide ($n=71$, $OR = 3.41$, 95% confidence intervals (CI) $2.59-4.49$; 95% prediction intervals (PI) $= .42 - 28.1$; $I^2 = 89.4$, $Q\text{-value} = 661$, $df(Q) = 70$, $P(Q) = <.001$). Studies conducted in primary care and other non-psychiatric settings had similar pooled odds to studies of current and former psychiatric patients ($OR = 3.86$ versus $OR = 3.23$, $P\text{-value} = .7$). The pooled sensitivity of suicidal ideation for later suicide was 41% (95% CI 35% - 48%) and the pooled specificity was 86% (95% CI 76 % - 92 %) both with high between-study heterogeneity. Studies of suicidal ideation expressed by current and former psychiatric patients had a significantly higher pooled Sensitivity (46% versus 22%) and lower pooled Specificity (81 % versus 96 %) than studies conducted in non-psychiatric settings. The PPV among non-psychiatric cohorts (0.3% 95% CI .1%-.5%) was significantly lower ($Q\text{-value} = 35.6$, $P<.001$) than among psychiatric samples (3.9% 95% CI 2.2%-6.6%).

Conclusions

Estimates of the extent of the association between suicidal ideation and later suicide are limited by unexplained between study heterogeneity. However, the utility of suicidal ideation as a test for later suicide is limited by a modest Sensitivity and low PPV.

Association between suicidal ideation and suicide: meta-analyses of odds ratios, sensitivity, specificity and positive predictive value*

Catherine M. McHugh, Amy Corderoy, Christopher James Ryan, Ian B. Hickie and Matthew Michael Large

Background

The expression of suicidal ideation is considered to be an important warning sign for suicide. However, the predictive properties of suicidal ideation as a test of later suicide are unclear.

Aims

To assess the strength of the association between suicidal ideation and later suicide measured by odds ratio (OR), sensitivity, specificity and positive predictive value (PPV).

Method

We located English-language studies indexed in PubMed that reported the expression or non-expression of suicidal ideation among people who later died by suicide or did not. A random effects meta-analysis was used to assess the pooled OR, sensitivity, specificity and PPV of suicidal ideation for later suicide among groups of people from psychiatric and non-psychiatric settings.

Results

There was a moderately strong but highly heterogeneous association between suicidal ideation and later suicide ($n = 71$, $OR = 3.41$, 95% CI 2.59–4.49, 95% prediction interval 0.42–28.1, $I^2 = 89.4$, Q -value = 661, d.f.(Q) = 70, $P \leq 0.001$). Studies conducted in primary care and other non-psychiatric settings had similar pooled odds to studies of current and former psychiatric patients ($OR = 3.86$ v. $OR = 3.23$, $P = 0.7$). The pooled sensitivity of suicidal ideation for later suicide was 41% (95% CI 35–48) and the pooled specificity was 86% (95% CI 76–92), with high between-study heterogeneity. Studies of suicidal ideation expressed by current and former psychiatric patients had a significantly higher pooled sensitivity (46% v. 22%) and lower pooled specificity (81% v. 96%) than studies conducted in non-psychiatric settings. The PPV among non-psychiatric cohorts (0.3%, 95% CI 0.1%–0.5%) was significantly lower (Q -value = 35.6, $P < 0.001$) than among psychiatric samples (3.9%, 95% CI 2.2–6.6).

Conclusions

Estimates of the extent of the association between suicidal ideation and later suicide are limited by unexplained between-study heterogeneity. The utility of suicidal ideation as a test for later suicide is limited by a modest sensitivity and low PPV.

Declaration interest

M.M.L. and C.J.R. have provided expert evidence in civil, criminal and coronial matters. I.B.H. has been a Commissioner in Australia's National Mental Health Commission since 2012. He is the Co-Director, Health and Policy at the Brain and Mind Centre (BMC) University of Sydney. The BMC operates an early-intervention youth services at Camperdown under contract to Headspace. I.B.H. has previously led community-based and pharmaceutical industry-supported (Wyeth, Eli Lilly, Servier, Pfizer, AstraZeneca) projects focused on the identification and better management of anxiety and depression. He is a Board Member of Psychosis Australia Trust and a member of Veterans Mental Health Clinical Reference group. He was a member of the Medical Advisory Panel for Medibank Private until October 2017. He is the Chief Scientific Advisor to, and an equity shareholder in, InnoWell. InnoWell has been formed by the University of Sydney and PricewaterhouseCoopers to administer the \$30 M Australian Government Funded Project Synergy. Project Synergy is a 3-year programme for the transformation of mental health services through the use of innovative technologies.

Keywords

Suicide; mortality; risk assessment.

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Health professionals are expected to have the skills to assess and manage patients with suicidal thoughts.¹ The presence of thoughts of suicide and the expression of suicidal ideation are signs of significant distress, and all patients who express suicidal ideation require a careful clinical assessment^{2,3} leading to a comprehensive treatment plan.³ In addition, suicidal ideation is sometimes considered to be the most important sign of short-term suicide risk,⁴ and it has been argued that questions about suicidal ideation play a crucial role in suicide screening.^{5,6}

Despite the undoubted clinical importance of suicidal ideation, meta-analysis has only been used recently to estimate the statistical strength of suicidal ideation as a test for later suicide. Several meta-analyses have highlighted the modest strength of the association between suicidal ideation and later suicide^{7–10} and one has

quantified the positive predictive value (PPV).⁸ To date, no meta-analysis has examined the sensitivity and specificity of suicidal ideation for suicide. Knowledge of the sensitivity of suicidal ideation for later suicide is particularly important because screening tests should be sufficiently sensitive, such that a high proportion of affected people screen positive.¹¹ Moreover, existing meta-analyses of the association between suicide and suicidal ideation have been limited to studies with a cohort design,⁹ only included patients with particular diagnoses⁷ or included studies where suicidal ideation was established post-mortem using psychological autopsy methods.⁸

We report a meta-analysis of cohort and case-control studies that examined the presence or absence of expressed suicidal ideation among those who later did or did not die by suicide.

Aims and hypotheses

The first aim of this study was to calculate a comprehensive set of measures of prediction of suicidal ideation for later suicide,

* The article number of this paper has been updated since original publication. A notice detailing the change has also been published at <https://doi.org/10.1192/bjo.2018.88>

including of effect size as measured by the pooled odds ratio (OR), sensitivity, specificity, meta-analytically derived receiver operator curve (ROC) and area under the curve (AUC) and the PPV. The second aim was to explore the extent of, and moderators of, between-study heterogeneity in these predictive measures. We hypothesised that suicidal ideation would be a more sensitive and specific test for suicide in non-psychiatric settings, where patients with suicidal ideation can be expected to have fewer additional and potentially confounding risk factors.

Methods

We conducted a registered meta-analysis (Prospero 42017059236) according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (see supplementary Table 1 available at <https://doi.org/10.1192/bjo.2018.88>).¹²

Searches

Multiple search strategies were initially explored using the databases Medline, Embase and PsycINFO from inception to January 2017. These searches yielded an excessive number of titles when the term 'suicide' was used as a keyword (>200 000) or in the title (>70 000). Moreover, placing limits in the searches using relevant search terms (such as 'ideation' or 'mortality') missed numerous relevant papers that were known to the authors through earlier hand searching. However, PubMed indexed all but one English-language publication located by searches of multiple databases in earlier studies.^{7,8} Therefore, and in order to obtain a large and representative sample of relevant studies, one author (M.M.L.) examined the titles of English-language publications with an accompanying abstract that contained variants of the single term 'suicide' (suicid*) in their title and were published in PubMed from inception to 14 September 2017 and hand searched the references list of relevant review articles.^{7-10,13,14} Two authors (M.M.L. and C.M.M.) winnowed the resulting abstracts and full-text publications (Fig. 1).

Included studies

Studies were included if they reported the expression or non-expression of suicidal ideation among people who later died by suicide or did not, such that all individuals could be classified into the following groups: true positive (those with suicidal ideation and suicide), false positive (those with suicidal ideation but without suicide), false negative (those without suicidal ideation but with suicide) or true negative (those without suicidal ideation or suicide). Studies were included if they provided effect size or other data that was sufficient to enable the calculation of the numbers of people in the true positive, false positive, false negative and true negative categories.

We included studies of patients who had received psychiatric care and people recruited from non-psychiatric settings including primary healthcare, general population samples, military populations and prisons. We excluded studies in which the dependent variable was suicide attempts, or when suicidal ideation was assessed by psychological autopsy methods, when all the controls were deceased or all of the individuals had made suicide attempts. We excluded studies of patients with severe medical illnesses such as malignancies or human immunodeficiency virus.

Definitions of suicide and suicidal ideation

Two authors (M.M.L. and C.M.M.) independently extracted the numbers of individuals with suicidal ideation among those who

had died by suicide and controls and the moderator variables. A third author (A.C.) re-examined the data points. The discrepant points were re-examined by two authors. We accepted the definition of suicidal ideation used in the primary research, acknowledging that the primary research might not have fully reflected differences in the way suicidal ideation was expressed. Studies were coded into four categories according to their definition of suicidal ideation: studies that reported a composite measure of suicidality (inclusive of both suicidal ideation and behaviour); studies that reported suicide plans (including suicide 'threats' as reported in the primary studies); studies that recorded a wish to die; and the majority of studies in which the nature of the suicidal ideation or suicidal thoughts was not specified.

Moderator variables

We collected data about potential moderators of the association between suicidal ideation and suicide; (a) whether the individuals were from psychiatric or non-psychiatric samples; (b) whether the samples consisted of hospital-treated patients; (c) the mean sample age; (d) the duration of follow-up after the assessment for suicidal ideation; (e) whether the study had a cohort or control design; (f) whether patients with suicidal behaviour were regarded as having suicidal ideation; (g) the year of study publication; (h) the proportion of individuals included with suicidal ideation; and (i) the incidence of suicide in the study.

Assessment of strength of reporting

Two researchers (M.M.L. and C.M.M.) independently assessed the reporting strength (and hence the risk of bias) of each primary study's research using a scale with four further moderator variables (scored 0–4) derived from the Newcastle Ottawa Scale.¹⁵ One point was allocated according to each of the following criteria: (a) use of a structured method to assess suicidal ideation; (b) collection of data about suicidal ideation in a method that was masked to the patient's suicide (either by a masking method or by electronic recording at the point of assessment); (c) if all the suicides were defined using a mortality database; and (d) inclusion of open verdicts as suicide. Studies counting open verdicts were rated as having stronger reporting because open verdicts are thought to be similar to suicides in some jurisdictions¹⁶ and because the presence of a history of suicidal ideation might make a coronial verdict of suicide more likely.

Data synthesis

Random effects meta-analysis was chosen *a priori* for all estimates (OR, sensitivity, specificity, PPV) because of the diversity of study populations and the differences in methods used in the primary research. Between-study heterogeneity in effect sizes was examined using I^2 , Q-value statistics and prediction intervals. The possibility of publication bias was assessed using a funnel plot and Egger's regression,¹⁷ and was quantified using Duval & Tweedie's trim and fill method.¹⁸ Subgroup analysis (random effects within subgroups) and random-effects meta-regression (method of moments) were used to explore the extent to which between-study heterogeneity was explained by categorical and continuous variables (including the year of publication and the proportion of all participants with suicidal ideation).

Moderator variables (including strength of reporting score items) that were significantly associated with between-study heterogeneity in sensitivity and specificity at $P \leq 0.05$ were included in multiple meta-regression models. Multiple meta-regression was not used to examine heterogeneity in ORs because of the absence of significant moderator variables. Comprehensive Meta-Analysis

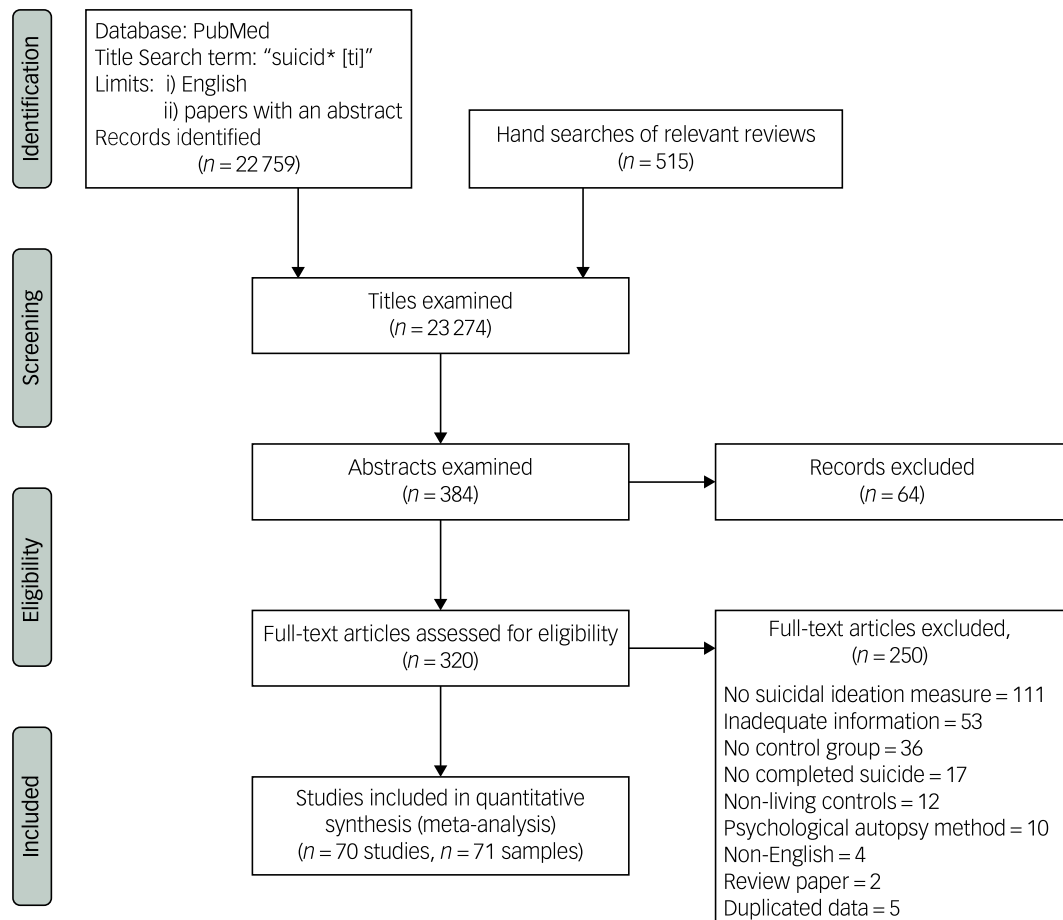


Fig. 1 Flow chart of searches.

(Version 3, Biostat, Englewood NJ) was used for the main analysis and a meta-analytic estimate of the ROC and AUC was calculated using Meta-DiSc.¹⁹

Results

Searches and data extraction

The initial searches yielded 320 potentially relevant papers that were examined in full text. There were 70 papers,^{20–89} reporting 71 studies in which true positive, false positive, false negative and true negative could be ascertained. Eight differences in the effect size in the independent data extraction were resolved by re-examination of the data (Table 1 and see supplementary Table 2 for the data used in meta-analysis).

The earliest study was published in 1961 and the latest in 2017. The median publication date was 2006. In total, 42 studies had a case-control design and 29 were cohort studies. Of the studies, 58 studies were of current or former psychiatric patients including 42 studies of current or former psychiatric in-patients.

In 52 studies suicidal ideation was defined clinically and 19 studies used a structured method. Twelve studies reported a composite measure of suicidality (inclusive of suicide attempts). Four studies reported on suicide plans and two studies recorded a wish to die rather than active suicidal ideation.

The 71 studies included in total of 4 669 303 individuals who had been assessed for suicidal ideation (mean 65 765, median 235) of whom 5 811 died by suicide (mean 81.8, median 49). In total there were 2082 people in the true positive, 125 034 in the

false positive, 3729 in the false negative and 4 538 458 in the true negative groups.

Meta-analyses

Meta-analysis of odds ratios

The pooled OR of suicide associated with suicidal ideation was 3.41 (95% CI 2.59–4.49; 95% prediction interval (PI) 0.42–28.1). There was very marked between-study heterogeneity, I^2 89.4, Q -value = 661, d.f.(Q) = 70, $P < 0.001$. The range of ORs was 0.28 to 81, the first quartile, 2.03, median, 2.96 and the third quartile 6.45 (Fig. 2).

This was associated with a meta-analytic AUC of 0.676 (s.e. = 0.021) (Fig. 3). The funnel plot appeared symmetrical (Fig. 4) but an Egger's regression was borderline significant (intercept 1.55, t -value = 2.07, d.f. = 69, $P = 0.04$). Duval & Tweedie's trim and fill did not identify any hypothetically missing studies.

Structured methods to assess suicidal ideation were associated with a non-significantly lower OR (OR = 2.38, 95% CI 1.14–4.99) than clinically defined suicidal ideation (OR = 3.72, 95% CI 2.96–4.67, Q -value = 1.28, d.f.(Q) = 1, $P = 0.26$). There was no evidence that studies that reported on a composite measure of suicidality spanning suicidal behaviour and suicidal ideation (OR = 3.09, 95% CI 2.02–4.72) differed from studies that simply reported on suicidal ideation (OR = 3.54, 95% CI 2.57–4.88, $Q = 0.26$, d.f.(Q) = 1, $P = 0.61$). Suicide plans were more strongly associated with suicide (four studies, OR = 8.51, 95% CI 5.51–13.06) than studies that reported a wish to die (two studies, OR = 3.01, 95% CI 1.49–6.06) and studies that did not specify the degree of intent or planning (65 studies, OR = 3.2, 95% CI 2.41–4.29, Q -value = 14.6, d.f.(Q) = 2, $P = 0.001$).

Table 1 Included studies

Study	Individuals included in the study	Measure of suicidal ideation	Measure of suicide	Odds ratio (95% CI)
Allebeck <i>et al</i> (1987) ³⁰	32 former in-patients with schizophrenia and 64 matched controls	Clinical definition in the medical records	Suicides and open verdicts obtained from a mortality register	2.34 (0.96–5.73)
Al-Sayegh <i>et al</i> (2015) ²¹	13 suicides among a cohort of 6293 members of the general population	Structured interview for suicidal thoughts and behaviours	Suicides and open verdicts obtained from a mortality register	2.10 (0.65–6.83)
Appleby <i>et al</i> (1999) ²²	149 discharged mental health patients and 149 matched controls	Clinical definition in the medical records	Suicides and open verdicts obtained from a mortality register	2.42 (1.52–3.87)
Baader-Matthaei <i>et al</i> (2004) ²³	32 mental health patients and 32 matched controls	Clinical definition in the medical records	Mortality register	3.82 (1.24–11.80)
Beck <i>et al</i> (1999) ²⁴	30 suicides among a cohort of 3701 mental health out-patients	Scale for suicide ideation	Mortality register	13.84 (5.64–33.98)
Beisser & Blanchette (1961) ²⁵	71 current mental health in-patients and 71 matched controls	Suicide threats documented in the medical records	Clinically defined	5.61 (2.54–12.41)
Berg (2010) ²⁶	3 suicides among 20 patients who had received electroconvulsive therapy	Clinical definition in the medical records	Mortality register	1.63 (0.11–22.98)
Bertelsen <i>et al</i> (2007) ²⁷	7 suicides among a cohort of 547 people with first-episode psychosis	Items in the Clinical Assessment in Neuropsychiatry instrument	Mortality register	0.55 (0.07–4.59)
Bickley <i>et al</i> (2013) ²⁸	100 recently discharged mental health patients and 100 matched controls	Retrospectively assessed by treating clinicians	Suicides and open verdicts obtained from a mortality register	2.03 (0.82–5.03)
Blumenthal <i>et al</i> (1989) ²⁹	12 former mental health in-patients and 12 matched controls	Suicide ideation or behaviours assessed with the Present State Examination	Clinically defined	0.50 (0.10–2.60)
Borg & Stahl (1982) ³⁰	34 first assessed mental health patients and 34 matched controls	Passive suicide ideation determined in a semi-structured interview	Suicides and open verdicts obtained from a mortality register	3.18 (0.76–13.13)
Bradvik & Bergland (1993) ³¹	89 melancholically depressed former in-patients and 89 matched controls	Clinical definition in the medical records	Mortality register	1.30 (0.64–2.63)
Cheng <i>et al</i> (1990) ³²	55 people with schizophrenia and 52 matched controls	Suicide ideation and behaviours documented in the medical records	Clinically defined	8.52 (1.04–70.07)
Conlon <i>et al</i> (2007) ³³	39 mental health patients and 39 matched controls	Suicide ideation documented in the medical records	Identified by a coronial investigator	1.91 (0.51–7.16)
Coryell & Young (2005) ³⁴	33 suicides among a cohort of 782 patients with a depressive disorder	Schedule for Affective Disorder item 246 > 2	Mortality register	2.84 (0.99–8.19)
Coryell <i>et al</i> (2016) ³⁵	7 suicides among a cohort of 1748 patients with bipolar disorder	Suicidal ideation using the Schedule for Affective Disorder	Clinical with missing individuals assessed with a mortality register	0.63 (0.13–3.11)
Coryell <i>et al</i> (2016) ³⁵	12 suicides among a cohort of 288 patients with bipolar disorder	Suicidal ideation using the Schedule for Affective Disorder	Clinical with missing individuals assessed with a mortality register	2.21 (0.68–7.15)
Crandall <i>et al</i> (2006) ³⁶	449 suicides among a cohort of 218 304 people attending an emergency department	Suicidal ideation documented in the medical records	Mortality register	6.45 (4.81–8.64)
De Hert <i>et al</i> (2001) ³⁷	63 formerly in-patients with schizophrenia and 63 matched controls	Suicidal threats documented in the medical records	Clinically defined	7.92 (3.51–17.89)
Didham <i>et al</i> (2006) ³⁸	221 suicides among primary care patients and 663 matched controls	Suicidal ideation documented in the medical records	Mortality register	17.31 (3.81–78.73)
Dingman & McGlashen (1986) ³⁹	38 suicides among a cohort of 451 former in-patients	Suicide threat and behaviours documented in the medical records	Clinically defined	2.95 (1.32–6.60)
Dobscha <i>et al</i> (2014) ⁴⁰	261 veterans treated in primary care and 522 matched controls	Suicide ideation and behaviours documented in the medical records	Mortality register	7.35 (4.45–12.14)
Dong <i>et al</i> (2005) ⁴¹	92 in-patient suicides and 92 matched controls	Suicidal ideation documented in the medical records	Suicides and open verdicts obtained from a mortality register	4.68 (2.32–9.44)
Drake <i>et al</i> (1986) ⁴²	15 suicides among a cohort of 104 former in-patients with schizophrenia	Suicidal ideation documented in the medical records	Clinically defined	8.33 (1.77–39.12)
Dutta <i>et al</i> (2007) ⁴³	8 suicides among a cohort of 239 former in-patients with bipolar disorder	Suicidal ideation documented in the medical records	Suicides and open verdicts obtained from a mortality register	2.92 (0.15–58.74)
Farberow <i>et al</i> (1966) ⁴⁴	218 mental health in-patient suicides and 220 in-patient controls	Suicidal threats documented in the medical records	Clinically defined	7.03 (4.10–12.07)

(Continued)

Table 1 (Continued)

Study	Individuals included in the study	Measure of suicidal ideation	Measure of suicide	Odds ratio (95% CI)
Fernando & Storm (1984) ⁴⁵	22 current or former mental health in-patients and 22 matched controls	Suicidal ideation documented in the medical records	Clinically defined	6.40 (1.65–24.77)
Flood & Seager (1968) ⁴⁶	73 former mental health in-patients and 70 matched controls	Suicidal ideation documented in the medical records	Mortality register	0.43 (0.19–0.95)
Fosse <i>et al</i> (2017) ⁴⁷	36 former mental health in-patients and 120 matched controls	Suicidal ideation item on the Suicide Risk Check List	Mortality register	2.63 (1.20–5.74)
Fowler <i>et al</i> (1979) ⁴⁸	15 suicides among a cohort of 225 patients with unipolar depression	Suicidal ideation documented in the medical records	Clinically defined	13.41 (0.79–227.6)
Fruehwald <i>et al</i> (2004) ⁴⁹	220 suicides of prisoners and 440 matched controls	Suicidal threats documented in custodial records	Mortality register	14.86 (8.15–27.08)
Funahashi <i>et al</i> (2000) ⁵⁰	80 people with schizophrenia and 80 matched controls	Suicidal ideation documented in the medical records	Clinically defined	81.0 (18.45–355.6)
Goldstein <i>et al</i> (1991) ⁵¹	46 suicides among a cohort of 1906 former in-patients with affective disorder	Suicidal ideation documented in the medical records	Mortality register	2.96 (1.63–5.36)
Green <i>et al</i> (2015) ⁵²	43 suicides among a cohort of 5200 mental health out-patients	Beck Depression Inventory suicide item >1	Mortality register	5.14 (2.62–10.10)
Hoyer <i>et al</i> (2009) ⁵³	135 current and former mental health in-patients and 135 matched controls	Suicidal ideation documented in the medical records	Mortality register	1.48 (0.91–2.40)
Hunt <i>et al</i> (2007) ⁵⁴	222 current mental health in-patients and 222 controls	Retrospectively assessed by treating clinicians	Suicides and open verdicts obtained from a mortality register	1.70 (0.94–3.08)
Hunt <i>et al</i> (2013) ⁵⁵	107 recently admitted mental health patients and 107 controls	Retrospectively assessed by treating clinicians	Suicides and open verdicts obtained from a mortality register	1.56 (0.73–3.35)
Hunt <i>et al</i> (2009) ⁵⁶	238 recently discharged mental health patients and 238 controls	Retrospectively assessed by treating clinicians	Suicides and open verdicts obtained from a mortality register	2.31 (1.24–4.32)
Hynan <i>et al</i> (2012) ⁵⁷	24 suicides among a cohort of 4 070 167 military personnel	Systematically collected department of defence data	Mortality register	10.45 (6.92–15.79)
Kan <i>et al</i> (2007) ⁵⁸	97 recently discharged mental health in-patients and 97 matched controls	Suicidal ideation documented in the medical records	Suicides and open verdicts obtained from a mortality register	1.88 (1.04–3.41)
Kessler <i>et al</i> (2015) ⁵⁹	68 suicides among a cohort of 316 686 veterans who were former in-patients	Systematically collected department of defence data	Mortality register	2.23 (1.07–4.68)
Khang <i>et al</i> (2010) ⁶⁰	13 suicides among a cohort of 5414 members of the general population	Suicide ideation item in a national health survey	Mortality register	2.58 (0.87–7.70)
Khanra <i>et al</i> (2016) ⁶¹	10 current mental health in-patients and 50 matched controls	Suicidal ideation documented in the medical records	Clinically defined	6.71 (1.12–40.07)
Kim <i>et al</i> (2012) ⁶²	324 depressed veterans and 312 matched controls	Suicide ideation and behaviours documented in the medical records	Mortality register	5.80 (3.86–8.71)
Kjelsberg <i>et al</i> (1994) ⁶³	35 former adolescent mental health in-patients and 35 matched controls	Suicidal ideation documented in the medical records	Mortality register	3.00 (1.03–8.70)
Kleiman & Liu (2014) ⁶⁴	25 suicides among a cohort of 19 989 members of the general population	Suicide ideation item in a national health survey	Mortality register	2.82 (0.97–8.22)
Li <i>et al</i> (2008) ⁶⁵	64 in-patients with schizophrenia and 64 matched controls	Suicidal ideation documented in the medical records	Clinically defined	31.0 (6.98–137.7)
Lin <i>et al</i> (2014) ⁶⁶	41 current mental health in-patients and 164 controls	Suicidal ideation documented in the medical records	Mortality register	3.44 (1.65–7.17)
Lopez-Morinigo <i>et al</i> (2016) ⁶⁷	71 people with schizophrenia and 355 controls	Suicide ideation item in a semi-structured risk assessment	Suicides and open verdicts obtained from a mortality register	3.57 (1.41–9.07)
Louzon <i>et al</i> (2016) ⁶⁸	310 suicides among a cohort of 391 492 veterans	Item 9 of the Patient Health Questionnaire	Mortality register	0.28 (0.22–0.36)
Lukaschek <i>et al</i> (2014) ⁶⁹	101 former mental health in-patients and 101 matched controls	Suicidal ideas and behaviours documented in the medical records	Railway suicides obtained using a mortality register	1.80 (0.97–3.34)
McEwan <i>et al</i> (2010) ⁷⁰	3 suicides among a cohort of 138 stalkers	Suicidal ideation documented in the medical records	Clinically defined	4.69 (0.40–55.34)
Mock <i>et al</i> (1996) ⁷¹	21 suicides in primary care and 63 matched controls	Suicidal ideation documented in the medical records	Mortality register	3.00 (0.18–50.10)
Motto & Bostrom (1990) ⁷²	38 suicides among a cohort of 2999 recently admitted mental health patients	Moderate or severe suicidal ideation items from semi-structured interview	Clinically defined	3.96 (1.87–8.39)

(Continued)

Table 1 (Continued)

Study	Individuals included in the study	Measure of suicidal ideation	Measure of suicide	Odds ratio (95% CI)
Murphy <i>et al</i> (1990) ⁷³	67 patients with alcoholism and 106 controls	Suicidal ideation documented in medical records or survey results	Clinically defined	12.93 (6.15–27.22)
Park <i>et al</i> (2017) ⁷⁴	96 suicides among a cohort of 8403 recently discharged mental health patients	Suicidal ideation documented in the medical records	Mortality register	2.80 (1.86–4.21)
Powell <i>et al</i> (2000) ⁷⁵	112 current mental health in-patients and 112 controls	Suicidal ideation documented in the medical records	Suicides and open verdicts obtained from a mortality register	9.94 (5.08–19.45)
Roy (1982) ⁷⁶	30 people with schizophrenia and 30 controls	Suicidal ideation documented in the medical records	Clinically defined	3.17 (0.75–13.51)
Salama (1988) ⁷⁷	5 suicides among a cohort of 139 current in-patients with schizophrenia	Suicidal ideation documented in the medical records	Clinically defined	23.94 (1.29–422.9)
Sani <i>et al</i> (2011) ⁷⁸	96 former mental health in-patients and 192 matched controls	Suicidal ideation documented in the medical records	Clinically defined	2.14 (1.24–3.69)
Shah & Ganesvaran (1997) ⁷⁹	60 current or recently discharged suicides and 60 matched controls	Suicidal ideation documented in the medical records	Clinically defined	2.31 (1.10–4.85)
Sharma <i>et al</i> (1998) ⁸⁰	44 current mental health in-patients and 44 matched controls	Suicidal ideation documented in the medical records	Clinically defined	3.40 (1.41–8.19)
Simon <i>et al</i> (2013) ⁸¹	46 suicides among a cohort of 84 414 mental health out-patients	Suicidal ideation documented in the medical records	Suicides and open verdicts obtained from a mortality register	7.98 (4.47–14.27)
Sinclair <i>et al</i> (2005) ⁸²	127 current or recently discharged patients with depression and 195 matched controls	Suicidal ideation documented in the medical records	Suicides and open verdicts obtained from a mortality register	1.89 (1.18–3.03)
Sinclair <i>et al</i> (2004) ⁸³	51 current or recently discharged patients with schizophrenia and 82 matched controls	Suicidal ideation documented in the medical records	Suicides and open verdicts obtained from a mortality register	2.88 (1.29–6.47)
Spiesl <i>et al</i> (2002) ⁸⁴	30 suicides among a cohort of 21 062 mental health in-patients	Suicidal ideation documented in the medical records	Clinically defined	0.98 (0.45–2.14)
Stephens <i>et al</i> (1999) ⁸⁵	28 suicides among a cohort of 1212 in-patients with schizophrenia	Suicidal ideation documented in the medical records	Clinically defined	5.54 (2.60–11.82)
Thong <i>et al</i> (2008) ⁸⁶	123 mental health patients and 123 matched controls	Suicidal ideation documented in the medical records	Mortality register	7.99 (3.41–18.70)
Weiser <i>et al</i> (2016) ⁸⁷	54 suicides among a cohort of 89 049 young men receiving primary mental healthcare	Suicidal ideation and behaviour documented in the medical records	Mortality register	1.64 (0.88–3.06)
Werbeloff <i>et al</i> (2016) ⁸⁸	8 suicides among a birth cohort of 4914	Suicidal ideation item on a research questionnaire	Mortality register	1.64 (0.20–13.38)
Yim <i>et al</i> (2004) ⁸⁹	73 recently discharged mental health in-patients and 73 matched controls	Suicidal ideation and behaviour documented in the medical records	Mortality register	2.81 (1.39–5.68)

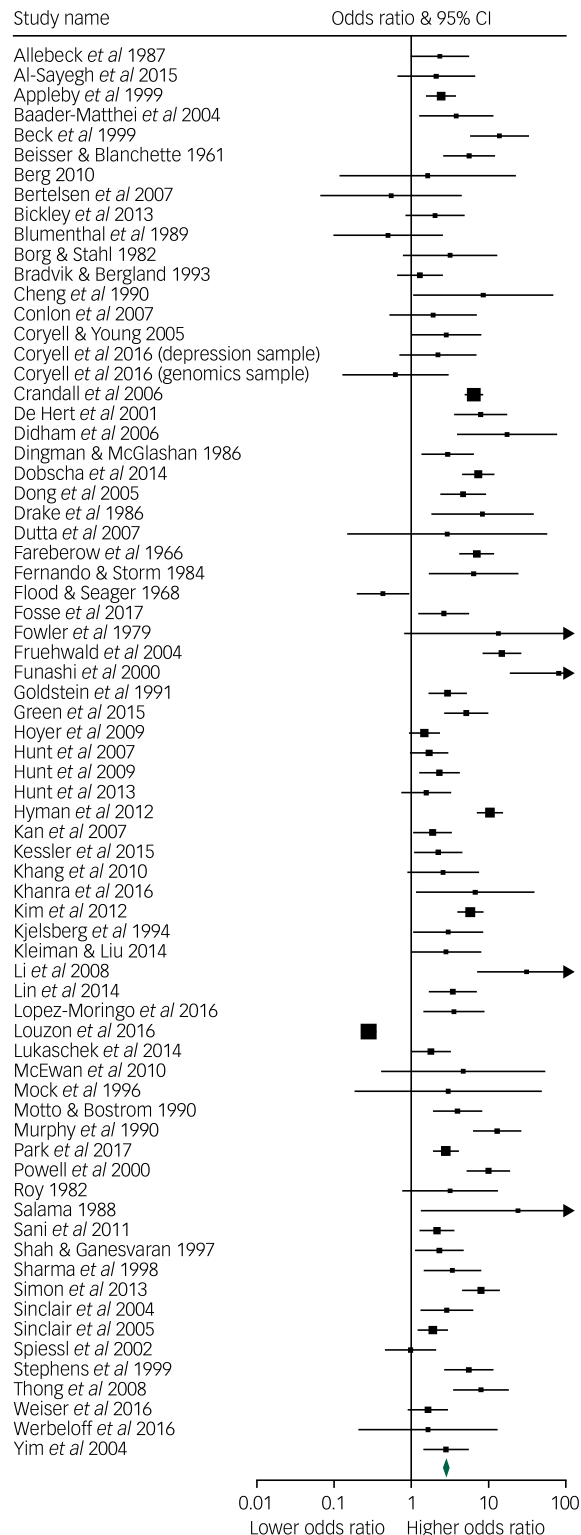


Fig. 2 Forest plot of the odds of the association between suicidal ideation and suicide.

Studies that were considered to have stronger reporting on the basis of a total strength of reporting score of ≥ 2 had a non-significantly weaker association (Q -value = 3.58, $d.f.(Q) = 1$, $P = 0.06$) between suicidal ideation and later suicide ($n = 37$, $OR = 2.70$, $95\% CI 1.81$ – 4.01) than studies with a strength of reporting score of < 2 ($n = 34$, $OR = 4.41$, $95\% CI 3.20$ – 6.08).

Between-study heterogeneity was not significantly explained by any of our predetermined moderator variables (Table 2). Studies of

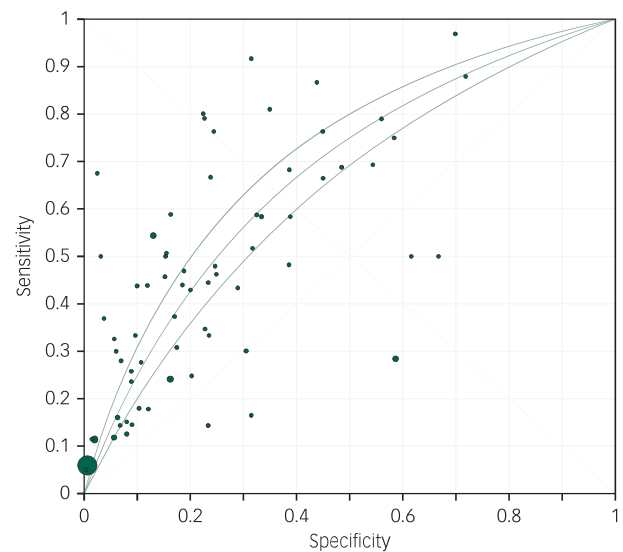


Fig. 3 Meta-analytic area under the curve.

non-psychiatric samples ($n = 13$, $OR = 3.86$, $95\% CI 2.67$ – 3.97) had similar ORs to studies of psychiatric patients ($n = 58$, $OR = 3.23$, $95\% CI 2.64$ – 3.96 ; Q -value = 0.119, $d.f.(Q) = 1$, $P = 0.7$). The main result and the analyses of moderators were not sensitive to the exclusion of two non-psychiatric studies with very large sample sizes that when combined included over 90% of individuals and 3.5% of the study weight in the random-effects meta-analysis.^{36,57}

Meta-analysis of sensitivity

The pooled sensitivity of suicidal ideation for suicide was 41% ($95\% CI 35$ – 48). There was very high between-study heterogeneity, $I^2 = 93.2$, Q -value = 1033, $d.f.(Q) = 70$, $P \leq 0.001$. The sensitivity ranged from 0 to 97%, first quartile 25%, median 44% and the third quartile 67%. An Egger's regression was non-significant (intercept 0.60, t -value = 0.61, $d.f. = 69$, $P = 0.54$).

Studies of non-psychiatric populations had a significantly lower sensitivity ($n = 13$, sensitivity 22%, $95\% CI 13$ – 53) than studies among psychiatric patients ($n = 58$, sensitivity 46%, $95\% CI 40$ – 52 ; Q -value = 10.6, $d.f.(Q) = 1$, $P = 0.001$). This result was not sensitive to the exclusion of the two non-psychiatric studies with very large sample sizes.

Use of a mortality database and more recent publication were associated with a lower sensitivity. Sensitivity was increased among studies of patients in hospital and in studies with a higher proportion of individuals with suicidal ideation (Table 3). The proportion of people with suicidal ideation was the only factor that was independently associated with between-study heterogeneity in a multiple meta-regression (supplementary Table 3). The multiple meta-regression model suggested that the proportion of people with suicidal ideation was the only independent moderator and explained 58% of the between-study heterogeneity in sensitivity.

Meta-analysis of specificity

The pooled specificity of suicidal ideation for later suicide was 86% ($95\% CI 76$ – 92). There was very high between-study heterogeneity, $I^2 = 99.9$, Q -value > 10 000, $d.f.(Q) = 70$, $P \leq 0.001$. The specificity ranged from 28 to 100%, first quartile 69%, median 83% and the third quartile 93%. An Egger's regression was non-significant (intercept -7.27 t -value = 0.74, $d.f. = 69$, $P = 0.46$).

Studies of non-psychiatric populations had a higher specificity ($n = 13$, specificity 96%, $95\% CI 84$ – 99) than studies of psychiatric

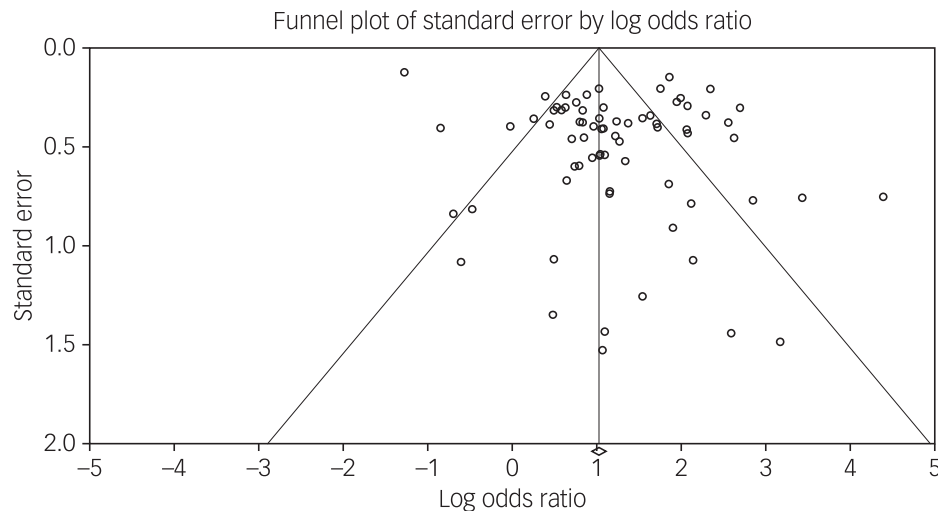


Fig. 4 Funnel plot of the odds of the association between suicidal ideation and suicide.

Table 2 Meta-regression of moderators of the odds ratio of suicidal ideation for later suicide

Variable	Coefficient	Standard error	Lower limit	Upper limit	Z-value	P
Non-psychiatric samples	0.16	0.37	-0.56	0.87	0.43	0.66
Hospital treated	-0.32	0.29	-0.89	0.25	-1.11	0.26
Mean sample age ^a	-0.41	0.26	-0.92	0.09	-1.62	0.1
Follow-up period ^b	-0.008	0.02	-0.04	0.03	-0.47	0.64
Structured method for suicidal ideation	-0.44	0.29	-1.01	0.14	-1.49	0.14
Use of a mortality database	-0.47	0.30	-1.06	1.22	-1.55	0.12
Cohort study	-0.28	0.29	-0.84	0.28	-0.96	0.34
Included suicide behaviour in the definition	-0.18	0.37	-0.90	0.53	-0.50	0.61
Included open verdicts	-0.18	0.31	-0.80	0.43	-0.59	0.55
Masking of the researchers to suicide	-0.23	0.28	-0.78	0.33	-0.81	0.42
Year of publication	-0.008	0.01	-0.03	0.01	-0.80	0.42
Proportion of individuals with suicidal ideation	-0.94	0.67	-2.25	0.37	-1.40	0.16
Incidence of suicide	0.26	0.51	-0.75	10.27	0.51	0.61

a. 58 studies in the analysis.

b. 68 studies included in the analysis.

Table 3 Meta-regression of moderators of the sensitivity of suicidal ideation for later suicide

Variable	Coefficient	Standard error	Lower limit	Upper limit	Z-value	P
Non-psychiatric samples	-1.11	0.31	-1.71	-0.49	-3.55	<0.001
Hospital treated	0.69	0.26	0.19	1.19	2.70	0.007
Mean age ^a	0.14	0.31	-0.48	0.76	0.44	0.66
Follow-up period ^b	-0.02	0.02	-0.02	0.06	0.96	0.34
Structured method for suicidal ideation	-0.09	0.29	-0.67	0.49	-0.30	0.76
Use of a mortality database	-1.01	0.26	-1.51	-0.49	-3.85	<0.001
Cohort study	0.07	0.26	-0.44	0.59	0.28	0.78
Included suicide behaviour in the definition	0.43	0.33	-0.22	1.08	1.29	0.20
Included open verdicts	-0.09	0.29	-0.64	0.48	-0.30	0.77
Masking of the researchers to suicide outcomes	-0.11	0.26	-0.62	0.39	0.44	0.66
Year of publication	-0.02	0.01	-0.04	-0.003	-2.26	0.02
Proportion of individuals with suicidal ideation	5.10	0.50	4.12	6.09	10.1	<0.001
Study incidence of suicide	0.19	0.64	-1.06	1.45	0.3	0.76

a. 58 studies included in the analysis.

b. 68 studies in the analysis.

populations ($n = 58$, specificity 81%, 95% CI 76–85, Q -value = 4.78, $d.f.(Q) = 1$, $P = 0.03$). This result was not sensitive to the exclusion of the non-psychiatric studies with very large sample sizes.

Suicidal ideation was a less specific indicator of suicide among studies with a high proportion of people with suicidal ideation and among samples of hospital-treated patients. A multivariate model found that hospital treatment and the proportion of people with suicidal ideation in the study population were significant

variables, explaining 79% of the between-study heterogeneity in specificity. (Table 4 and supplementary Table 4).

Meta-analysis of PPV

The pooled PPV for suicidal ideation as a test for later suicide among the 29 cohort studies was 1.7% (95% CI 0.9–3.2) over an average duration of follow-up of 9.1 years. There was very

Table 4 Meta-regression tests of potential moderators of the specificity of suicidal ideation for later suicide

Variable	Coefficient	Standard error	Lower limit	Upper limit	Z-value	P
Non-psychiatric samples	1.65	0.79	0.10	3.20	2.09	0.04
Hospital treated	-1.67	0.62	-2.88	-0.45	-2.69	0.007
Mean sample age ^a	-0.50	0.37	-1.23	0.23	-1.34	0.18
Follow-up period ^b	-0.003	0.03	-0.06	0.06	-0.10	0.92
Structured method for suicidal ideation	0.34	0.53	-0.69	1.39	0.65	0.61
Use of a mortality database	0.37	0.64	-0.89	1.62	0.57	0.57
Cohort study	0.09	0.60	-1.09	1.27	0.15	0.88
Included suicide behaviour in the definition	-0.97	0.87	-2.68	0.74	-1.11	0.26
Included open verdicts	0.05	0.67	-1.25	1.36	-0.08	0.93
Masking of the researchers to suicide outcomes	0.27	0.60	-0.91	1.45	0.46	0.64
Year of publication	0.03	0.02	-0.01	0.08	1.52	0.12
Proportion of individuals with suicidal ideation	-5.73	0.75	-7.21	-4.26	-7.64	<0.001
Study incidence of suicide	-1.05	0.87	-2.80	0.64	-1.23	0.22

a. 58 studies in the analysis.

b. 68 studies included in the analysis.

high between-study heterogeneity, $I^2 = 97.9$, Q -value = 1186, d.f.(Q) = 28, $P \leq 0.001$. An Egger's regression was non-significant (intercept 2.81, t -value = 1.13, d.f. = 27, $P = 0.27$). The PPV among nine non-psychiatric cohorts (0.3% 95% CI 0.1–0.5) was significantly lower (Q -value = 35.6, d.f.(Q) = 1, $P < 0.001$) than among psychiatric samples (3.9% 95% CI 2.2–6.6).

Discussion

Main findings

Clinicians sometimes rely on suicidal ideation as a crucial test for short-term suicide risk,⁴ and it has been argued that asking about suicidal ideation could form part of a screening test for later suicide.^{5,6} Our finding of a pooled OR of suicide associated with suicidal ideation of 3.41 and the meta-analytic AUC of 0.676 indicate a statistical association between suicidal ideation and later suicide with moderate strength.⁹⁰ However, this should be interpreted very cautiously because of the very high and largely unexplained heterogeneity between studies. Moreover, the low PPV of suicidal ideation for suicide, which flows from the low incidence of suicide outcomes, even among psychiatric cohorts, highlights the limitations of suicidal ideation as a practical test of future suicide.

We had hypothesised that suicidal ideation would be a more sensitive and specific test for suicide in non-psychiatric settings, where patients with suicidal ideation might have fewer other risk factors. We found no evidence that suicidal ideation is more strongly associated with suicide in non-psychiatric settings than in psychiatric settings. Contrary to our hypothesis we found that suicide ideation was a less sensitive test for later suicide in non-psychiatric settings, and that the prevalence of suicidal ideation is associated with the sensitivity for later suicide.

Our results can be compared with those of recent meta-analyses of the psychometric properties of suicide risk scales^{91,92} and multivariate models of suicide risk,⁹³ which found similar odds of suicide, sensitivity, specificity and PPV among studies conducted in psychiatric settings as well as similar between-study heterogeneity despite examining quite different study sets. Collectively, these studies highlight a high degree of uncertainty about the statistical strength of commonly used approaches to suicide risk assessment.

The current paper advances knowledge of the association between suicidal ideation and suicide by reporting the pooled sensitivity and specificity of suicidal ideation for suicide. The main finding is the limited sensitivity of suicidal ideation for suicide, such that approximately 60% of people who go on to die by suicide have not expressed suicidal ideation at a specified earlier

time. In contrast, the non-expression of suicidal ideation is fairly specific to not dying by suicide in the study period, with only 14% of those not dying by suicide expressing suicidal ideation.

Implications

Knowledge of the sensitivity and specificity of suicidal ideation for suicide is important because any given OR can be achieved with differing trade-offs between sensitivity and specificity. In this study we found firm evidence that such trade-offs differ between studies, in part as a result of the proportion of individuals expressing suicidal ideation. The proportion of people with suicidal ideation was strongly associated with sensitivity and was inversely associated with specificity, such that similar odds of suicide were found in populations with higher rates of suicidal ideation (i.e. psychiatric patients) and lower rates of suicidal ideation (i.e. non-psychiatric populations).

In general, screening tests should be sensitive enough to capture most cases.¹¹ Our study suggests that suicidal ideation is not sensitive enough to be very helpful as a stand-alone screening test for suicide in psychiatric or non-psychiatric settings, a limitation that is compounded by the modest specificity. Clinicians should not assume that patients experiencing mental distress without suicidal ideation are not at elevated risk of suicide. It is notable that our subgroup analysis of non-psychiatric settings found that nearly 80% of people who later die by suicide had not expressed suicidal ideation. Conversely suicidal ideation is somewhat specific to suicide, particularly in settings where the prevalence of suicidal ideation is low. In this sense, the presence of suicidal ideation conveys more salient information about later suicide than the absence of suicidal ideation.

The finding that the proportion of individuals with suicidal ideation was strongly associated with sensitivity and inversely associated with specificity requires some consideration. To some extent this result is a logical consequence of the definition of sensitivity as the proportion of all cases detected – hypothetically, an extremely sensitive test that included the slightest degree of suicidal ideation would likely select almost the entire population and would approach a 100% sensitivity. Although variation in the threshold test for suicidal ideation might have contributed to variation in the prevalence of suicidal ideation between studies in non-extreme examples with typical rates of suicidal ideation, a very wide variation in the proportion of people with suicidal ideation can be associated with a wide variation of sensitivities.

In addition to highlighting uncertainty in the strength of the association between suicidal ideation and suicide, this study highlights an important clinical dilemma about the trade-off between

sensitivity and specificity. Although detailed questioning about suicidal ideation is often indicated, for example when there is suspicion of a suicide plan, and such questioning might bring about a greater sensitivity, it might be associated with a higher false positive rate than less detailed questioning.

Limitations

In addition to the main limitation posed by the extent of between-study heterogeneity, this meta-analysis has a number of other limitations. In most studies there was a lack of clarity about how suicidal ideation was determined and defined. However, this limitation might not have had very much impact on our results because we found little evidence that structured methods of assessing suicidal ideation predicted suicide more accurately than clinical methods. Although it is logical that there may be important threshold issues on the spectrum of severity of suicidal ideation – a possibility supported by our finding of an association between the rate of suicidal ideation and the sensitivity of suicidal ideation for later suicide – there were too few studies that reported different points on the spectrum of ideation to properly explore threshold issues. Another limitation is that we lacked any data about how factors such as gender, comorbid conditions and wider cultural factors might affect the association between suicidal ideation and suicide.

Our results should also be interpreted in light of the knowledge that suicidal ideation can fluctuate over short periods of time.⁹⁴ The primary studies we included measured suicidal ideation at the beginning of a follow-up period, often a follow-up of years. In cases of individuals who died by suicide without earlier suicidal ideation it is likely that suicidal ideation emerged closer to the time of the suicide. It remains to be seen if real time or more temporally proximal measures of suicidal ideation will be more strongly associated with later suicide.⁹⁵

In conclusion, enquiring about suicidal ideation will always be a central skill for mental health professionals, not because suicidal ideation is a meaningful forecast of suicide but because patients who express suicidal ideation are making important communications about their inner world and level of psychological distress. However, clinicians should be aware of the statistical limitations of ideation as a screening tool, and not be lured into either a false confidence generated by an absence of ideation, or determinism about the likelihood of suicide if it is present.

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Supplementary material

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2.2 Suicidal behaviour as a predictor of completed suicide

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2.2.1 Abstract

Objective

Suicidal ideation and suicidal behaviour are both regarded as important risk factors for suicide, but it is usually believed that suicidal ideation is less strongly linked to suicide than suicidal behaviours. In this study, we assessed and compared the strengths of the associations that suicidal ideation and suicidal behaviour have with later suicide using meta-analysis of primary studies reporting both these independent variables and the dependent variable of suicide.

Methods

A total of 51 English language publications describing cohort or controlled studies that reported on both the association between suicidal ideation and suicide and the association between suicidal behaviours and suicide were located using searches for titles in PubMed containing variants of the word suicide (suicid*). Suicides were considered to include reported suicides and open verdicts from mortality registers. The strengths of the two associations were examined in separate random effects meta-analyses and were then compared using mixed effects meta-regression. Subgroups were examined according to study characteristics including the definitions of suicidal ideation or behaviour used, setting (psychiatric or non-psychiatric), diagnostic mix of the study population, study design (cohort or control) and study quality.

Results

Suicidal ideation (odds ratio = 3.11, 95% confidence interval = 2.51, 3.86) and suicidal behaviours (odds ratio = 4.09, 95% confidence interval = 3.05, 5.49) were both significantly associated with suicide but there was no significant difference in the strengths of association ($p = 0.14$). Nor were there significant differences in the strengths of the two associations in multiple subgroup analyses.

Conclusion

Suicidal ideation and suicidal behaviour are both moderately associated with suicide. Existing data cannot conclusively demonstrate that suicidal behaviours are more strongly associated with suicide than suicidal ideation. Clinicians should not strongly prioritise suicidal behaviour over suicidal ideation when considering suicide risk.

Is suicidal behaviour a stronger predictor of later suicide than suicidal ideation? A systematic review and meta-analysis

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Abstract

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Keywords

Suicide, suicidal behaviour, suicidal ideation, prediction, suicide risk

Introduction

Previous suicidal behaviour is often regarded as a key risk factor and warning sign for later suicide (Berman, 2018; Bostwick et al., 2016; Gunnell and Lewis, 2005; Smith et al., 2013). A World Health Organization (WHO, 2018) fact-sheet states that ‘a prior suicide attempt is the single most important risk factor’ for suicide. The salience of the association between suicidal behaviour and suicide is also emphasised by leading psychological theories of suicide, such as Joiner’s interpersonal theory of suicide, which

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suggests that in order for completed suicide to occur, an individual must have both suicidal ideation and an acquired capability to engage in suicidal behaviour. An acquired capability to engage in suicidal behaviour may override the individual's innate fear of death and tendency towards perseverance of life and can develop as a result of exposure to trauma and violence, non-suicidal self-harming behaviours, substance use and access to means, all of which may increase an individual's capability to carry out an act that would result in death (Van Orden et al., 2010). Importantly, Joiner's theory suggests that suicidal ideation and behaviour are separate dimensions, rather than the same construct with differing degrees of severity. Although some studies have reported very strong associations between suicidal behaviour and suicide (Beck et al., 1999; Didham et al., 2006; Hyman et al., 2012), the strength of the association between suicidal behaviours and suicide was called into questioned by a recent meta-analysis by Ribeiro et al. (2016). Ribeiro et al. (2016) found a pooled odds ratio (OR) of suicide associated with suicide attempt of 2.03 (95% confidence interval [CI]= 1.61, 2.57) among a sample of 21 studies, consistent with a weak statistical association that they described as providing 'marginal improvement in diagnostic accuracy above chance'. Ribeiro et al. (2016) also examined a separate sample of six studies finding that suicidal ideation was associated with suicide with an OR of 1.95 (95% CI=1.31, 2.90) suggesting that suicidal ideation and behaviour are associated with suicide with a very similar effect size. Ribeiro et al.'s (2016) meta-analysis had the important strength of examining longitudinal studies that were free from possible hindsight and outcome bias in the assessment of suicidal ideation and behaviour. However, the inclusion of un-matched data sets and the exclusion of a large number of controlled studies left open some possibility that suicidal behaviour and suicidal ideation had a similar pooled OR by chance in their study, and that a larger study of matched data for the two independent variables would demonstrate that suicidal behaviour was more strongly associated with suicide than suicidal ideation.

Knowledge of the relative strengths of the associations between suicidal ideation and suicide and suicidal behaviours and suicide is of interest for both theoretical and practical reasons. First, if an acquired capability for suicidal behaviour is a necessary precursor for suicide, then it would be expected that suicidal behaviour would be more strongly associated with suicide than suicidal ideation because suicidal ideation may occur without an acquired capability. Second, people presenting with suicidal behaviour in clinical practice sometimes deny suicidal ideation, and people with suicidal ideation may have a history of suicide attempts (Berman, 2018; Smith et al., 2013). In both situations, the relative weight given to suicidal ideation and suicidal behaviour by clinicians might be important.

The aim of this study was to assess the strengths of the associations between the two independent variables (suicidal

ideation and suicidal behaviour) and the dependent variable of suicide in a sample of primary studies reporting both associations. The null hypothesis was that the effect size of the associations between suicidal ideation and suicide and suicidal behaviours and suicide would not be statistically different with an alpha of 0.05 in the main or in any subgroup analyses.

Methods

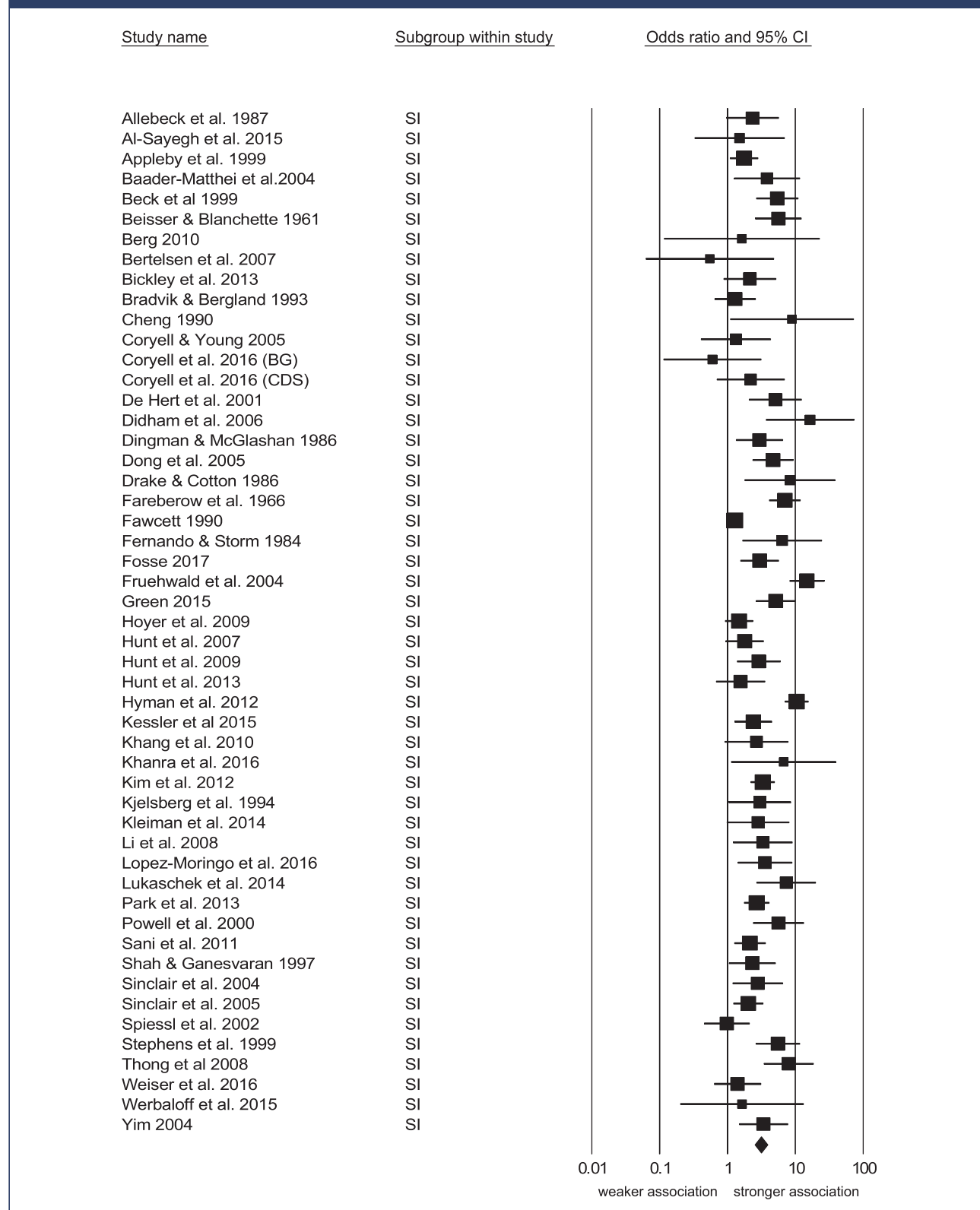
We extended a previous meta-analysis of the association between suicidal ideation and suicide (McHugh et al., 2019) to include studies also reporting on suicidal behaviour. The extended meta-analysis was registered with PROSPERO (133007) and conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009).

Searches

Preliminary searches of Medline, Embase and PsychINFO from inception to January 2017 looking for papers that examined the association between suicidal ideation and suicide using the word 'suicide' as a key word or in the title resulted in an excessive number of results (McHugh et al., 2019), while placing limits using relevant terms such as 'thoughts', 'ideation' or 'mortality' missed relevant papers that were known to the authors from earlier meta-analyses (Chapman et al., 2015; Large et al., 2011b, 2018). In contrast, searches of PubMed using variants of the word suicide in the title reliably located papers known to the authors and those found in searches of multiple databases in earlier studies (Chapman et al., 2015; Hubers et al., 2018). Therefore, and in order to obtain a large and representative sample of relevant studies, one author (M.M.L.) examined the titles of English language publications with an accompanying abstract that contained variants of the single term 'suicide' (suicid*) in their title and were published in PubMed from inception to 18 July 2018. The reference list of relevant review articles (Chapman et al., 2015; Franklin et al., 2017; Hubers et al., 2018; Large et al., 2011a, 2011b; McHugh et al., 2019; Ribeiro et al., 2016) was hand searched. Two authors (M.M.L. and C.M.) winnowed the resulting abstracts and full-text publications (see Figure 1, Supplementary Material).

Inclusion and exclusion criteria

Full-text papers were initially examined for cohort or controlled studies that reported the effect size data (ORs, counts or other measures of effect size discrimination) quantifying the association between suicidal ideation and suicide. The resulting papers were then examined for similar effect size data about the association between suicidal behaviours and suicide. Papers that only reported on the

Figure 1. Forest plot of studies reporting the association between suicidal ideation, behaviour and suicide.

association between suicidal ideation and suicide were excluded in order to examine the two independent variables in matched primary study populations and to avoid any possibility of systematic bias associated with an association between the study population and the choice of either suicidal ideation or suicidal behaviours. Hence, we included papers that reported on (1) the expression or non-expression of suicidal ideation, (2) the presence or absence of non-lethal suicidal behaviour and (3) relevant effect size data or counts (true positives, false positives, false negatives and true negatives) related to suicide. We included studies of patients who had received psychiatric care and people recruited from non-psychiatric settings as defined in an earlier meta-analysis of the association between suicidal ideation and suicide (Hubers et al., 2018; McHugh et al., 2019).

We excluded studies in which suicidal ideation and behaviour were assessed by psychological autopsy method, studies in which the non-suicidal controls were deceased and studies of patients with severe medical illnesses such as malignancies or human immunodeficiency virus.

Data extraction and definitions of suicide and suicidal ideation

Two authors (M.M.L. and C.M.) independently extracted the effect size data and the moderator variables. The OR was the preferred data format, followed by raw counts and other effect size data. A third author (A.C.) re-examined the data points. The discrepant points were re-examined by two authors until there was consensus. We accepted the definitions of suicidal behaviour (such as self-harm, suicide attempt, suicidal behaviour) and suicidal ideation (suicidal ideas/ideation/thoughts/threats) as used in the primary research. Data points regarding 'suicide plans' were excluded because suicide planning may be considered both ideation and behaviour, in particular if steps have been taken to enact a plan. When studies reported suicidal ideation and suicidal behaviour on a spectrum that assumed that all those with suicidal behaviour had suicidal ideation, estimates for the association between suicidal ideation and suicide were made using those without suicidal ideation or behaviours as the reference category. In these studies, estimates of the association between suicidal behaviour and suicide used those with no suicidal behaviour (including those with suicidal ideation) as the reference category. Where suicidal ideation and suicidal behaviours were recorded as separate categories, we analysed both variables separately using those without suicidal ideation and suicidal behaviours, respectively, as the reference group. In regarding suicidal ideation and suicidal behaviours as separate categories, we were aware that many patients with suicidal behaviour in the primary studies would have had suicidal ideation and some patients with suicidal ideation would have had suicidal behaviour.

When papers reported more than one data set for suicidal behaviour or suicidal ideation (e.g. a past history of suicide attempts and recent presentation with suicidal behaviour), we chose most contemporaneous assessment of the two independent variables.

Moderator variables

We collected five moderator variables: (1) study population (whether the study consisted of patients from non-psychiatric settings such as primary care or military settings adopting the nomenclature of earlier research) (Hubers et al., 2018) and samples of psychiatric patients defined by having a schizophrenia spectrum psychosis, a mood disorder or mixed or other psychiatric diagnoses; (2) duration of follow-up between the assessment of the independent variables and possible suicide; (3) whether the study used a cohort of control design; (4) whether the studies reported suicidal ideation and behaviour dimensionally (thus excluding those with suicidal behaviour from the suicidal ideation group) or reported suicidal ideation and suicidal behaviours as independent categories; (5) according to a strength of reporting scale.

Assessment of strength of reporting

Two researchers (M.M.L. and C.M.) independently assessed the reporting strength (and hence the risk of bias of each individual study) of the methods used in the primary research using a scale (scored 0–4) derived from the Strengthening the Reporting of Observational Studies in Epidemiology statement checklist (Von Elm et al., 2007) and used in a related study (McHugh et al., 2019). The term strength of reporting was used instead of study quality to acknowledge that the primary studies were not generally conducted to assess the association between suicidal ideation and suicidal behaviour and suicide and could be regarded as being of adequate quality for their research purpose. One point was allocated according to each of the following criteria: (1) use of a structured method to assess suicidal ideation, (2) collection of data about suicidal ideation and behaviour in a method that was blinded to the patient's suicide (either by a blinding method or by electronic recording at the point of assessment), (3) ascertainment of suicide using a mortality database and (4) inclusion of open verdicts as suicide. These items were added to produce a 5-point scale (0–4), with a score of 2 or more being considered high quality.

Data synthesis

Random effects meta-analysis was chosen a priori for all estimates because of the diversity of study populations and differences in the methods used in the primary research. As a first analytic step, the two independent variables of suicidal

ideation and suicidal behaviour and the dependent variable of suicide were examined in two separate meta-analyses. The effect size data in the primary research data and pooled effect size were expressed in OR. Between-study heterogeneity in effect sizes was examined using I^2 , Q value statistics. The possibility of publication bias was assessed using a funnel plot and Egger's regression (Egger et al., 1997). Subgroups were examined in both the estimates of suicidal ideation and suicidal behaviours using a mixed model that assumed a random effect within subgroups and a fixed effect between subgroups. The study null hypothesis was examined in the second analytic step in which the statistical difference between the strength of the associations between suicidal ideation and suicidal behaviour and the null hypothesis was compared using a mixed effects meta-regression of all the studies and within subgroups. For the purpose of the meta-regression, data reporting the association between suicidal ideation and suicide were coded as '0' and used as the reference variable and data reporting with suicidal behaviour were coded as '1' such that a positive coefficient indicated a stronger association between suicidal ideation than suicidal behaviours. Comprehensive Meta-Analysis (CMA; Version 3; Biostat, Englewood, NJ, USA) was used in all analysis.

Results

Systematic searching located 51 publications where both the associations between suicidal behaviour and suicide and the associations between suicidal ideation and suicide were reported (see Table 1). The studies reported on 7,415,193 individuals (mean per study=146,396, standard deviation [SD]=859,898), among whom there were 3921 suicides (mean per study=77, SD=150). The mean length of follow-up was 5.5 years. These included 8 studies from non-psychiatric populations and 43 from psychiatric populations including 9 studies of people with schizophrenia, 9 studies of people with affective disorder and 25 studies of people with mixed or other psychiatric diagnoses. There were 30 case-control studies and 21 cohort studies. In all, 20 were classified as of lower quality and 31 of higher quality according to our quality scale (see Table 1, Supplementary Material).

Suicidal ideation

Suicidal ideation was associated with suicide with a median OR of 2.90 and a study range of 0.55 to 16.5 with a pooled OR of 3.11 (see Figure 1). Studies conducted in non-psychiatric settings had the strongest pooled association between suicidal ideation and suicide, while studies of patients with affective disorder had a weaker association (see Table 2). The strength of the association between suicidal ideation and suicide was stronger in a small subgroup of studies that reported on people who were described as making a suicidal 'threat' (four studies; OR=7.82, 95%

CI=4.80, 12.47), than 47 studies that reported on patients with suicidal ideation (OR=2.83, 95% CI=2.30, 3.49; $Q=14.1$, $df=1$, $p=0.001$). The association between suicidal ideation and suicide was not associated with the mean duration of follow-up (coefficient=-0.02, 95% CI=-0.06, 0.01, $Z=-1.34$, $p=0.18$). There was no evidence of publication bias on examination of the funnel plot (see Figure 2, Supplementary Material) or by Egger's regression (intercept=1.03, $df=49$, $p=0.09$).

Suicidal behaviour

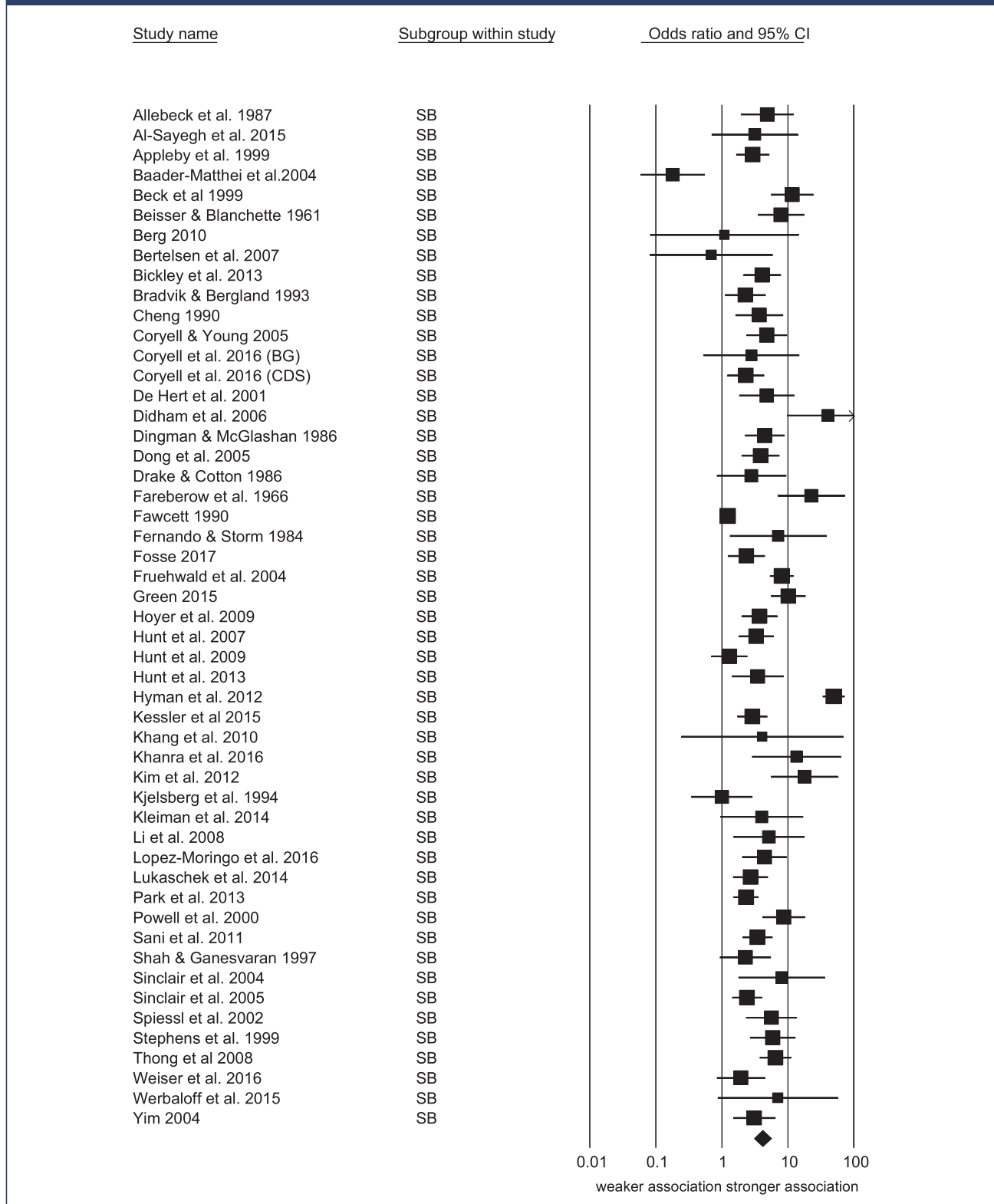
Suicidal behaviour was associated with suicide with median OR of 3.87 and study range of 0.18 to 49.4 with a pooled OR of 4.09 (see Figure 2). Studies conducted in non-psychiatric settings had the strongest pooled association between suicidal behaviour and suicide, while studies of patients with affective disorder had a weaker association (see Table 3). There was no difference in the strength of the association between suicidal behaviour and suicide between the 39 studies that reported on patients with suicide attempts (OR=4.39, 95% CI=3.08, 6.24) and 12 studies that reported on patients with self-harm (OR=3.25, 95% CI=1.95, 5.40; $Q=0.91$, $df=1$, $p=0.34$). The association between suicidal behaviour and suicide was not influenced by the mean duration of follow-up (coefficient=-0.01, 95% CI=-0.06, 0.04, $Z=-0.47$, $p=0.64$). There was no evidence of publication bias on examination of the funnel plot (see Figure 3, Supplementary Material) or by Egger's regression (intercept=0.99, $df=49$, $p=0.26$).

Comparison of the strength of the association between suicidal ideation and suicidal behaviours and later suicide

Suicidal behaviours were more strongly associated with suicide than suicidal ideation (OR=4.06 vs 3.02) but this did not reach significance as assessed with meta-regression (see Table 4). Among six studies that allowed us to exclude people with prior suicidal behaviour from the suicidal ideation group, there was a trend towards a weaker association between suicidal ideation and suicide (six studies; OR=2.57, 95% CI=1.63, 4.03) than the association between suicidal behaviour and suicide (six studies; OR=5.28, 95% CI=2.72, 10.2; $Q=3.11$, $df=1$, $p=0.08$). There was no difference between the strength of the associations between suicidal ideation and suicide and suicidal behaviour and suicide in subgroups of studies as defined by study setting (non-psychiatric or psychiatric), diagnostic mix of study population, study design (cohort or control) or study quality.

Discussion

Both the independent variables of suicidal ideation and suicidal behaviour are associated with suicide with an effect

Figure 2. Forest plot of studies reporting association between suicidal behaviour and suicide.

size that can be qualitatively assessed to be moderate (Rosenthal, 1995) and is similar in the strength of association as that found between male gender and suicide in most

countries (Large, 2018). In the main analysis and in each of the subgroup analyses, suicidal behaviour was more strongly associated with suicide than suicidal ideation but this

Table 1. Studies reporting on both the association between suicide ideation and suicide and suicide behaviour and suicide.

Author (year)	Subjects	Measure of suicidal ideation	Measure of suicidal behaviour	Measure of suicide	Suicidal behaviour Odds ratio (95% CI)	Suicidal ideation Odds ratio (95% CI)
Allebeck et al. (1987)	32 former inpatients with schizophrenia and 64 matched controls	Clinical documentation in the medical records	Suicide attempt	Suicides and open verdicts obtained from a mortality register	4.9 (1.9, 12.3)	2.3 (1.0, 5.7)
Al-Sayegh et al. (2015)	13 suicides among a cohort of 6293 members of the general population	Structured interview for suicidal thoughts and behaviours	Suicide attempt	Suicides and open verdicts obtained from a mortality register	3.1 (0.7, 14.3)	1.5 (0.3, 7.0)
Appleby et al. (1999)	149 discharged mental health patients and 149 matched controls	Clinical documentation in the medical records	Self-harm	Suicides and open verdicts obtained from a mortality register	2.9 (1.6, 5.3)	1.8 (1.1, 2.9)
Baader-Matthei et al. (2004)	32 mental health patients and 32 matched controls	Clinical documentation in the medical records	Suicidal behaviour	Mortality register	0.2 (0.1, 0.6)	3.8 (1.2, 11.8)
Beck et al. (1999)	30 suicides among a cohort of 3701 mental health outpatients	Scale for suicide ideation	Suicide attempt	Mortality register	11.6 (5.5, 24.6)	5.4 (2.6, 11.2)
Beisser and Blanchette (1961)	71 inpatient suicides and 71 matched controls	Suicide threats documented in the medical records	Suicide attempt	Clinically defined	7.9 (3.5, 17.8)	5.6 (2.5, 12.4)
Berg (2010)	3 suicides among 20 patients who had received electro-convulsive therapy	Clinical documentation in the medical records	Suicide attempt	Mortality register	1.1 (0.1, 14.7)	1.6 (0.1, 23.0)
Bertelsen et al. (2007)	7 suicides among a cohort of 547 people with first episode psychosis	Clinical Assessment in Neuropsychiatry instrument	Suicide attempt	Mortality register	0.7 (0.1, 5.9)	0.6 (0.1, 4.9)
Bickley et al. (2013)	100 recently discharged mental health patients and 100 matched controls	Retrospectively assessed by treating clinicians	Self-harm	Suicides and open verdicts obtained from a mortality register	4.1 (2.1, 7.9)	2.1 (0.9, 5.3)
Bradvik and Berglund (1993)	89 melancholically depressed former inpatients and 89 matched controls	Clinical documentation in the medical records	Suicide attempt	Mortality register	2.3 (1.1, 4.6)	1.3 (0.6, 2.6)
Cheng et al. (1990)	55 people with schizophrenia and 52 matched controls	Clinical documentation in the medical records	Suicide attempt	Clinically defined	3.7 (1.6, 8.6)	8.9 (1.1, 73.1)
Coryell and Young (2005)	33 suicides among a cohort of 782 patients with a depressive disorder	Schedule for Affective Disorder	Suicide attempt	Mortality register	4.8 (2.3, 9.8)	1.3 (0.4, 4.4)
Coryell et al. (2016)	7 suicides among a cohort of 1748 patients with bipolar disorder	Schedule for Affective Disorder	Suicide attempt	Clinically defined	2.8 (0.52, 15.0)	0.6 (0.1, 3.2)

(continued)

Table 1. (continued)

Author (year)	Subjects	Measure of suicidal ideation	Measure of suicidal behaviour	Measure of suicide	Suicidal behaviour Odds ratio (95% CI)	Suicidal ideation Odds ratio (95% CI)
Coryell et al. (2016)	12 suicides among a cohort of 288 patients with bipolar disorder	Schedule for Affective Disorder	Suicide attempt	Clinically defined	2.3 (1.2, 4.4)	2.2 (0.7, 7.0)
De Hert et al. (2001)	63 formerly inpatients with schizophrenia and 63 matched controls	Suicidal threats documented in the medical records	Suicide attempt	Clinically defined	4.8 (1.8, 12.7)	5.1 (2.1, 12.6)
Didham et al. (2006)	221 suicides among primary care patients and 663 matched controls	Clinical documentation in the medical records	Self-harm	Mortality register	40.5 (9.6, 170.3)	16.5 (3.7, 74.4)
Dingman and McGlashan (1986)	38 suicides among a cohort of 451 former inpatients	Suicidal threat documented in the medical records	Suicide attempt	Clinically defined	4.5 (2.2, 9.0)	3.0 (1.3, 6.6)
Dong et al. (2005)	92 inpatient suicides and 92 matched controls	Clinical documentation in the medical records	Self-harm	Suicides and open verdicts obtained from a mortality register	3.9 (2.0, 7.5)	4.7 (2.3, 9.4)
Drake et al. (1986)	15 suicides among a cohort of 104 former inpatients with schizophrenia	Clinical documentation in the medical records	Suicide attempt	Clinically defined	2.8 (0.8, 9.5)	8.3 (1.8, 39.1)
Farberow et al. (1966)	218 mental health inpatient suicides and 220 inpatient controls	Suicidal threats documented in the medical records	Suicide attempt	Clinically defined	22.7 (7.0, 74.2)	7.0 (4.1, 12.1)
Fawcett et al. (1990)	25 suicides among 954 patients with major affective disorder	Schedule for Affective Disorder	Suicide attempt	Clinically defined	1.2 (1.0, 1.5)	1.3 (1.0, 1.6)
Fernando and Storm (1984)	22 suicides by current or former mental health inpatients and 22 matched controls	Clinical documentation in the medical records	Deliberate self-harm	Clinically defined	7.1 (1.3, 38.8)	6.4 (1.7, 24.8)
Fosse et al. (2017)	36 former mental health inpatients and 120 matched controls	Suicide Risk Check List	Suicide attempt	Mortality register	2.3 (1.2, 4.5)	3.0 (1.5, 5.8)
Fruehwald et al. (2004)	220 suicides of prisoners and 440 matched controls	Suicidal threats documented in custodial records	Suicide attempt	Mortality register	8.1 (5.3, 12.3)	14.9 (8.2, 27.1)
Green et al. (2015)	43 suicides among a cohort of 5200 mental health outpatients	Beck depression inventory suicide	Suicide attempt	Mortality register	10.2 (5.5, 18.8)	5.1 (2.6, 10.1)
Hoyer et al. (2009)	135 current and former mental health inpatients and 135 matched controls	Clinical documentation in the medical records	Suicide attempt	Mortality register	3.7 (2.0, 7.0)	1.5 (0.9, 2.4)
Hunt et al. (2007)	222 current mental health inpatients and 222 controls	Retrospectively assessed by treating clinicians	Deliberate self-harm	Suicides and open verdicts obtained from a mortality register	3.3 (1.8, 6.2)	1.8 (0.9, 3.4)

(continued)

Table 1. (continued)

Author (year)	Subjects	Measure of suicidal ideation	Measure of suicidal behaviour	Measure of suicide	Suicidal behaviour Odds ratio (95% CI)	Suicidal ideation Odds ratio (95% CI)
Hunt et al. (2013)	107 recently admitted mental health patients and 107 controls	Retrospectively assessed by treating clinicians	Self-harm	Suicides and open verdicts obtained from a mortality register	3.5 (1.4, 8.7)	1.6 (0.7, 3.6)
Hunt et al. (2009)	238 recently discharged mental health patients and 238 controls	Retrospectively assessed by treating clinicians	Self-harm	Suicides and open verdicts obtained from a mortality register	2.9 (1.4, 6.1)	3.5 (1.4, 8.7)
Hyman et al. (2012)	24 suicides among a cohort of 4,070,167 military personnel	Systematically collected department of defence data	Suicide attempt	Mortality register	49.4 (33.4, 73.0)	10.5 (6.9, 15.8)
Kessler et al. (2015)	68 suicides among a cohort of 316,686 Veterans who were former inpatients	Systematically collected department of defence data	Suicide attempt	Mortality register	2.9 (1.7, 4.9)	2.4 (1.3, 4.6)
Khang et al. (2010)	13 suicides among a cohort of 5414 members of the general population	National health survey	Suicide attempt	Mortality register	4.1 (0.2, 69.7)	2.7 (0.9, 8.0)
Khanra et al. (2016)	10 current mental health inpatients and 50 matched controls	Clinical documentation in the medical records	Suicide attempt	Clinically defined	13.5 (2.8, 64.7)	6.7 (1.1, 40.1)
Kim et al. (2012)	324 depressed veterans and 312 matched controls	Clinical documentation in the medical records	Suicide attempt	Mortality register	17.9 (5.5, 58.2)	3.3 (2.2, 5.0)
Kleiman and Liu (2014)	25 suicides among a cohort of 19,989 members of the general population	National health survey	Suicide attempt	Mortality register	4.0 (0.9, 17.1)	2.8 (1.0, 8.2)
Kjelsberg et al. (1994)	35 former adolescent mental health inpatients and 35 matched controls	Clinical documentation in the medical records	Suicide attempt	Mortality register	1.0 (0.3, 2.9)	3.0 (1.0, 8.7)
Li et al. (2008)	64 inpatients with schizophrenia and 64 matched controls	Clinical documentation in the medical records	Suicide attempt	Clinically defined	5.2 (1.5, 18.0)	3.3 (1.2, 9.2)
Lopez-Morino et al. (2016)	71 people with schizophrenia and 355 controls	Semi-structured risk assessment	Suicide attempt	Suicides and open verdicts obtained from a mortality register	4.4 (2.0, 9.7)	3.6 (1.4, 9.1)
Lukaschek et al. (2014)	101 former mental health inpatients and 101 matched controls	Clinical documentation in the medical records	Suicide attempt	Railway suicides obtained using a mortality register	2.7 (1.5, 5.0)	7.4 (2.7, 20.3)

(continued)

Table 1. (continued)

Author (year)	Subjects	Measure of suicidal ideation	Measure of suicidal behaviour	Measure of suicide	Suicidal behaviour Odds ratio (95% CI)	Suicidal ideation Odds ratio (95% CI)
Park et al. (2017)	96 suicides among a cohort of 8403 recently discharged mental health patients	Clinical documentation in the medical records	Suicide attempt	Mortality register	2.3 (1.5, 3.6)	2.7 (1.7, 4.2)
Powell et al. (2000)	112 current mental health inpatients and 112 controls	Clinical documentation in the medical records	Self-harm	Suicides and open verdicts obtained from a mortality register	8.7 (4.1, 18.3)	5.6 (2.4, 13.5)
Sani et al. (2011)	96 former mental health inpatients and 192 matched controls	Clinical documentation in the medical records	Suicide attempt	Clinically defined	3.5 (2.0, 5.9)	2.1 (1.2, 3.7)
Shah and Ganesvaran (1997)	60 current or recently discharged suicides and 60 matched controls	Clinical documentation in the medical records	Suicide attempt	Clinically defined	2.3 (0.9, 5.6)	2.3 (1.0, 5.2)
Sindair et al. (2005)	127 current or recently discharged patients with depression and 195 matched controls	Clinical documentation in the medical records	Suicide attempt	Suicides and open verdicts obtained from a mortality register	2.4 (1.2, 6.6)	2.0 (1.2, 3.4)
Sindair et al. (2004)	51 current or recently discharged patients with schizophrenia and 82 matched controls	Clinical documentation in the medical records	Suicide attempt	Suicides and open verdicts obtained from a mortality register	8.1 (1.8, 36.9)	2.8 (1.2, 6.6)
Spiesl et al. (2002)	30 suicides among a cohort of 21,062 mental health inpatients	Clinical documentation in the medical records	Suicide attempt	Clinically defined	5.6 (2.3, 13.7)	1.0 (0.4, 2.1)
Stephens et al. (1999)	28 suicides among a cohort of 1212 inpatients with schizophrenia	Clinical documentation in the medical records	Suicide attempt	Clinically defined	5.9 (2.7, 13.1)	5.5 (2.6, 11.8)
Thong et al. (2008)	123 mental health patients and 123 matched controls	Clinical documentation in the medical records	Deliberate self-harm	Mortality register	6.5 (3.7, 11.4)	8.0 (3.4, 18.7)
Weiser et al. (2016)	54 suicides among a cohort of 89,049 young men receiving primary mental health care	Clinical documentation in the medical records	Suicide attempts	Mortality register	1.9 (0.8, 4.5)	1.4 (0.6, 3.1)
Werbeloff et al. (2016)	8 suicides among a birth cohort of 4914	Item on a research questionnaire	Suicide attempts	Mortality register	7.0 (0.9, 57.7)	1.6 (2, 13.4)
Yim et al. (2004)	73 recently discharged mental health inpatients and 73 matched controls	Clinical documentation in the medical records	Suicide attempts	Mortality register	3.1 (1.5, 6.5)	3.4 (1.5, 7.9)

CI: confidence interval.

Table 2. Main results and subgroup analysis of the association between suicidal ideation and suicide.

	Number of studies	Point estimate	Lower limit	Upper limit	I^2	Q value	df	p value
Main	51	3.11	2.51	3.86	75.4			
Non-psychiatric	8	4.41	2.08	9.35	81.4	15.3	3.00	0.002
Affective disorder	9	1.69	1.23	2.33	55.2			
Schizophrenia	9	3.76	2.67	5.93	0.00			
Mixed diagnosis	25	3.25	2.61	4.04	52.8			
Controlled studies	30	3.32	2.62	4.20	65.2	0.73	1.00	0.39
Cohort studies	21	2.70	1.77	4.07	82.4			
Lower quality	20	4.50	3.23	6.26	64.9	7.54	1.00	0.006
Higher quality	31	2.51	1.94	3.23	74.2			

Table 3. Main results and subgroup analysis of the association between suicidal behaviour and suicide.

	Number of studies	Point estimate	Lower limit	Upper limit	I^2	Q value	df	p value
Main	51	4.09	3.05	5.50	87.5			
Non-psychiatric	8	8.18	2.88	23.3	90.9	3.91	3.00	0.27
Affective disorder	9	2.89	1.74	4.81	79.9			
Schizophrenia	9	4.45	2.17	6.23	0.0			
Mixed diagnosis	25	3.74	2.79	5.02	75.6			
Controlled studies	30	3.78	2.91	4.90	70.9	0.23	1.00	0.63
Cohort studies	21	4.44	2.40	8.24	93.4			
Lower quality	20	4.60	3.08	6.87	76.5	0.43	1.00	0.51
Higher quality	31	3.80	2.55	5.66	90.3			

difference did not reach statistical significance and we were not able to reject the null hypothesis. There was a trend towards statistical significance in the subset of six studies in which those with suicidal behaviour were excluded from the suicidal ideation group. Our results should not be interpreted to suggest that future studies will not find a significant difference in the strength of the association between suicide and either suicidal ideation or suicidal behaviour. The consistency of non-significantly stronger association between suicidal behaviour in all subgroups does suggest that suicidal behaviour might be eventually shown to be more strongly associated with suicide than suicidal ideation as more data become available. However, our data suggest that any difference in statistical strength is likely to be small and of dubious clinical significance.

This study also provided an opportunity to assess whether measurement of dimensions of suicidal thoughts and behaviour impacts the strength of associations that are found between these distinct, but overlapping constructs,

and later suicide. As mentioned, our previous meta-analysis (McHugh et al., 2019) assessed the strength of association between suicidal ideation and later suicide. Of the 71 studies in that meta-analysis, 51 measured suicidal ideation and behaviour separately and were thus included in this meta-analysis. The remaining 22 studies were not included as they did not include a measure of suicidal behaviour. While in the previous meta-analysis we found a pooled OR for suicidal ideation of 3.41, the current meta-analysis found an OR of 3.11. This indicates that studies that only report on suicidal ideation and not suicidal behaviour may tend to report a slightly higher OR. This may also be true for studies that report on suicidal behaviour only; however, we were not able to compare that data as the prior review focused on ideation only.

The main weakness of this study flowed from the conceptualisation of suicidal ideation and suicidal behaviours as categorically independent entities in all but six studies. In reality, it is likely that most patients classified as

Table 4. Main result and subgroup meta-regression of suicide behaviour using suicide ideation as the reference variable.

	Number of studies	Coefficient	Standard error	Lower limit	Upper limit	Z value	p value
Main	51	0.27	0.19	-0.09	0.64	1.49	0.14
Non-psychiatric	8	0.66	0.66	-0.63	1.95	1.00	0.31
Affective disorder	9	0.52	0.30	-0.08	1.12	1.71	0.09
Schizophrenia	9	0.17	0.25	-0.31	0.65	0.69	0.49
Mixed diagnosis	25	0.13	0.19	-0.24	0.49	0.68	0.49
Controlled studies	30	0.12	0.18	-0.23	0.47	0.69	0.49
Cohort studies	21	0.53	0.38	-0.22	1.28	1.38	0.16
Lower quality	20	0.01	0.27	-0.51	0.53	0.05	0.95
Higher quality	31	0.43	0.24	-0.04	0.90	1.78	0.08

having suicidal behaviours had suicidal ideation and that many patients with suicidal ideation had a history of suicidal behaviour. This overlap between the two variables would lessen the extent of any difference in the strength of the two associations in 45 of the 51 included studies and in our meta-analytic result. Specifically, the inclusion of patients with suicidal behaviour in the suicidal ideation group might increase the observed association between suicidal ideation and suicide, lessening the possibility of finding a difference in the extent of the associations between these two variables and suicide. Despite the above caveat, we believe that the result of our study is somewhat surprising to the extent that we found that the objective sign of suicidal behaviour was not very much more strongly associated with suicide than the subjective symptom of suicidal ideation and that this difference did not reach statistical significance despite a highly powered meta-analysis. Prior to conducting this study, we held the opinion that suicidal behaviours were likely to be more strongly associated with suicide than suicidal ideation and formulated our hypothesis accordingly. We believed a priori that suicidal ideation would be less strongly associated with suicidal behaviours because they can be regarded as a communication of a persons' inner world and level of distress rather than behaviour per se. Further suicidal ideation is much more common than suicidal behaviours (Johnston et al., 2009) and can be conceptualised as being dynamic and fluctuating over time, lessening the likely strength of any association. In contrast, suicidal behaviour is more static and objective and therefore a potentially reliable marker of suicide in line with a large body of research that suggests that actuarial prediction usually outperforms clinical prediction (Dawes et al., 1989). Moreover, one might expect suicidal behaviour to be more strongly associated with suicide because it is more similar to suicide, with both involving self-destructive behaviour and an acquired capability for self-harm (Van Orden et al.,

2010). After this study, we modified our opinions about the relative strengths of the association between suicidal ideation and suicidal behaviours and considered that our results might be because people may be more reliable in their reporting of suicidal ideation than might generally be believed (Berman, 2018) and/or that the recording of suicidal behaviour is either less reliable (Eikelenboom et al., 2014) or less accurate (Hart et al., 2013) than one might imagine.

Conclusion

The results of this study are clinically relevant in that it is not rare for patients to present with suicidal behaviour yet deny current suicidal ideation while other patients will present with suicidal ideation in the absence of suicidal behaviour. This study suggests that, to the extent to which suicidal ideation and behaviours are conceptualised as risk factors, patients with either of these phenomena are more or less equal but only modestly increased risk of suicide. Patients with suicidal ideation only should not be dismissed as not having suicidal behaviour and there is no strong reason why people with suicidal behaviours should receive more restrictive mental health care than those with suicidal ideation only. The study also has some implications for future primary studies. Studies that report suicidal ideation and suicidal behaviours as both dimensional and categorical risk factors could more fully discriminate between the two risk factors. Highly powered primary studies and future meta-analyses might further clarify the relative strengths of these two common and important clinical aspects of suicidality.

While we urge clinicians to make very careful assessments of both past suicidal behaviour and of suicidal ideation, our results suggest that presently there are no strong grounds to put particular emphasis on suicidal behaviour over suicidal ideation.

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Supplemental Material

Supplemental material for this article is available online.

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2.3 Chapter summary

In [Chapter 2](#) systematic review and meta-analyses reviewed 70 years of research to assess the role of two key risk factors for suicide used to direct clinical care, suicidal ideation (SI) and suicidal behaviour (SB). In [Chapter 2.1](#), meta-analysis was used to test the performance of suicidal ideation as a screening measure for later suicide. A comprehensive set of performance measures calculated for suicidal ideation as a predictor of future suicide, highlighted weaknesses of suicidal ideation applied as a screening tool given its low sensitivity and only moderate specificity. While there were no significant differences based on the age of the sample, there were significant differences between sensitivity and specificity in studies that sampled from the general population versus those that focused on psychiatric settings, such that SI is an even less effective screening tool in non-psychiatric samples. [Chapter 2.2](#) found SB associated with a slightly greater odds of future suicide, though there were no significant differences between the two. Studies in non-psychiatric settings or in samples with psychosis or mixed psychiatric diagnoses, found SB associated with a greater odds of suicide death. Both reviews highlight the importance of considering sample and setting when interpreting outcomes in suicide research.

With the limitations in the existing suicide research in mind, [Chapter 3](#) will explore the application of new approaches to predictive modelling using machine learning. Firstly [Chapter 3.1](#) presents a narrative synthesis of findings from initial machine learning models of suicidal behaviour. In [Chapter 3.2](#) machine learning is then applied to build predictive models of self-harm and suicidal behaviour in a longitudinal cohort of young people accessing early intervention mental health services. A set of ML algorithms will be applied to a comprehensive set of validated social, psychological and clinical measures using a data driven approach to identify key predictors.

Chapter 3: Applying machine learning to the prediction of suicidal behaviour

3.1 A narrative review of machine learning in suicide research

McHugh, C., Large MM. (2020) ‘Can machine-learning methods really help predict suicide?’ *Current opinion in psychiatry*. DOI: [10.1097/YCO.0000000000000609](https://doi.org/10.1097/YCO.0000000000000609)

3.1.1 Abstract

Purpose of review

In recent years there has been interest in the use of machine learning in suicide research in reaction to the failure of traditional statistical methods to produce clinically useful models of future suicide. The current review summarizes recent prediction studies in the suicide literature including those using machine learning approaches to understand what value these novel approaches add.

Recent findings

Studies using machine learning to predict suicide deaths report area under the curve that are only modestly greater than, and sensitivities that are equal to, those reported in studies using more conventional predictive methods. Positive predictive value remains around 1% among the cohort studies with a base rate that was not inflated by case–control methodology.

Summary

Machine learning or artificial intelligence may afford opportunities in mental health research and in the clinical care of suicidal patients. However, application of such techniques should be carefully considered to avoid repeating the mistakes of existing methodologies. Prediction studies using machine-learning methods have yet to make a major contribution to our understanding of the field and are unproven as clinically useful tools.



Can machine-learning methods really help predict suicide?

Catherine M. McHugh^a and Matthew M. Large^b

Purpose of review

In recent years there has been interest in the use of machine learning in suicide research in reaction to the failure of traditional statistical methods to produce clinically useful models of future suicide. The current review summarizes recent prediction studies in the suicide literature including those using machine learning approaches to understand what value these novel approaches add.

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Summary

Machine learning or artificial intelligence may afford opportunities in mental health research and in the clinical care of suicidal patients. However, application of such techniques should be carefully considered to avoid repeating the mistakes of existing methodologies. Prediction studies using machine-learning methods have yet to make a major contribution to our understanding of the field and are unproven as clinically useful tools.

Keywords

artificial intelligence, machine learning, prediction, suicidal behaviour, suicide

INTRODUCTION: BACKGROUND

The prediction of suicide has been a focus of mental health research for decades. However, a practical method for anticipating individual suicides or even usefully stratifying patients according to suicide risk has remained elusive [1,2]. While the fallibility of suicide risk assessment is now more clearly understood [3,4] suicide risk assessment is still held to be a key element of suicide prevention [5,6]. Perceived suicide risk can be used to justify coercive and restrictive care of individual patients, for example by involuntary hospitalization, with the reasoning that the certain but limited harms associated with the treatment are outweighed by the less certain but catastrophic effects of suicide [7]. Similarly, it has been suggested that suicide prevention can be achieved by targeted interventions given to groups at higher suicide risk [8]. In recent years, there has been a surge of interest in the prediction of suicidal behaviour that seems to have been fuelled by reports that artificial intelligence or machine learning can produce predictive models with a higher degree of accuracy than has been achieved by clinical or more traditional statistical methods [9]. Proponents of

machine learning have suggested a central limitation in suicide research has been the number and complexity of interacting suicide risk factors. Traditional statistical approaches such as logistic regression and various survival analyses methods have a limited ability to analyse a large numbers of variables and cannot consider more complex and contingent interactions. In contrast machine learning has the potential to recognize complex patterns of interacting risk factors and might, as a result have more utility.

Perhaps the most important limitation in suicide prediction that needs to be overcome is the base rate problem. In line with Bayes' Theorem, events like suicide that have a very low base rate can only be predicted using methods that have an extraordinary

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KEY POINTS

- The low base rate of suicide deaths limits the predictive power of any model, machine learning or otherwise.
- Continued research in predictive models may be of clinical utility in some subpopulations if an outcome with a high enough base rate is chosen and if a meaningful positive predictive value can be achieved.
- Clinicians and policy makers must be aware of the risks of the application of machine learning algorithms to clinical problems.
- Machine learning offers an opportunity to analyse large amounts of data from novel sources, such as smartphone, wearables, that may add to increased understanding of the suicidal phenotypes.

ability to discriminate between lower and higher risk groups [10]. Some researchers have argued that in the face of base rate issues, and the limited predictive value of current methods, future studies should focus on more common outcomes such as suicide attempts [11]. However, there is strong evidence that suicide attempts are distinct to suicide deaths. For example, suicide attempts are more strongly associated with female sex and younger age while suicide occurs more frequently among men and older people [12].

Another central issue in suicide prediction research has been the nature and quality of the risk factor variables. For example, a lifetime history of suicidal ideation or behaviour are commonly used as predictor variables when current or recent suicidal thoughts and behaviour might be more pertinent [13] because suicidal ideation is known to fluctuate over short periods of time, and even highly lethal suicidal behaviour can occur with little planning [14]. However, a lack of distinction between static risk factors (such as previous suicide attempts or childhood trauma) and dynamic or fluctuating risk factors (such as depressed mood, hopelessness, agitation, intoxication) may not be the most important limitation of risk factor data. Recent research has suggested that the recording of historical data about suicide attempts is less accurate than might be imagined [15] and one recent study found that suicide prediction is enhanced if more accurate data about past hospitalization is available [16].

Suicide prediction using established statistical techniques

Putting aside concerns about the nature and quality of suicide risk factors, in recent years the statistical

limitations of both individual risk factors and combinations of risk factors have come into focus. After performing a meta-analytic review of over 50 years of suicide research into the association between risk factors and suicide, Franklin *et al.* [1] emphasized the surprisingly modest predictive strength of well known risk factors in longitudinal studies and in a related study Ribeiro *et al.* [3] found that a history of self-injurious thoughts and behaviours ‘only provide marginal improvement in diagnostic accuracy above chance’. Similarly a recent meta-analytic review of studies reporting the association between suicidal ideation and later suicide found a meta-analytic area under the curve (AUC) of .676 and positive predictive value (PPV) of 1.7% over a mean study duration of 9.1 years [17]. These metrics were associated with pooled sensitivity for suicide of 40%, and studies outside of specialist psychiatric settings had a lower sensitivity such that four in five of suicides would be missed if suicidal ideation was used as the sole test of later suicide.

It is likely that the number and complexity of contributing suicide factors places a limit on the statistical association between any single risk factor and suicide. To test this hypothesis, Large *et al.* examined 50 years of studies that used two or more clinical risk factors in longitudinal studies of suicide prediction. Overall they found that a higher risk category was associated with an odds ratio of 4.84 compared with the lower risk category with a sensitivity of 56% and PPV of 5.5% over 5 years of follow-up [2]. The authors found that models that included a greater number of suicide risk factors were not associated with better predictive metrics. This surprising finding led them to conclude that risk assessment using multiple factors has much the same statistical limitations as individual risk factors [18]. However, the vast majority of the studies included in the meta-analysis used experimenter derived scales or regression models to combine suicide risk factors. The inability of researcher designed risk scales or regressions methods to utilize complex and possibly contingent interactions between risk factors may have accounted for the disappointing results.

In 2019, a review by Belsher *et al.* [19²²] examined 17 studies with suicide prediction models that had been tested in both experimental and validation models. This study concluded the ability of such models to predict future suicidal events was near zero. These authors suggested that any predictive model that is accurate should be evaluated within clinical frameworks to assess the potential impact on clinical pathways and other outcomes, such as adverse events and costs to the service. Further the authors suggest that policy makers and researchers

should consider what an acceptable PPV may be, and if it is too low to actually inform change in clinical care then such modelling should be abandoned.

Suicide prediction using machine learning

In recent years, there has been growing interest in using machine learning, used here synonymously with artificial intelligence to predict suicide

(Table 1) [20²²,21²²,22,23,24²⁴]. While these studies examine a diverse group of patients, and used differing methods, two observations can be made. First, the AUC results seem to be only modestly greater than those reported in studies using more conventional predictive methods. Second, the sensitivities in the highest risk group vary, but might not greatly exceed the sensitivity of 56% derived by meta-analysis of more conventional studies. Third, the PPV

Table 1. Studies using machine learning to predict suicide

	Study description	Base rate of suicide	Model	AUC, and sensitivity and PPV of highest risk category
Amini <i>et al.</i> 2016	457 Suicides among a cohort of 5414 people with suicide attempts in Hamadan province, Iran (2008–2010)	8.4%	Support vector machines	AUC = 0.72 Sensitivity = 53% PPV = 13.1%
			Artificial neural networks	AUC = 0.75 Sensitivity = 75% PPV = 14.7%
DelPozo-Banos <i>et al.</i>	2604 Suicides and 52 080 controls identified in Welsh database of routine health records (2001–2015)	4.5%	Artificial neural networks	AUC = 0.8 Sensitivity = 64.5% PPV = 14.3%
Choi <i>et al.</i> 2018	2546 Suicides among a national cohort of 819 951 South Koreans (2004–2013)	0.3%	Support vector machines	AUC = 0.69
			Deep neural networks	AUC = 0.68
Gradus <i>et al.</i> 2020	10 152 Male and 3951 female suicides and 130 591 male and 134 592 female controls from Danish health registries (1995–2015)	Men = 7.8% Women = 2.9%	Classification trees	Men AUC = 0.80 Sensitivity = 32% PPV = 48%
				Women AUC = 0.88 Sensitivity = 54.4% PPV = 31%
Kessler, Stein <i>et al.</i> 2017	240 Suicides among a cohort of 238 888 USA military veterans who had mental health outpatient visits but had not been psychiatrically admitted (2004–2009)	0.1%	Naive Bayes, random forests, support vector regression and elastic net penalized regression	AUC = 0.59 Sensitivity = 22.4% PPV = 0.4%
Kessler, Hwang <i>et al.</i> 2017	6360 Suicides among 2112 008 USA military veteran controls (2009–2011)	0.3%	Penalized logistic regression, Bayesian additive regression tree	Sensitivity = 2.7% PPV = 8.1%
Simon <i>et al.</i> 2018	1240 Suicides among two cohorts of 2960 929 insured patients, USA (2009–2011)	0.04%	Penalized LASSO	Mental health specialty visits: AUC = 0.86 Sensitivity = 48% PPV = 0.26%
				Primary care visits AUC = 0.83 Sensitivity = 43% PPV = 0.13%

Note that sensitivity was tabulated because it reflects the capture of suicides in the high-risk group and PPV was tabulated because it is associated with the number of high risk false positive cases per predicted suicide. AUC, area under the curve; LASSO, least absolute shrinkage and selection operator; PPV, positive predictive value.

was limited, in most studies about 1% among the cohort studies with a base rate that was not inflated by case–control methodology. Moreover, two studies explicitly compared the predictive metrics of machine learning methods and more conventional statistical approaches. Choi *et al.* [25²⁵] found that Cox regression and the machine-learning methods of support vector machine and deep neural networks produced similar AUC statistics of 0.688, 0.687 and 0.683 respectively. Amini *et al.* [26] also compared a variety of prediction methods examining logistic regression decision trees, support vector machine and artificial neural networks finding similar AUC statistics of 0.752, 0.725, 0.719 and 0.748, respectively.

Other studies have examined the utility of machine learning to predict suicide attempts. Walsh *et al.* [27,28²⁸] examined the predictive accuracy of a machine-learning algorithm to detect suicide attempts in adults, and later adolescents, from hospital health record data and found an AUC of 0.8–0.9. Barak-Corren *et al.* used Bayesian modelling to predict future suicidal behaviour (attempts or deaths) using a retrospective cohort design of electronic health records of 1728 549 individuals who had visited a large healthcare centre three or more times over a 15-year period. The authors reported the model had an accuracy of approximately 90% [29]. However, this apparent level of overall accuracy was associated a sensitivity (33–45%), specificity (90–95%) and positive predictive value of (3–5%) – figures that are quite similar those derived using traditional statistical techniques. The reported accuracy in each of these studies benefited from a relatively higher base rate of suicide attempt when compared with suicide. In addition, reporting ‘accuracy’ may be misleading. Accuracy refers to the true positives and true negatives divided by the total number of Individuals, thus when the base rate of an outcome is low (i.e. low number of true positives) a high level of accuracy can still be achieved by a large number of true negatives as is generally the case in suicide research.

Potential imitations of machine learning prediction studies

Some authors believe that prediction studies using machine learning may have been limited by the way they reported their findings. In addition to the difficulty of interpreting accuracy, Fazel and O’Reilly [30³⁰] highlight that the calibration of the models is rarely reported limiting the interpretation of the metrics of sensitivity, specificity and AUC. This lack calibration reporting has been raised consistently as a limitation of machine-learning outside

suicide research [31³¹]. In a recent review of prediction studies in neurosciences, Poldrack *et al.* (2019) raised another limitation of prediction studies using machine learning, which is the practice of using the same or overlapping data to train the models on and then to test [32³²]. This methodological issue may limit the generalizability of the findings and may be a particularly relevant in suicide research because health services can be highly specific to the populations they serve [33³³].

It is also uncertain how the detection of suicide risk from electronic health data can be applied in practice [19¹⁹]. However, lead researchers in the field of machine learning and suicide believe that machine learning predictive models may be worthwhile even if they have statistical limitations because of the low cost. For example a clinician might be reminded to screen a patient for suicidal risk on the basis of an artificial intelligence algorithm that works seamlessly with the medical record [34]. However, the utility such an application is questionable given guidelines for primary care already include screening for common mental disorders and suicidal ideation in high risk groups [35].

While it may be that machine learning can achieve somewhat stronger suicide predictions than more conventional methods, this does not mean that machine-learning tools are not vulnerable to the pitfalls that have hindered the adoption earlier suicide prediction methods. For example, the goal of clinical risk prediction is rarely to predict whether individuals will engage in suicidal behaviour in the next 12 months, as is a common outcome in predictive studies [36]. Rather, the clinical goal of a suicide risk assessment is usually to identify people who are sufficiently high risk to justify a set of clinical interventions over much shorter periods. When studies of very short-term prediction are conducted, they will be faced with an even more challenging base rate problem.

One ethically concerning suggestion is that predictive analytics could be used to rule out those who do not truly have risk despite presenting for mental healthcare [33³³]. In medicine a ‘rule out’ test, must have high sensitivity, so as not to exclude suicide cases, a sensitivity that has not been achieved by machine learning (Table 1). More broadly machine learning does not impact the distinction between statistical validity and the clinical utility. In the past it has been argued that the low PPV of suicide risk assessment limits the range of indicated treatments to those that are benign and tolerable to the numerous false positives. Following on from this critics have suggested risk assessment is not useful in guiding treatment because benign and tolerable interventions should also be offered to low risk groups

among whom many if not most suicides will occur [37,38]. We fear that the distinction between statistical validity and clinical utility might be lost in the enthusiasm for machine learning, particularly given the difficulty clinicians and policy makers may have in understanding the statistical methods. For example, the reported high degree of accuracy reported in some studies may sound more convincing than other less intuitive predictive metrics that might be less remarkable. This enthusiasm for new methods might even trump concern about the lack of the transparency in decisions from 'black boxes' of machine learning [30].

Applications of artificial intelligence and prediction beyond identifying risk

Some authors suggest that the identification of individuals at risk may be less relevant in clinical services than practice of managing risk factors. Torous and Walker suggest that artificial intelligence may be useful in identifying risk where previous suicide attempt or diagnosis of mental illness are not present. These authors also identify opportunities for using artificial intelligence to efficiently disseminate interventions, particularly in the areas of safety planning, lethal means reduction and providing supportive contacts [39]. Artificial intelligence might be a driver of more sophisticated interventions such virtual counsellors, although such technology is still in the early stages, and early reviews by users suggest these methods will not be alternatives to face to face therapy in the near future [40].

Artificial intelligence might also be used to analyse continuously collected data, including data extracted or monitored on social media. To date the understanding of proximal and fluctuating risk factors for suicide has been limited by practical research considerations. An increased capacity to study proximal factors using technology has been identified as a major direction of future research [41]. Use of smartphones, wearable devices, social media and other connected devices to conduct ecological momentary assessment might allow for collection of data in the real-world settings and across different time periods. Such sources create complex data sets which would be unanalysable without machine learning and might hold opportunities for both the understanding of suicidal behaviour and its prevention.

CONCLUSION

Machine learning is likely to afford opportunities in mental health, but the application of artificial

intelligence should be carefully considered to avoid repeating the mistakes of existing methodologies. The application of artificial intelligence without a thorough understanding its limits may build in bias into new models. Prediction studies using machine learning have not yet added convincingly to our understanding of suicide and superiority in accuracy of machine learning over other methods is yet to be established. Prediction studies based on electronic health records are likely to be limited by the quality of the input data but novel data sources from outside health systems might add meaningfully to prediction and understanding of suicide. Predicting future suicidal behaviour is likely to be an elusive goal, but this should not detract from the importance of delivering suicide prevention interventions.

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Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

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3.2 Predictive modelling using machine learning in clinical population of young people

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3.2.1 Abstract

Purpose

Machine learning (ML) has shown promise in modelling future self-harm but is yet to be applied to key questions facing clinical services. In a cohort of young people accessing early intervention youth mental health care, this study aimed to establish 1) the performance of models predicting deliberate self-harm (DSH) compared to suicide attempt (SA), 2) the performance of models predicting new onset or repeat behaviour, and 3) the relative importance of factors predicting these outcomes.

Methods

802 young people aged 12-25 years attending early intervention youth mental health services had detailed social and clinical assessments at baseline and 509 completed 12 months follow-up. Four ML algorithms, as well as logistic regression, were applied to build four distinct models.

Results

The mean performance of models predicting SA (AUC: 0.82) performed better than the models predicting DSH (AUC: 0.72), with mean positive predictive values (PPV) approximately twice that of the prevalence (SA prevalence 14%, PPV: 0.32, DSH prevalence 22%, PPV: 0.40). All ML models outperformed standard logistic regression. The most frequently selected variable in both models was a history of DSH via cutting.

Conclusion

History of DSH and clinical symptoms of common mental disorders, rather than sociodemographic factors, were the most important variables in modelling future behaviour. The performance of models predicting outcomes in key sub-cohorts, those with new-onset or repetition of DSH or SA during follow up, was poor. These findings indicate that the performance of models of future DSH or SA may depend on knowledge of the individual's recent history of either behaviour.



Predictive modelling of deliberate self-harm and suicide attempts in young people accessing primary care: a machine learning analysis of a longitudinal study

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Abstract

Purpose Machine learning (ML) has shown promise in modelling future self-harm but is yet to be applied to key questions facing clinical services. In a cohort of young people accessing primary mental health care, this study aimed to establish (1) the performance of models predicting deliberate self-harm (DSH) compared to suicide attempt (SA), (2) the performance of models predicting new-onset or repeat behaviour, and (3) the relative importance of factors predicting these outcomes.

Methods 802 young people aged 12–25 years attending primary mental health services had detailed social and clinical assessments at baseline and 509 completed 12-month follow-up. Four ML algorithms, as well as logistic regression, were applied to build four distinct models.

Results The mean performance of models predicting SA (AUC: 0.82) performed better than the models predicting DSH (AUC: 0.72), with mean positive predictive values (PPV) approximately twice that of the prevalence (SA prevalence 14%, PPV: 0.32, DSH prevalence 22%, PPV: 0.40). All ML models outperformed standard logistic regression. The most frequently selected variable in both models was a history of DSH via cutting.

Conclusion History of DSH and clinical symptoms of common mental disorders, rather than social and demographic factors, were the most important variables in modelling future behaviour. The performance of models predicting outcomes in key sub-cohorts, those with new-onset or repetition of DSH or SA during follow-up, was poor. These findings may indicate that the performance of models of future DSH or SA may depend on knowledge of the individual's recent history of either behaviour.

Keywords Suicidal behaviour · Suicide attempt · Deliberate self-harm · Machine learning · Youth · Adolescence

Introduction

Self-harm and suicidal behaviours are common in young people and are associated with significant morbidity and increased risk of repeat suicidal behaviour and premature death by suicide [1, 2]. Population studies of young people who engage in self-harm have suggested that the majority of self-harm resolves without intervention [1]. Yet in clinical populations of young people, there is evidence that early self-harm and suicidal behaviour predicts onset and chronicity of major mental illness [2]. Evidence from population studies may be inappropriately applied to suicide prevention in clinical populations if the relationship between particular risk factors, or processes, and suicidal behaviour differ between these two settings. For example, male gender is commonly cited as a significant risk factor for suicide in the population, but appears to be less

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associated with increased death due to suicide in clinical settings [3]. It has also been argued that the phenomenological differences between non-suicidal deliberate self-harm and suicide attempts that have been reported in population samples may not be as readily apparent in clinical populations [4]. In population samples, non-suicidal self-harm is associated with less lethality or severity, more repetition and a greater likelihood of cutting than overdose or other high-risk methods [5, 6]. Kapur et al. have argued that in clinical settings, episodes of non-suicidal self-harm are not so easy to distinguish from episodes of self-harm with suicidal intent, as they may be in non-clinical populations [4]. In clinical populations having multiple, interacting risk factors is the norm, rather than the exception, and understanding how those factors interact is complex [7].

Studies of complex processes have been aided by developments in machine learning (ML), which allows for the analysis of the high-dimensional data sets, where the number of potential predictors exceed the outcome of interest. Initial ML studies in suicide research have focused on identifying those at risk of suicidal behaviour in generalist settings such as emergency departments or military health services, rather than in mental health services [8, 9]. Though important, these findings may over-emphasise the clinical utility of such models in mental health services where the prevalence of suicidal ideation and behaviour and associated risk factors is higher, and identification of suicidality via assessment and screening is much more likely to be standard practice [10, 11].

Theories of suicidal behaviour, such as the Ideation-to-Action framework, have also emphasised the limited clinical utility of research that identifies predictors of suicidal behaviour relative to healthy controls, as these features will not necessarily distinguish those with suicidal ideation from those who engage in a suicidal act, which is the focus of clinical services [6]. These limitations are important in machine learning, because performance metrics such as accuracy are influenced by the ratio of those with the outcome to those without, that is the prevalence of the outcome in a population [12, 13]. Recent reviews of predictive modelling of future suicidal behaviour have emphasised the importance of understanding sample and setting when interpreting performance metrics [13] and have recommended developing predictive models specific to sub-populations where positive predictive value is likely to be high enough to meaningfully guide adoption of clinical interventions within services [14, 15].

The current study draws on the approach used by Iorfino et al., which applied a set of machine learning (ML) algorithms to routinely collected clinical information to develop predictive models of self-harm and suicidal behaviour in young people accessing mental health care services [16]. Although the use of routinely collected administrative data

and/or clinical information in electronic health records (EHR) has been a focus of much machine learning health research, variables collected in EHRs can have limitations. For example, many EHRs may include diagnostic data, but not validated measures of symptoms or psychological constructs.

In the current study, a set of machine learning algorithms were applied to a comprehensive assessment battery containing validated self-report and clinician measures of social, clinical and psychological risk factors collected in a cohort of young people accessing community-based mental health services [17]. The set of algorithms was used to build four distinct ML models designed to address key questions facing clinical services delivering suicide prevention interventions. The study first aimed to establish performance of models predicting DSH or SA in the entire cohort, and whether performance differed by outcome. The second aim was to establish the performance of models predicting outcomes in key sub-groups, those with new-onset DSH or SA, and those who repeat DSH or SA. Finally, the study aimed to assess the relative importance of clinical and psychosocial factors predicting these outcomes.

Methods

This study describes a longitudinal cohort study of 802 young people aged 12–25 years old accessing primary youth mental health care, known as the Transitions study [17]. The Transitions study was designed to assess a range of clinical, social and functional outcomes (including suicidal behaviour) of young people accessing youth-specific primary mental health services, known as ‘headspace’ clinics [17, 18]. Young people can self-refer, or be referred by clinicians, family members or school counsellors. Although the services provided by individual headspace clinics varies, the clinics included in this study contained a mix of primary mental health care and more specialised mental health services. Therefore, the presentations of young people attending these clinics ranges from non-specific and early-stage presentations to more discrete episodes of mental illness, including major mood disorder and psychosis [17].

The current study includes 802 young people who attended one of four clinics in Melbourne or Sydney, between January 2011 and August 2012. 509 young people completed a follow-up assessment at 12 months. Participants were invited to participate in the study by a trained research assistant (RA) after their initial clinical visit. Further details of the study methodology have been previously published [17]. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used [19].

Social and clinical assessment

The assessment battery included validated measures of clinical and psychosocial risk factors, which included both interviewer-led and self-report measures [17]. Measures included as part of the baseline assessment are detailed in Table 1 and are also detailed in the original study protocol [17]. Participants completed comprehensive assessments at two timepoints, baseline and 12-month follow-up. Assessment interviews were conducted by RAs, who were trained in use of study assessment measures and achieved an inter-rater reliability of at least 0.8 for interview-led measures. Demographic factors collected included age, gender, sexual orientation, ethnicity and country of participant's birth and parent's birth.

Self-harm and suicidal behaviour outcome measures

Questions assessing deliberate self-harm (DSH) and suicide attempts (SA) in the 12 months prior to each timepoint were interviewer-led and were previously adapted by Patton et al. from the Beck Suicide Inventory [20]. Further details of the assessment are included in Supplementary material Table 1. To ensure that participants who engaged in both deliberate self-harm and suicide attempts were not double counted, those who engaged in a suicide attempt were analysed in the suicide attempt group. History of DSH and/or suicide attempt was coded into three categories based on presence of a behaviour in the 12 months prior to each assessment; (1) those without self-harm, (2) a deliberate self-harm group (with DSH but had no suicide attempts); and (3) a suicide attempt group (those who reported having made a suicide attempt and may or may not have engaged in DSH also).

Statistical analysis

Baseline social and clinical factors were analysed by outcome at 12 months, using chi-squared tests for categorical predictors and ANOVA for continuous predictors. The Bonferroni method was used to adjust for multiple testing. Post hoc tests were carried out using Scheffé's test to determine where significant differences were. The baseline characteristics of the 293 participants who did not complete follow-up assessment were compared to the remaining sample, using t-tests for continuous variables and chi-squared tests for categorical variables (Supplementary table 3). Missing data from the 509 participants who did complete follow-up were inspected and found to be consistent with a missing-at-random pattern (Supplementary table 2). No variable was missing more than 10% of data. Missing data were imputed using the 'multivariate imputation by chained equations' ('mice')

package in R [21]. Five imputations were run, using predictive mean matching for continuous variables and logistic regression for categorical variables, both used all available data. Imputed datasets were modelled separately, and coefficients, standard errors and test statistics were pooled. All analyses were performed in R (version 3.6.3) [22].

Model building

We applied four different machine learning algorithms, as well as logistic regression, to build four different machine learning (ML) models representing different clinical samples to address our key questions (Fig. 1). The term ML model is used here to refer to a set of algorithms. Each algorithm was run for 100 trials and thus, the performance of each model represents the mean performance metrics over 500 trials (i.e. 5 algorithms $\times$ 100 trials).

Model 1 compared the group of participants who reported DSH at follow-up (but no SA), to all participants who reported no self-harm during follow-up. *Model 2* compared all participants who reported SA during follow-up, to all who reported no self-harm during follow-up. *Model 3* and 4 analysed predictors of specific sub-groups, those who repeated DSH or SA during care, or those who had new-onset DSH or SA during care. *Model 3* sampled only participants who reported no self-harm at baseline and compared those who reported new-onset DSH or SA at follow-up with those who had no self-harm at follow-up. *Model 4* sampled only participants who reported either DSH or SA at baseline and compared those who went on to repeat either behaviour during follow-up to those who reported no further DSH or SA.

Machine learning algorithms and regression

Each ML model was built by applying multiple machine learning algorithms to the set of 50 potential predictors (Table 1). This approach is designed to improve predictive performance of a model, as well as the validity of variable selection out of a large number of potential predictors [12]. We followed the methods described in Demetriou et al. [23]. The algorithms selected were Area Under the Curve Random Forests (AUCRF), Boruta, Least absolute shrinkage selection operator (LASSO) regression, elastic-net regression and logistic regression. In this study LASSO and elastic-net regression were forms of logistic regression given the binary outcome. Both AUCRF and Boruta are variants of the random forest (RF) algorithm. For each RF model we generated 1000 decision trees. For both RF (AUCRF and Boruta) and the penalised logistic regression techniques (LASSO and elastic-net regression), we used the internal fivefold cross-validation to identify the optimal lambda and alpha coefficient. Lambda controls the strength of penalization in

Table 1 Social and clinical assessment battery

Domain	Sub-domains	Measure	Interpretation
Demographics	Age	In years	
	Gender		Male, female, other
	Sexuality		Heterosexual or same sex attracted
Clinical symptoms (clinician-rated)			
Depression	Mood and cognitive symptoms	QIDS-8 [21]	Higher score denotes greater symptom severity
Sleep and energy	Suicidal ideation	QIDS, item 12	Yes/no, where a score of 2 or more indicates yes
	Initial insomnia	QIDS, item 1	
	Mid-nocturnal insomnia	QIDS, item 2	
	Early morning waking	QIDS, item 3	
	Hypersomnia	QIDS, item 4	
	Fatigue	QIDS, item 14	
	Psychomotor slowing	QIDS, item 15	
	Psychomotor agitation	QIDS, item 16	
Mania	Mania symptoms	YMRS, 11 items [22]	Higher score indicates greater symptom severity in the last 48 h
Clinical stage	Stage 1A	Clinical staging model [23]	Non-specific symptoms
	Stage 1B		Attenuated syndrome
	Stage 2 +		First episode of discrete disorder or persistent, recurrent mental illness)
Clinical symptoms (self-report ^a)			
Rumination	Rumination	Rumination scale, 10 items [24]	Higher score indicates greater rumination
Psychological distress	Psychological symptoms	SPHERE-12, 6 items [25]	Higher score indicates greater symptom severity
	Somatic symptoms	SPHERE-12, 6 items	
Anxiety	Generalised anxiety symptoms	GAD, 7 items [26]	Higher score indicates greater symptom severity
	Frequency, severity and impact of anxiety symptoms	OASIS, 5 items [27]	Higher score indicates greater symptom severity
Disordered eating and associated behaviours	Preoccupation with weight or shape	SCOFF, 5 items [28]	Higher score indicates greater symptom severity
	Purging		
	Weight loss		
Substance use	Alcohol	WHO-ASSIST, Q2 [29]	High risk/ low risk
	Cannabis		High risk indicates at least monthly use in last 3 months
	Tobacco		
	Other illicit drugs (excluding above)	WHO-ASSIST, Q1	High risk/ low risk
			High risk indicates any history of use over the lifetime
Psychological and developmental factors (self-report ^a)			
Personality	Reward-responsiveness	BIS/BAS, 24-item scale [30]	Higher score indicates higher expression of trait
	Fun-seeking		
	Drive		
	Behavioural inhibition		
Childhood abuse	Physical abuse	CTQ, sub-scales [31]	Higher score indicates greater severity of abuse history
	Sexual abuse		
	Emotional abuse		
Parenting	Care	PBI [32]	Higher score indicates greater experience of sub-domain
	Over-protectiveness	Paternal	
	Authoritarian	Maternal	

Table 1 (continued)

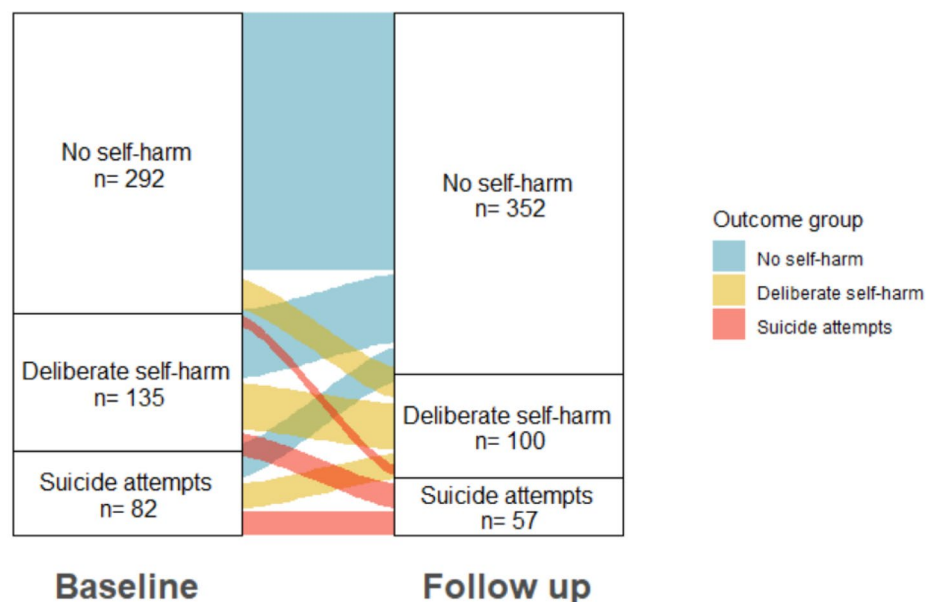
Domain	Sub-domains	Measure	Interpretation
Social factors (self-report ^a)			
Current employment or education	Education or employment, full-time or part-time	NEET [33]	Yes/no, where no indicates not in either employment or education
Social and occupational functioning	Level of functioning (clinician-rated)	SOFAS [34]	Higher score indicates higher functioning
Financial stress	Difficulty paying rent or utilities in last 6 months	ABS 2006 census [33]	Higher score indicates greater severity of stress
Recent adverse life events	Adverse life events	Brugha life stress scale, 11 items [35]	Higher score indicates greater severity of stress
Social support	Support from friends Support from family Conflict with friends Conflict with family	Schuster Social support scale, 20 items [39]	Higher score indicates greater experience of sub-domain

Somatic symptoms: refers to symptoms that may occur as part of a somatisation process whereby psychological distress is experienced as physical symptoms, including musculoskeletal pain, fatigue, poor sleep and/or gastrointestinal symptoms (nausea, diarrhoea, constipation)

ABS Australian Bureau of Statistics, BIS/BAS behavioural inhibition/behavioural activation system, CTQ childhood trauma questionnaire, GAD-7 generalised anxiety disorder scale, NEET Not in education or employment, PB parental bonding instrument, QIDS quick inventory of depressive symptoms, SPHERE somatic and psychological health report, SOFAS social and occupational functioning assessment scale, OASIS overall anxiety severity and impairment scale, WHO-ASSIST World Health Organisation Alcohol, Smoking and Substance Involvement Screening Test

^aself-report unless otherwise indicated

Fig. 1 Machine learning model building. Model 1 predicts all participants who report DSH at follow-up ($n=100$, yellow group) relative to those with no self-harm at follow-up ($n=352$, blue group). Model 2 predicts participants who report SA at follow-up ($n=57$, red group) relative to those with no self-harm at follow-up ($n=352$) (blue group). Model 3 samples only those without self-harm at baseline ($n=292$). Model 4 samples only those with either DSH or SA at baseline ($n=217$)



LASSO and elastic-net regression and alpha controls the balance between L1- and L2-regularisation in elastic-net regression. Logistic regression, using a backwards stepwise approach, was included to allow for comparability between the other four algorithms and traditional statistical approach.

Another common problem faced in suicide research using machine learning is the issue of unbalanced datasets [12]. To account for unbalanced samples the synthetic minority over-sampling technique (SMOTE) algorithm

was used [24], which allows for the number of patients in the minority class to be doubled by synthetic generation of cases. Borderline samples were identified via Gower distance and removed in order to increase the separation between sample classes [25]. Additionally, random under sampling of the majority class was used to balance with the minority class.

Model validation and performance

Models were built and trained using 10 repeats of tenfold cross-validation, to address the risk of over-fitting the data as can occur in high-dimensional data sets [26, 27]. In each fold, samples were trained on 90% of data, and tested on 10% of data. The test set remained unaltered to assess the ML models' performance on the real-world prevalence of deliberate self-harm and suicide attempts. Where the outcome variables were balanced, neither SMOTE nor random under sampling was implemented.

The performance of each algorithm within a model was compared using metrics including Area Under the Receiver-Operating Curve (AUROC), Area under the Precision–Recall Curve (AUPRC), sensitivity, specificity, brier score and positive predictive value. AUROC is a measure of the ability of a statistical model to discriminate between a binary outcome at all possible thresholds between 0 and 1. The ROC curve plots the true positive rate (also referred to as sensitivity or recall) against the false-positive rate ($1 - \text{specificity}$). An AUROC of 0.5, indicates a statistical model is no better at predicting an outcome than chance. An AUROC > 0.8 would generally be considered a strong performance, and 0.7–0.8 as good, 0.6–0.7 as sufficient and 0.5–0.6 as weak [28]. The area under the precision–recall curve is considered a more valid measure of performance of imbalanced datasets when detecting positive cases is important [29]. The AUPRC plots the precision against recall, and hence the baseline for comparison should be the prevalence of the outcome in the sample. For example, if the prevalence of an outcome is 20%, then an AUPRC of 0.6 would be considered good, whereas if the prevalence is 60% an AUPRC of 0.6 would indicate the performance of the algorithm is no better than chance. Brier score measures discrimination and calibration, that is the magnitude of error in the probability estimates [30]. A brier score ranges from 0 (perfect accuracy) to 1 (perfect inaccuracy). Positive predictive value (PPV) was calculated for each algorithm to allow for an assessment of how clinically useful such an algorithm, and the ML model it informs, may be. PPV is influenced by the prevalence of an outcome in the sample and is dependent on a specific probability threshold, unlike AUROC and AUPRC.

Variable selection

As each of the five algorithms produced 100 trials, we present summarised statistics for variable selection. For AUCRF and Boruta, a variable is deemed selected if it is present in the final iteration of the random forest trial algorithm. For the remaining regression-based techniques, a variable is deemed selected if the coefficient is not zero.

The frequency with which a variable was selected was summed across the 500 trials and ranked against other variables for each ML model. Final variable importance was determined based on whether a variable was selected in greater than 70% of trials per algorithm. Variables were also ranked by frequency of selection in descending order, with those ranked 1–10 indicating greatest importance.

Results

Of the 802 participants who completed the baseline assessment, 509 participants (mean age 18.3 years, 69% females) completed the follow-up assessment at 12 months. Factors associated with the 37% (293/802) lost to follow-up were being of male gender, having lower baseline social and occupational functioning, being of earlier clinical stage and being more likely to report lifetime drug use (Supplementary table 3). Bivariate associations between baseline clinical and social variables and outcome group are presented in Supplementary Table 4.

Prevalence and method of self-harm and suicide attempts at baseline

At baseline, 26.7% (214/802) reported engaging in deliberate self-harm but no suicide attempts and 15.8% (128/802) reported having made a suicide attempt (Table 2). All those who reported a suicide attempt had also engaged in an episode of deliberate self-harm. Therefore 42.3% (342/802) engaged in at least one episode of deliberate self-harm in the 12 months prior to baseline. Cutting or burning was the most common method of deliberate

Table 2 Prevalence of suicidal behaviour at baseline and follow-up

Baseline	Follow-up				
	No self-harm	Deliberate self-harm	Suicide attempt	No follow-up	Total
No self-harm, <i>n</i> (%)	251 (54.6)	30 (6.5)	11 (2.4)	168 (36.5)	460 (100)
Deliberate self-harm, <i>n</i> (%)	67 (31.3)	45 (21.0)	23 (10.7)	79 (36.9)	214 (100)
Suicide attempt, <i>n</i> (%)	34 (26.6)	25 (19.5)	23 (18.0)	46 (35.9)	128 (100)
Total	352	100	57	293	802

self-harm, reported by 70% (238/342) of those who self-harmed, while overdose or poisoning was the most common method of suicide attempt, reported by 50% (64/128) of those who reported a suicide attempt. Engaging in multiple methods of self-harm or suicidal behaviour was also common, with more than 38% (130/342) reporting engagement in two or more methods.

Prevalence and rates of repetition of self-harm and suicide attempts at follow-up

Of the 509 participants assessed at follow-up 11.2% (57 of 509) reported having made a suicide attempt and engaged in deliberate self-harm and 19.6% (100 of 509) reported an episode of deliberate self-harm without suicide attempt in the 12-month follow-up period. All those who made a suicide attempt also reported an episode of DSH. The proportion of young people with DSH or SA at baseline, who repeated DSH or SA in 12 months of follow-up was high (53.5%, 116/217). Of those who completed follow-up and had no history of self-harm or suicide attempts at baseline, 14% (41 of 292) reported new-onset self-harm or suicidal behaviour (DSH without SA 10.3%, SA 3.8%) in the follow-up period.

Risk of DSH or SA during follow-up varied by type of baseline self-harm behaviour (i.e. intent and method used) (Fig. 2A). Young people who reported having made a suicide attempt at baseline assessment were twice as likely to report having made a suicide attempt during follow-up than those who had engaged in DSH only at baseline (OR 15.4, CI 6.9–34, vs. OR 7.8, CI 3.6–16.9); however, it should be noted that both ORs were associated with a wide confidence interval, which overlapped. DSH via cutting or burning at baseline was associated with the

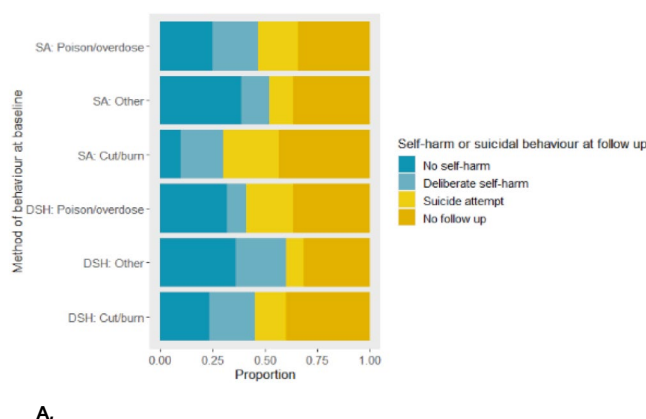
greatest odds of either DSH or SA during follow-up (see Fig. 2B). Suicide attempt at baseline by cutting or burning and DSH by poison or overdose were both also associated with an increased OR of suicide attempt during follow-up.

Machine learning algorithms and model selection

The mean and standard deviation for performance metrics of each algorithm, AUCRF, Boruta, Elastic-net regression, LASSO and logistic regression, are described in Table 3. The performance of each algorithm on the training dataset is available in Supplementary material (Supplementary Fig. 1A–D). The elastic-net regression algorithm was associated with a slightly better mean AUROC in each ML model, aside from Model 3 where it was ranked behind LASSO and Boruta. Logistic regression, which was included for comparison, was ranked 5th in terms of performance metrics in each ML model, aside from Model 1, where Boruta was ranked last and logit performance was on par with the AUCRF. Aside from logistic regression, which was associated with reduced performance, other algorithms had similar performance.

Model performance

The mean performance of models predicting either DSH (Model 1) or SA (Model 2) were both strong. The ML model predicting SA was associated with greater mean performance metrics than the model predicting DSH (SA: AUC: 0.82 sensitivity: 0.72, specificity: 0.78, DSH: AUC: 0.72 sensitivity: 0.62, specificity: 0.73). The mean positive predictive value (PPV) of the ML model predicting SA was approximately twice that of the prevalence (SA prevalence



	DSH OR (95% CI)	SA OR (95% CI)
SA: Poison/overdose	1.85 (0.8–4.6)	1.5 (0.6–4.2)
SA: Other	0.45 (0.2–1.3)	0.6 (0.2–2.0)
SA: Cut/burn	2.54 (0.5–11.9)	8.3 (1.8–37.1)
DSH: Poison/overdose	0.9 (0.2–5.0)	6.7 (1.5–29.4)
DSH: Other	2.84 (1.5–5.4)	1.6 (0.6–3.9)
DSH: Cut/burn	5.4 (3.2–9.1)	8.5 (4.3–16.6)

B.

Fig. 2 Method of behaviour at baseline and likelihood of further DSH or SA. Samples only those young people who reported DSH or SA at baseline ($n=342$) and includes those lost to follow-up. **A** presents the proportion of young people in each outcome group by method of

DSH or SA at baseline, and **B** presents the odds ratio of either outcome, DSH or SA, according to baseline behaviour and method. Reference group for odds ratio calculations was those who completed follow-up and reported no further self-harm

Table 3 Performance metrics of each algorithm by model

ML model	Sample	Algorithm	AUROC, mean (SD)	AUPRC, mean (SD)	Brier score, mean (SD)	Sensitivity, mean (SD)	Specificity, mean (SD)	PPV, mean (SD)
Model 1 (<i>n</i> =452)	DSH at follow-up (<i>n</i> =100) vs. No self-harm at follow-up (<i>n</i> =352)	AUCRF	0.71 (0.10)	0.39 (0.10)	0.20 (0.02)	0.57 (0.16)	0.75 (0.08)	0.40 (0.11)
		Boruta	0.68 (0.11)	0.37 (0.11)	0.21 (0.03)	0.56 (0.16)	0.74 (0.08)	0.38 (0.10)
		Elastic-net	0.74 (0.09)	0.42 (0.12)	0.20 (0.03)	0.62 (0.16)	0.74 (0.08)	0.41 (0.09)
		LASSO	0.74 (0.09)	0.42 (0.11)	0.20 (0.03)	0.62 (0.15)	0.75 (0.07)	0.42 (0.09)
		Logit	0.71 (0.09)	0.39 (0.11)	0.24 (0.05)	0.61 (0.15)	0.70 (0.08)	0.37 (0.07)
	Prevalence of outcome 22%							
Model 2 (<i>n</i> =409)	SA at follow-up (<i>n</i> =57) vs. No self-harm at follow-up (<i>n</i> =352)	AUCRF	0.79 (0.09)	0.32 (0.12)	0.17 (0.03)	0.71 (0.18)	0.75 (0.07)	0.32 (0.09)
		Boruta	0.80 (0.10)	0.34 (0.13)	0.17 (0.03)	0.69 (0.19)	0.76 (0.08)	0.33 (0.11)
		Elastic-net	0.82 (0.09)	0.36 (0.11)	0.17 (0.04)	0.71 (0.20)	0.78 (0.07)	0.35 (0.11)
		LASSO	0.82 (0.09)	0.35 (0.11)	0.18 (0.04)	0.70 (0.20)	0.78 (0.07)	0.35 (0.10)
		Logit	0.68 (0.11)	0.10 (0.09)	0.29 (0.08)	0.61 (0.18)	0.72 (0.09)	0.27 (0.09)
	Prevalence of outcome 13.9%							
Sub-group analyses								
Model 3 (<i>n</i> =292)	New-onset DSH or SA (<i>n</i> =41) vs. No history of self-harm at BL or FU (<i>n</i> =251)	AUCRF	0.57 (0.14)	0.17 (0.06)	0.23 (0.04)	0.39 (0.25)	0.69 (0.10)	0.17 (0.10)
		Boruta	0.58 (0.15)	0.17 (0.06)	0.22 (0.03)	0.41 (0.25)	0.70 (0.10)	0.18 (0.10)
		Elastic-net	0.57 (0.15)	0.18 (0.08)	0.26 (0.06)	0.43 (0.26)	0.67 (0.12)	0.18 (0.12)
		LASSO	0.58 (0.14)	0.18 (0.08)	0.26 (0.05)	0.43 (0.25)	0.67 (0.12)	0.18 (0.11)
		Logit	0.51 (0.14)	0.12 (0.07)	0.41 (0.10)	0.45 (0.24)	0.58 (0.11)	0.15 (0.08)
	Prevalence of outcome 14%							
Model 4 (<i>n</i> =217)	Repeat DSH or SA (<i>n</i> =116) vs. No repeat DSH or SA (<i>n</i> =101)	AUCRF	0.61 (0.11)	0.59 (0.09)	0.26 (0.04)	0.50 (0.14)	0.66 (0.15)	0.64 (0.13)
		Boruta	0.62 (0.11)	0.59 (0.09)	0.27 (0.04)	0.50 (0.14)	0.67 (0.14)	0.64 (0.12)
		Elastic-net	0.64 (0.11)	0.60 (0.08)	0.25 (0.03)	0.47 (0.15)	0.71 (0.15)	0.66 (0.12)
		LASSO	0.62 (0.12)	0.59 (0.09)	0.25 (0.03)	0.45 (0.17)	0.71 (0.16)	0.38 (0.19)
		Logit	0.55 (0.12)	0.54 (0.08)	0.35 (0.07)	0.46 (0.14)	0.61 (0.16)	0.58 (0.12)
	Prevalence of outcome 53.4%							

Each algorithm was run over 100 trials, thus results of 500 trials were used to calculate mean and standard deviation of each performance metric. In the ML models with samples that were unbalanced in terms of outcome groups (Models 1–3) random under sampling of controls and synthetic generation of cases were used to adjust for this. ML Model 4 which compared participants with repeat DSH/SA versus those without repeat behaviour was balanced by outcome so these techniques were not required

AUCRF area under the curve random forest, *AUROC* area under the receiver-operator curve, *AUPRC* area under the precision–recall curve, *BL* baseline, *DSH* deliberate self-harm, *FU* follow-up, *ML* machine learning, *PPV* positive predictive value, *SA* suicide attempt, *SD* standard deviation

14%, PPV: 0.32), as was the ML model predicting DSH (prevalence 22%, PPV: 0.4).

Model 3 which tested the ability of the algorithms to predict new-onset DSH or SA during follow-up amongst participants who reported no history of DSH or SA at baseline performed poorly (AUROC 0.55, AUPRC: 0.16, sensitivity: 0.26, specificity: 0.76). Both AUROC and AUPRC indicated that Model 3 is little better than chance at predicting new-onset DSH or SA. Model 4 which tested the ability of the algorithms to predict repetition of DSH

or SA among those who reported either behaviour at baseline, performed slightly better (AUROC 0.63, sensitivity: 0.53, specificity: 0.67). The mean positive predictive values of Models 3 and 4 were only slightly greater than prevalence (Model 3 prevalence 14%, PPV: 0.17, Model 4 prevalence 53%, PPV: 0.63).

Variable selection

Models 1 and 2 were used for variable selection as the performance metrics of these models indicated they were

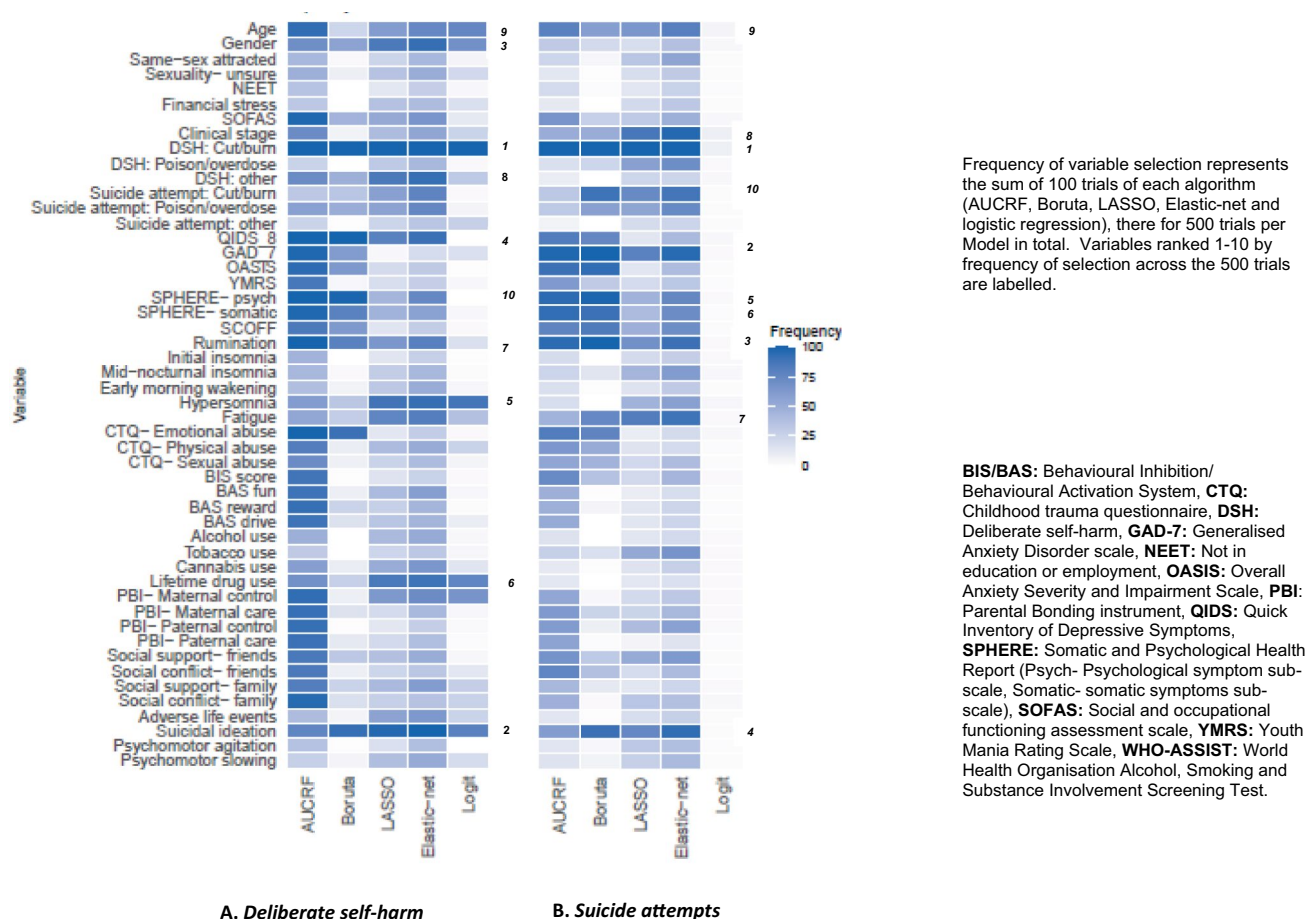


Fig. 3 Heatmap displaying frequency of variable selection by each algorithm in ML Model 1 and Model 2. Frequency of variable selection represents the sum of 100 trials of each algorithm (AUCRF, Boruta, LASSO, Elastic-net and logistic regression), there for 500 tri-

als per Model in total. Variables ranked 1–10 by frequency of selection across the 500 trials are labelled. **A** presents variable selection in Model 1 (deliberate self-harm) and **B** presents variable selection in Model 2 (suicide attempts)

accurate enough to be used for variable selection. Models 3 and 4 were no better at predicting outcomes than chance, thus using these models for variable selection was not appropriate. Figure 3 presents a heatmap of the frequency of variable selection by each algorithm in Model 1 (Fig. 3A) and 2 (Fig. 3B). History of deliberate self-harm via cutting at baseline was the most frequently selected predictor in both models, being selected in all 500 trials of algorithms predicting DSH at follow-up and 408 trials of algorithms predicting SA at follow-up. While half of the variables ranked 1–10 by frequency of selection across algorithm trials were common to models of both outcomes (DSH via cutting, suicidal ideation, general psychological distress, rumination and younger age), there was also evidence for a distinct pattern of variable selection between the models predicting DSH or SA. Symptoms of generalised anxiety, fatigue, somatic symptoms, a history of suicide attempt by cutting, more advanced clinical stage (> stage 1B), and eating disorder symptoms, were variables important to the prediction of SA (i.e. Model

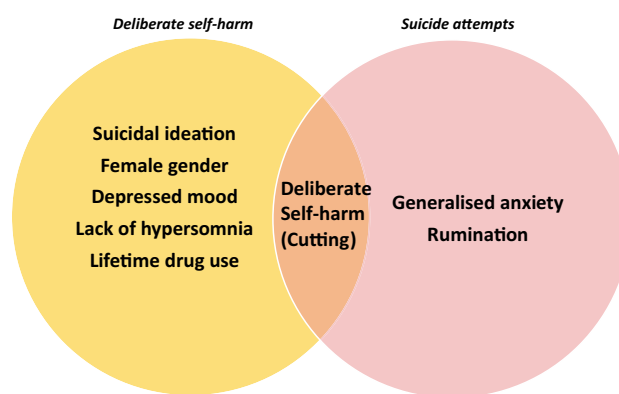


Fig. 4 Variables important to the prediction of DSH and/or SA. Important variables were those that were selected in at least 70% of algorithm trials

2, Fig. 3B) but not DSH (i.e. Model 1, Fig. 3A). Variables that were ranked within 1–10 in models of DSH but not SA were an absence of hypersomnia, female gender, depressive symptoms (QIDS-8), a history of recreational drug use, and deliberate self-harm by engaging in high-risk behaviours.

Figure 4 presents variables selected in at least 70% of algorithm trials. Those selected in algorithms predicting DSH were suicidal ideation (446/500), female gender (374/500), depressive symptoms (QIDS-8) (371/500), absence of hypersomnia (365/500), and lifetime drug use (350/500). After DSH by cutting, only two other variables were selected in at least 70% of algorithm trials predicting SA, generalised anxiety symptoms (GAD-7) (377/500) and ruminative thinking (358/500).

Discussion

Machine learning models predicting deliberate self-harm and suicide attempts differed in terms of their ability to predict future events, as well as in the variables selected to do so. Both models predicting either DSH or SA performed well, though the model predicting SA was superior with greater mean AUROC, as well as greater mean sensitivity and mean specificity. While a number of variables were frequently selected in both, there was also evidence that some factors were important to either DSH or SA models but not both (Fig. 4). Our findings suggest risk factors within clinical populations of young people are different to those of population samples of young people. For example, our findings suggest that in clinical samples, method of self-harm or suicidal behaviour may be as important as whether the behaviour is associated with suicidal intent in determining future risk of suicide attempt. For example, cutting, with or without suicidal intent was more important in predicting future suicide attempt than other methods where suicidal intent was present. Similarly, deliberate self-harm (without suicidal intent) via poisoning was more frequently selected by algorithms predicting future suicide attempts, but not deliberate self-harm. In population samples, overdose and poisoning are usually more strongly associated with suicide attempts than non-suicidal self-harm [6], and our findings suggest that in clinical samples an overdose should be considered a greater risk of future suicidal behaviour regardless of whether suicidal intent is expressed.

Aside from age and a history of self-harm or suicide attempts the highest-ranking variables in each model were almost entirely validated symptom scales of common mental disorders, rather than other social or demographic factors. Although social factors are important risk factors at a population level, our findings suggest that common symptoms of mental disorder play a pivotal role in the expression of self-harm and suicidal behaviour in clinical settings. Rather than

indicate that social factors are not important contributors to suicide risk it appears that such risk factors were similarly prevalent in young people in clinical settings with or without self-harm or suicidal behaviour. There was also evidence for a distinct pattern of predictors between the two outcomes. Gender was an important variable in the model of DSH but was not frequently selected in the prediction of SA, adding further evidence to the more limited effect of gender on suicidal behaviour in clinical services [31, 32]. More advanced clinical stage (> stage 1B), somatic symptoms, generalised anxiety and symptoms of disordered eating and disturbance of body image ranked highly in the prediction of SA but not DSH. These symptom clusters are often associated with more severe disorders in young people that tend to follow a more chronic or relapsing course. For example, fatigue and somatic symptoms are associated with more severe variants of depression, including bipolar depression and treatment resistant depression [33]. Co-morbid symptoms of generalised anxiety or disordered eating may increase treatment resistance [33].

Our findings of the importance of clinical symptoms to future self-harm or suicidal behaviour suggest that leading theories of suicidal behaviour may require adaption to clinical settings. Theorists have suggested that mental disorders contribute to suicidal behaviour via their effect on suicidal ideation or in certain conditions by increasing agitation, but not beyond that [34]. In the context of clinical services, it must be considered that a diagnosis of a major mental illness such as a moderate to severe major depressive episode, can account for many features of the leading ideation-to-action theories, including the experience of hopelessness, worthlessness, withdrawal from relationships and perceived isolation. The experience of mental illness, which is often episodic and relapsing in course, may also increase the likelihood of experiencing prolonged or recurrent symptoms and, thus, result in greater degree of social and functional impairment and have a greater impact on an individual's sense of belonging and development of intimate relationships. Further research into the impact of symptom improvement on future suicidal behaviour in cohorts of young people accessing clinical care is needed.

Our second aim was to understand how predictive modelling performed when predicting new-onset or repeat DSH or SA. Models of new-onset or repeat DSH or SA were developed by sampling sub-groups of participants to understand how the models performed when baseline DSH or SA is known, which is often the case in clinical services. Both models performed poorly and were only slightly better at predicting outcome than chance. These findings re-affirm the importance of previous self-harm or suicidal behaviour in determining risk of future behaviour and suggest that performance of predictive modelling on heterogeneous

samples where history of suicidal behaviour is not controlled for may be inflated. Despite this, the prevalence of repeat DSH or SA (53.4%) in those who reported either at baseline was high enough to justify a set of enhanced clinical interventions for this group. On the other hand, the incidence of new DSH or SA, in those without either behaviour at baseline was similar to the incidence in the age-matched population [35]. Understanding what type of clinical suicide prevention interventions should be delivered to this sub-group remains a challenge. More longitudinal data on outcomes in this group may help clarify how suicide prevention should be prioritised relative to other clinical priorities. As highlighted by Bossarte et al. [36] future ML studies may move away from a focus on prediction of future suicidal behaviours, and instead focus on predicting response to treatment.

There were a number of limitations in this study. Although analysing high-dimensional data sets without over-fitting is considered a distinct advantage of machine learning, the smaller sample size of the sub-group analyses remains a limitation. A number of techniques were used to reduce the risk of over-fitting (cross-validation, test–train splitting, SMOTE). However, dimensionality reduction prior to predictive modelling, for example through principal component analysis, is another approach recommended to improve performance metrics and validity, and reduce any effect of collinearity [37]. The use of additional approaches to dealing with imbalanced data, such as weighting the algorithm loss function to penalise false-negative results more than false-positive results may have increased the robustness of the analysis [38].

As a rule, variable selection should be interpreted with caution in machine learning studies as ML has a limited ability to examine associations between predictors. In the current study some validated measures, were broken down into key symptom clusters and included as separate variables. This was decided a priori to examine specific symptom clusters that have been shown to have an association with suicidal behaviour independent of the disorder measured by the parent scale [39, 40]. However, this may have increased the interaction between variables, and thus reduced the validity of the variable selection process.

It should also be noted the current study focus on a community-based mental health service for young people (12–25 years) and collected history of DSH or suicide attempt via clinical interview. Loss to follow-up was also greater in those at an earlier clinical stage. This may limit the generalisability of the findings to other clinical mental health settings, such as emergency departments, or cohorts of different ages, or in samples with suicidal behaviour that has been confirmed by assessment during a hospital presentation.

Conclusion

Modelling of future self-harm and suicidal behaviour should be specific to particular clinical settings and clinical questions. This is crucial as the performance of predictive models is related not only to the prevalence of the outcome of interest in the sample but also on whether a service or clinician has prior knowledge of the individual's history of deliberate self-harm or suicide attempts. Predictors of DSH or SA in clinical populations of young people differ from those of population samples. Method of DSH or SA used may be as important to prediction of future behaviours as the expression of suicidal intent. While a history of DSH via cutting was the most important variable in predicting both outcomes, other highly ranked predictors represented a greater experience of clinical symptoms. Given the significant role clinical symptoms play in predicting deliberate self-harm or suicide attempts in young people accessing clinical services, the key suicide prevention in this cohort should be the delivery of high-quality clinical care that aims for recovery, of which amelioration of symptoms is one component.

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Data availability The Transitions cohort data is not open access but may be made available upon request to the original study authors and subject to ethical and organisational review.

Declarations

Conflict of interest Catherine M. McHugh, Frank Iorfino, Jacob J Crouse, Alissa Nichles, Natalia Zmicerevska, Nicholas Ho, and Nick Glozier report no conflicts of interest. Elizabeth Scott is the clinical director of the St Vincent's Youth Mental health programme. She has received honoraria for educational seminars related to the clinical management of depressive disorders supported by Servier and Eli-Lilly pharmaceuticals. She has participated in a national advisory board for the antidepressant compound Pristiq, manufactured by Pfizer. She was the National Coordinator of an antidepressant trial sponsored by Servier. Ian Hickie was an inaugural Commissioner on Australia's National Mental Health Commission (2012–18). He is the Co-Director, Health and Policy at the Brain and Mind Centre (BMC) University of Sydney. The BMC operates an early-intervention youth services at Camperdown under contract to headspace. Professor Hickie has previously led community-based and pharmaceutical industry-supported (Wyeth, Eli Lilly, Servier, Pfizer, AstraZeneca) projects focused on the identification and better management of anxiety and depression. He was a member of the Medical Advisory Panel for Medibank Private until October 2017, a Board Member of Psychosis Australia Trust and a member of Veterans Mental Health Clinical Reference group. He is the Chief Scientific Advisor to, and an equity shareholder in, Innowell. Innowell has been formed by the University of Sydney and PwC to deliver the \$30 m Australian Government-funded 'Project Synergy'.

Project Synergy is a three-year programme for the transformation of mental health services through the use of innovative technologies.

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3.3 Chapter summary

[Chapter 3](#) explored the application of machine learning (ML) modelling to prediction of suicidal behaviours. In [Chapter 3.1](#) a narrative review of the field summarised initial studies applying machine learning to suicide prediction and concluded that despite the reported highly accurate performance of these models, many of the same limitations apparent in earlier statistical approaches to modelling remained. Regardless of whether machine learning, or statistical approaches were used models predicting suicide deaths were likely to be of limited clinical utility given the low PPV associated with models predicting rare outcomes. Another limitation of the field identified in [Chapter 3.1](#) was the use of administrative data rather than variables that represent validated clinical constructs, such as clinical symptoms or diagnosis.

Building on these findings, [Chapter 3.2](#) then applied a machine learning approach to a comprehensive set of validated social, psychological, and clinical measures collected in a clinical cohort of young people with a high base rate of SI or SB. Predictive models of future suicide attempts (SA) were associated with slightly superior performance than those predicting future deliberate self-harm (DSH). Models predicting new-onset or repeat DSH/SA performed poorly, however the PPV of models predicting repeat behaviour were high enough to justify assertive clinical interventions. After a history of previous DSH or SA, clinical symptoms of common mental disorders were the most important predictors in modelling future behaviour.

In [Chapter 4](#) the opportunities presented by incorporating new forms of data into models of suicidal behaviour are explored. Cognitive domains, measured by behavioural tasks, represent potential biomarkers of a number of mental disorders and outcomes, including suicidal behaviour. [Chapter 4.1](#) reviews the evidence for an association between impulsivity and suicidal behaviour in young people. [Chapter 4.2](#) then explores the impact of adding neurocognition into standard clinical assessment on predicting future suicidal behaviours.

Chapter 4: Neurocognition in the suicidal behaviour of young people

4.1 A meta-analytic review of impulsivity in the suicidal behaviour of young people

McHugh, C., Lee, R.S., Hermens, D., Corderoy, A., Large, M.M., Hickie I.B. (2019)
'Impulsivity and Suicidal Behaviour in young people: A systematic review and meta-analysis' *Journal of Psychiatric Research*. 116 (3): 51-60. DOI:
[10.1016/j.jpsychires.2019.05.012](https://doi.org/10.1016/j.jpsychires.2019.05.012)

4.1.1 Abstract

Background

Impulsivity is considered a possible phenotype underlying the expression of self-harm and suicidal behaviours. Yet impulsivity is not a unitary construct and there is evidence that different facets of impulsivity follow different neurodevelopmental trajectories and that some facets may be more strongly associated with such behaviours than others. Moreover, it is unclear whether impulsivity is a useful predictor of self-harm or suicidal behaviour in young people, a population already considered to display heightened impulsive behaviour.

Methods

A systematic review and meta-analysis of studies published in Medline, PubMed, PsychInfo or Embase between 1970 and 2017 that used a neurocognitive measure to assess the independent variable of impulsivity and the dependent variable of self-harm and/or suicidal behaviour among young people (mean age < 30 years old).

Results

6183 titles were identified, 141 full texts were reviewed, and 18 studies were included, with 902 young people with a self-harm or suicidal behaviour and 1591 controls without a history of these behaviours. Deficits in inhibitory control (13 studies, SMD 0.21, p-value= 0.002, 95% confidence interval (CI) (0.08- 0.34), prediction interval (PI)=0.06-0.35) and impulsive decision-making (14 studies, SMD 0.17, p-value=0.008, 95% CI (0.045-0.3), PI=0.03-0.31) were associated with self-harm or suicidal behaviour. There were no significant differences between measures of different facets of impulsivity (ie. delay discounting, risky decision-making, cognitive or response inhibition) and self-harm or suicidal behaviour.

Conclusion

Multiple facets of impulsivity are associated with suicidal behaviour in young people. Future suicide research should be designed to capture impulsive states and investigate the impact on different subtypes of impulsivity.



Impulsivity in the self-harm and suicidal behavior of young people: A systematic review and meta-analysis

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ABSTRACT

Background: Impulsivity is considered a possible phenotype underlying the expression of self-harm and suicidal behaviors. Yet impulsivity is not a unitary construct and there is evidence that different facets of impulsivity follow different neurodevelopmental trajectories and that some facets may be more strongly associated with such behaviors than others. Moreover, it is unclear whether impulsivity is a useful predictor of self-harm or suicidal behavior in young people, a population already considered to display heightened impulsive behavior. **Methods:** A systematic review and meta-analysis of studies published in Medline, PubMed, PsychInfo or Embase between 1970 and 2017 that used a neurocognitive measure to assess the independent variable of impulsivity and the dependent variable of self-harm and/or suicidal behavior among young people (mean age < 30 years old).

Results: 6183 titles were identified, 141 full texts were reviewed, and 18 studies were included, with 902 young people with a self-harm or suicidal behavior and 1591 controls without a history of these behaviors. Deficits in inhibitory control (13 studies, SMD 0.21, p-value = 0.002, 95% confidence interval (CI) (0.08–0.34), prediction interval (PI) = 0.06–0.35) and impulsive decision-making (14 studies, SMD 0.17, p-value = 0.008, 95% CI (0.045–0.3), PI = 0.03–0.31) were associated with self-harm or suicidal behavior. There were no significant differences between measures of different facets of impulsivity (i.e. delay discounting, risky decision-making, cognitive or response inhibition) and self-harm or suicidal behavior.

Conclusion: Multiple facets of impulsivity are associated with suicidal behavior in young people. Future suicide research should be designed to capture impulsive states and investigate the impact on different subtypes of impulsivity.

1. Introduction

Impulsivity has emerged as a promising phenotype underlying suicidal and self-harm behavior (Mann et al., 2009). Though impulsivity has long been considered an important contributor to the expression of these behaviors, research into the association has been limited by the use of heterogeneous definitions of impulsivity (Anestis et al., 2014; Gvion 2011). Impulsivity is now widely considered ‘a predisposition toward rapid, unplanned reactions to internal or external stimuli with diminished regard to the negative consequences of these reactions to the impulsive individual or to the other’ (Moeller et al., 2001).

Historically, much of the literature examining impulsivity and self-harm or suicidal behavior has used self-report measures of impulsivity exclusively, such as the Barratt Impulsivity scale (Anestis et al., 2014; Hamza et al., 2015), though recent reviews have made distinctions between self-report and neurocognitive measures (Liu et al., 2017). Neurocognitive testing for impulsivity has been growing in favor, in part due to the ability of these tests to capture best performance through experiential testing and a growing interest in proximal, or state-based, factors associated with self-harm and suicidal behavior (Christensen et al., 2016). In a recent meta-analysis, Liu et al. (2017) found the relationship between impulsivity measured proximally

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	Definition
Impulsivity	A predisposition toward rapid, unplanned reactions to internal or external stimuli with diminished regard to the negative consequences of these reactions to the impulsive individual or to others (Moeller, Barratt et al. 2001)
Response inhibition	The process of the overriding of a planned or already initiated action (Bari and Robbins 2013)
Cognitive inhibition	The stopping or overriding of a mental process, in whole or in part, with or without intention (MacLeod 2007)
Delay discounting	The tendency to choose small rewards that are given immediately over larger rewards that are given after a relative delay (Fineberg, Chamberlain et al. 2014) Also referred to as temporal discounting, or time-preference.
Probabilistic discounting	The tendency to choose larger but less likely option, over the smaller, more likely option. (Robbins and Dalley 2016)
Suicidal behavior	Any intentional action that may cause a person to die.
Suicide attempt	A potentially self-injurious behavior associated with at least some intent to die.
Non-suicidal self-injury	Self-injurious behavior with no intent to die.
Deliberate self-harm	Any type of self-injurious behavior, including suicide attempts and non-suicidal self-injury.
Suicidal ideation	Active: Thoughts about taking action to end one's life, including identifying a method, having a plan, or having intent to act. Passive: Thoughts about death or wanting to be dead without any plan or intent

Fig. 1. Definitions of impulsivity and suicidal behavior.

(within the last month) to suicide attempts was much stronger than attempts occurring at a more distal time point. Self-report measures, which have generally been designed to capture trait-based impulsivity, may be less objective than neurocognitive tasks in capturing impulsive states. Neurocognitive models of impulsivity have delineated several separate, but related, constructs including impulsive decision-making deficits (delay discounting and risky decision-making) and inhibitory control (response and cognitive inhibition) (Dalley and Robbins, 2017). Though definitions of impulsivity are closer to consensus than in the past, there is still no agreed set of measures used by researchers and clinicians (Fineberg et al., 2014). This review considers varying definitions of impulsivity based on the instruments used within selected studies (Fig. 1) and uses the term impulsivity to refer to impulsive decision-making deficits and deficits of inhibitory control. Importantly previous reviews have not assessed whether the association between impulsivity and self-harm and suicidal behavior is moderated by the facet of impulsivity measured (Liu et al., 2017; Hamza et al., 2015; Lockwood et al., 2017).

This review considers self-harm and suicidal behavior as a broad construct that includes a number of more specific constructs such as suicide attempts (SA), non-suicidal self-injury (NSSI) and deliberate self-harm (DSH) and uses the terms as they have been used in the primary studies. Despite evidence these behaviors are distinct from each other, in terms of intent, severity, frequency and method, previous findings have suggested these behaviors may represent differing degrees of severity within the same phenotype or differing phenotypes with significant overlap. (Muehlenkamp and Gutierrez, 2007; Hawton et al., 2012) The high degree of co-morbidity of these behaviors in young people would support such an idea (Muehlenkamp and

Gutierrez, 2007; Nock et al., 2006). Yet it is not clear whether a particular behavior, whether suicide attempt or non-suicidal self-injury, may be more strongly associated with impulsivity. Liu et al. (2017) found impulsivity more strongly associated with suicide attempts than non-suicidal self-injury. Hamza et al. (2015) found neurocognitive measures were not associated with NSSI, though both reviews included relatively few studies of NSSI.

1.1. Neurocognitive development and suicidal behavior

Deficits in executive function are associated with expression of suicidal behavior, including decision-making and problem-solving deficits, memory biases (overgeneralization, preferential recall of negatively valenced stimuli) and attentional biases (Iorfino et al., 2016; Carballo et al., 2008). Impulsive decision-making and deficits of inhibitory control of cognition and behavior have been linked with self-harm and suicidal behaviors in older age groups and with other associated psychopathology, such as substance abuse (Bickel et al., 2007; Dombrovski et al., 2011; Richard-Devantoy et al., 2012). Less is known about the role of these deficits in the suicidal behavior of young people. Cognitive and motor inhibitory control do not reach full maturity until early adulthood (Hooper et al., 2004). Decision making in developmentally normative young people is considered more impulsive than adults. This impulsivity has been characterized as being a result of higher reward dependency, greater sensation seeking and reduced tolerance for ambiguity of outcome (Steinberg, 2008; Blakemore and Robbins, 2012; Tymula et al., 2012). Thus, the question should be asked: how does the suicide and self-harm literature on impulsivity apply to young people, and in an already impulsive cohort is it useful in

identifying those at risk? Further characterizing impulsivity in young people engaging in self-harm or suicidal behaviors may be an important step in understanding the contribution of these development-related vulnerabilities to the expression of the behavior.

1.2. The stress-diathesis model: the importance of the impulsive state

While ethical and practical issues have constrained our ability to do research in populations of individuals who are acutely suicidal and distressed, there is evidence that in individuals who have very recently engaged in near fatal deliberate self-harm, intensity of suicidal ideation and intent can fluctuate rapidly (Douglas et al., 2004). Suicidal ideation and behavior have only a weak predictive ability for later completed suicide (Ribeiro et al., 2016; McHugh et al., 2019). Similarly there is evidence that suicide attempters with high trait impulsivity are as likely to plan an attempt as suicide attempters with low trait-impulsivity (May and Klonsky, 2016; Witte et al., 2008). These findings have raised important questions about the relevance of measuring suicidal intent or planning, which has been an essential component of suicide prevention in clinical settings. The limitations of this approach have driven the investigation of cognitive phenotypes, which recognize the importance of the gene-environment interaction in the development of psychopathology (Mann et al., 2009). Mann's stress-diathesis model (1999) of suicidal behavior proposes that individuals may have a trait-like disposition (diathesis) to expressing suicidal behavior when exposed to stressors, or state variables, such as symptoms of psychiatric illness, psychosocial stress or substance use.

Until recently, most research into associations between impulsivity and self-harm and suicidal behaviors have approached impulsivity as a 'state-independent' trait. It has been considered a personality trait, yet personality is now understood to be more dynamic with maladaptive features becoming accentuated in times of stress (Newton-Howes et al., 2015; McHugh and Balaratnasingam, 2018). What is not clear is how an impulsive trait may interact with impulsive cognitive states to produce suicidal behaviors.

1.2. Measures of impulsivity

1.2.1. Impulsive decision-making

Impulsive decision making can be considered to include several facets, including delay discounting, probabilistic discounting and reflection impulsivity. Delay discounting in economics refers to the individual's tendency to reduce value attached to an outcome based on time until outcome (Bickel et al., 2007). That is, the choice to accept smaller sooner rewards, rather than larger, later rewards. This is also referred to as temporal discounting or time preference. Tests of delay discounting may be self-report or experiential, the latter of which involves real monetary or food rewards. Probabilistic discounting refers to the choice between a smaller reward with higher probability of return, or larger reward, with lower probability of return. Decision-making tasks such as the Iowa Gambling Task (IGT), or the Cambridge Gambling Task (CGT) can be considered to measure probabilistic discounting, but also tap into other neurocognitive constructs such as reinforcement learning (IGT) or delay aversion (CGT) (Brevers et al., 2013; Cambridge Cognition, 2018). As these measures are not purely measures of probabilistic discounting they will be referred to as measures of risky decision-making. In this review, the term impulsive decision-making will be used to refer measures of delay discounting and these risky decision-making tasks. Explanations of neurocognitive tests of discounting discussed in this review are included in Appendix A1.

1.2.2. Inhibitory control

Inhibitory control consists of cognitive and motor inhibition and is an essential executive function. In decision making terms, having sufficient inhibitory control may allow an individual to consider value and response selection, and enable them to choose the option with the

highest objective value, or utility. Motor inhibition, hereafter referred to as response inhibition, is the failure to inhibit pre-potent responses to stimuli. Behavioral tests of response inhibition include the Go/No Go impulsivity paradigm (Dougherty et al., 2005) and the Stop signal test (SST) (Cambridge Cognition, 2018).

Cognitive inhibition, 'the stopping or overriding of a mental process, in whole or in part, with or without intention' (MacLeod, 2007), requires mediating control of attentional processes and working memory. Measures of selective and sustained attention, such as the continuous performance task (CPT), are also often used to measure this type of impulsivity (Dougherty et al., 2002). Commission errors are believed to reflect response initiation aspects of impulsivity because they result from incomplete processing of stimuli leading to rapid but incorrect responses. The Stroop test is another commonly used measure of cognitive inhibition. Explanations of neurocognitive tests of inhibitory control discussed in this review are included in Appendix A1.

The current review aims to establish whether these neurocognitive measures of impulsivity can be used to differentiate young people engaging in self-harm or suicidal behaviors from those who do not, and which, if any, sub-type of impulsivity is more strongly associated with these behaviors. We aim to establish whether age or gender moderates the relationship between impulsivity and such behaviors. A further aim of this review was to understand whether use of neurocognitive measures of impulsivity has identified evidence of impulsivity being more strongly associated with recent self-harm or suicidal behavior, rather than a lifetime history of these behaviors.

2. Methods

Methods of review including eligibility criteria, data collection and synthesis were specified in advance in the form of a review protocol and registered with PROSPERO (CRD42017081260). PRISMA guidelines for systematic review were followed (Liberati et al., 2009).

2.1. Search strategy

Medline, PubMed, PsychInfo, Embase databases were searched for relevant key words and MeSH terms which included 'suicid*' OR 'suicide, attempted' OR 'self-injurious behavior' OR 'auto-mutilation' AND 'impulsiv*' OR 'decision making' OR 'delay discounting' OR 'inhibitory control' OR 'response inhibition' OR 'executive function' OR 'cognitive control'. Studies identified from references of relevant articles were also included. Search criteria selected only studies that were reported in English and published between January 1980 and December 2017.

2.2. Eligibility criteria

Using a proforma the first author (CM) screened titles and abstracts for the following inclusion criteria: i) a mean age between 12 and 30 years, ii) compared a group with a self-harm or suicidal behavior to a group without such behaviors iii) used a neurocognitive measure of impulsivity. Self-harm or suicidal behavior was defined as any non-fatal self-injurious behavior, with intent to harm self and/or intent to end one's life, and included suicide attempts (SA), non-suicidal self-injury (NSSI) and deliberate self-harm (DSH). Terms were used as they were in the original studies. A neurocognitive test was considered any task designed to measure impulsivity. Studies with mean age between 12 and 30 years were included to capture changing impulsivity with development.

Studies were excluded if they measured suicidal ideation without behavior, had a control group with self-harm or suicidal behavior, did not report on the association between impulsivity and these behaviors or used a self-report measure of impulsivity exclusively. Articles published in languages other than English were also excluded.

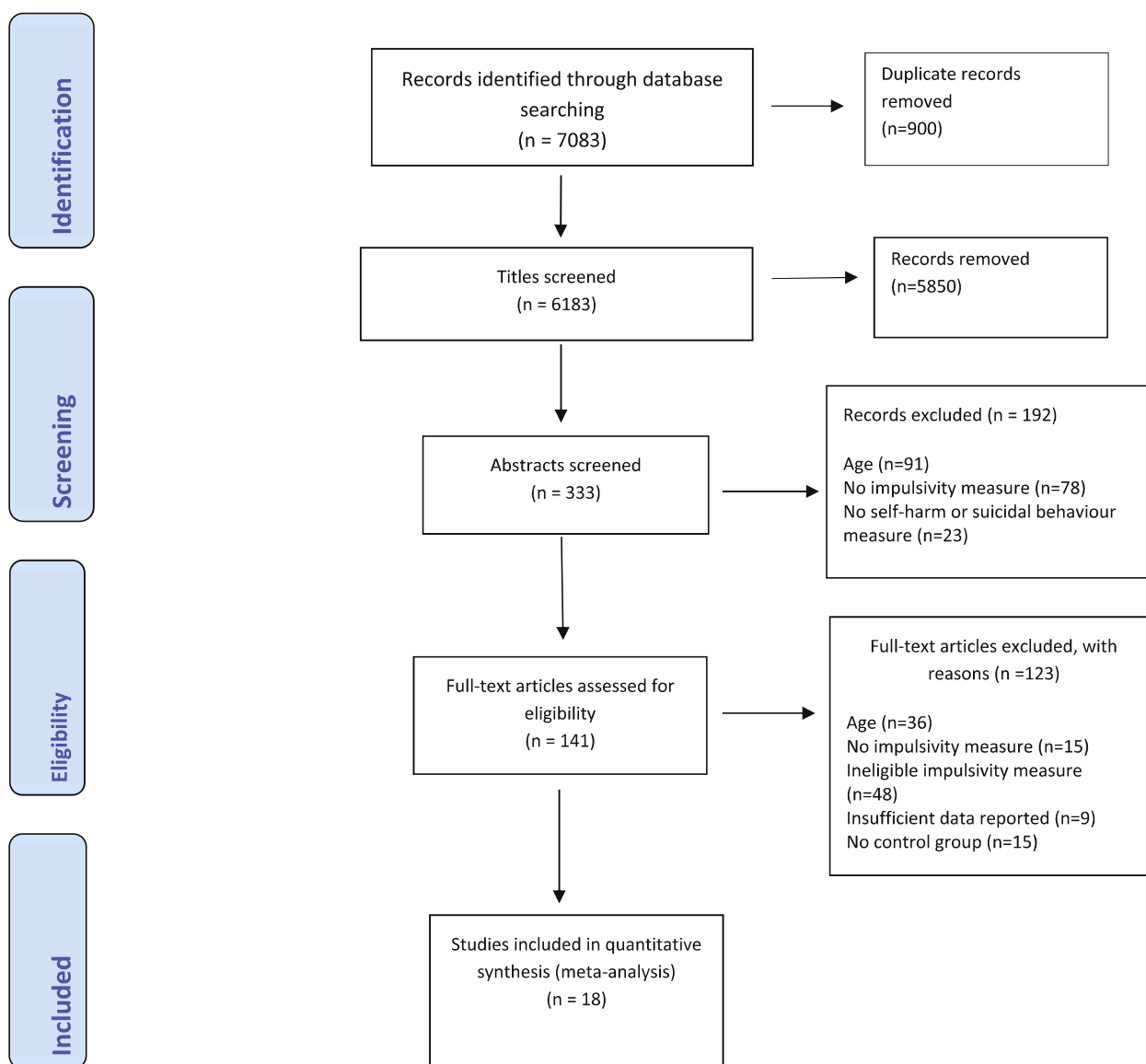


Fig. 2. PRISMA flowchart.

2.3. Identification of studies

Fig. 2 outlines the process undertaken to identify studies for this review. 6183 titles were screened to determine appropriateness for screening of abstract. 333 titles and abstracts were screened by two authors (CM and AC). At that stage 192 studies were excluded based on eligibility criteria. The eligibility stage led to 141 full texts being assessed and subsequently a further 123 studies being excluded. The remaining 18 studies were included in this review.

2.4. Synthesis of results

A proforma was used to extract data from the included studies. This included information on study design (cross-sectional, longitudinal and period of follow up), sample characteristics (sample size, age, gender, population), outcome measures (NSSI, SA, or DSH), recency of self-harm or suicidal behavior (lifetime, or within 1 year), measure of impulsivity used, key findings and limitations. Key findings were evidence of an association between the impulsivity measure and outcome measure.

Neurocognitive measures were grouped together a priori based on

the facet (or subtype) of impulsivity the measure was considered to capture—delay discounting, risky decision-making, response inhibition or cognitive inhibition. Key metrics were extracted and examined to ensure appropriateness of entering into meta-analysis. Where studies reported several metrics from the same measure efforts were made to extract the same metrics from each study (ie. commission errors on the CPT, overall proportional bets on IGT) Where studies reported multiple outcome groups (ie. multiple attempts vs. single attempts separately) the two groups were pooled, due to the small number of studies reporting these as separate groups.

2.5. Assessment of study quality

Study quality was assessed using the Newcastle-Ottawa scale for case-control studies and cohort studies (Wells et al, 2018). Studies scoring 5 or less were considered to be of low quality and at greater risk of bias.

2.6. Meta-analysis

The pooled effect size across all facets of impulsivity was estimated

with a random effects meta-analysis chosen a priori for all estimates because of the diversity of study populations and differences in the methods used in the primary research. Between-study heterogeneity in effect sizes was examined using I-square, Q-value statistics and prediction intervals. The possibility of publication bias was assessed using Egger's regression (Egger et al., 1997) and was quantified using Duval and Tweedie's trim and fill method (Egger et al., 1997; Duval and Tweedie, 2000). Subgroups according to the facets of impulsivity, strength of reporting and age and sex distribution of the samples were compared using a mixed effects model. Comprehensive Meta-Analysis (CMA; Version 3, Biostat, Englewood NJ) was used for the main analysis.

3. Results

3.1. Study characteristics

Eighteen studies were included in the meta-analysis. Fourteen studies with a total of 632 subjects measured impulsive decision-making, four measured delay discounting, 3 via delay discounting (DD) tasks and 1 via Two Choice Impulsivity Paradigm (TCIP). Nine studies measured risky decision-making, 4 via IGT, 4 via CGT, 1 via the Information Sampling Task (IST).

Thirteen studies with a total of 1195 subjects measured inhibitory control. Eight studies measured response inhibition (6 via SST, 3 via Go No-go or goStop Impulsivity paradigm), six studies measured cognitive inhibition (5 via CPT, 1 via the Stroop test). Three studies used multiple measures, allowing for comparison between different neurocognitive measures of impulsivity. Table 1 summarizes the characteristics of included studies.

3.1.1. Assessment of study quality

The median NOS score of the 18 included studies was 4 (range 3–7). Additional detail is included in the supplementary material (Appendix A: 2).

3.2. Meta-analysis

Young people engaging in self-harm or suicidal behavior were significantly more impulsive than those without such behavior (standardized difference in mean 0.19, 95% CI = 0.10–0.28, p -value < 0.000, $PI = 0.0934$ –0.29), see Fig. 3. The degree of variance was less than expected due to sampling error alone ($Q = 23.05$, $df = 26$, I -squared = 0). The funnel plot showed no evidence of publication bias (Appendix A: 3). Egger's regression was not significant (intercept = 0.03, t -value = 0.0034, $df = 25$, p -value = 0.49). Duval and Tweedie's trim and fill did not identify any missing hypothetical studies.

Both impulsive decision-making and deficits of inhibitory control were significantly associated with self-harm and suicidal behavior. Deficits in inhibitory control were associated with a greater effect size (SMD 0.21, p -value = 0.002, 95% CI (0.08–0.34), $PI = 0.06$ –0.35), than impulsive decision-making (SMD 0.17, p -value = 0.01, 95% CI (0.05–0.3), $PI = 0.03$ –0.31), though the difference between the two groups was non-significant (Q -value = 0.13, $df = 1$, p -value = 0.72).

Measures of risky decision-making (SMD 0.26, p -value = 0.001, 95% CI 0.11–0.42) and response inhibition (0.22, p -value = 0.005, 95% CI (0.06–0.38), differentiated young people with such behaviors from those without. Measures of cognitive inhibition (ie. CPT) (SMD 0.14, p -value = 0.24, CI -0.09–0.37) and measures of delay discounting (SMD -0.02, p -value = 0.9, CI -0.3–0.3) did not differentiate the suicidal young people from controls. Despite response inhibition and risky decision-making being significantly associated with self-harm or suicidal behavior, but not cognitive inhibition or delay discounting, subtype of impulsivity measure used did not significantly moderate the relationship between impulsivity and these behaviors (Q -value = 3.09, $df = 3$, p -value = 0.38).

3.2.1. Moderator analysis

None of the variables selected a priori significantly moderated the effect between impulsivity and self-harm and suicidal behavior. In some cases, subgroups reached statistical significance while others did not. See Table 2. Young people who had engaged in self-harm or suicidal behavior were significantly more impulsive than healthy controls (20 studies, SMD = 0.19, 95% CI = 0.09–0.30, p -value = 0.0002), but not psychiatric controls ($n = 7$, SMD = 0.18, 95% CI = -0.14–0.49, p -value = 0.27), though this was a non-significant difference (Q -value = 0.01, $df = 1$, p -value = 0.92). Study quality, whether low quality (24 studies, SMD = 0.206, 95% CI = 0.111–0.302, p -value = 0.000) or high quality (3 studies, SMD = 0.016, 95% CI = -0.315–0.348, p -value = 0.923), did not moderate the relationship between impulsivity and outcome measure.

Type of self-harm or suicidal behavior measure, whether suicide attempt ($n = 15$, SMD = 0.18, 95% CI = 0.02–0.34, p -value = 0.003) or NSSI ($n = 11$, SMD = 0.20, 95% CI = 0.07–0.33, p -value = 0.003), did not moderate the relationship between impulsivity and such behaviors (Q -value = 0.04, $df = 1$, p -value = 0.85). Timing of self-harm or suicidal behavior, whether lifetime history ($n = 13$, SMD = 0.17, 95% CI = 0.04–0.31, p -value = 0.02) or recent ($n = 14$, SMD = 0.21, 95% CI = 0.07–0.34, p -value = 0.002), was associated with similar effect sizes (Q -value = 0.12, $df = 1$, p -value = 0.73).

Age of sample was not a moderator of the relationship between impulsivity and self-harm or suicidal behavior. The relationship between impulsivity and these behaviors was similar in samples of young adults ($n = 15$, SMD = 0.19, 95% CI = 0.07–0.30, p -value = 0.002) and adolescents (age < 18 years old) ($n = 12$, SMD = 0.19, 95% CI 0.01–0.37, p -value = 0.04, Q -value = 0.003, $df = 1$, p -value = 0.96). Gender distribution of the sample also did not moderate the relationship. Though studies with sample sizes of more than 70% females ($n = 13$, SMD = 0.15, 95% CI = 0.004–0.29, p -value = 0.04) had a smaller effect size than those with more even gender distribution ($n = 14$, SMD = 0.23, 95% CI = 0.10–0.36, p -value < 0.001, Q -value = 0.72, $df = 1$, p -value = 0.40), the difference was non-significant.

4. Discussion

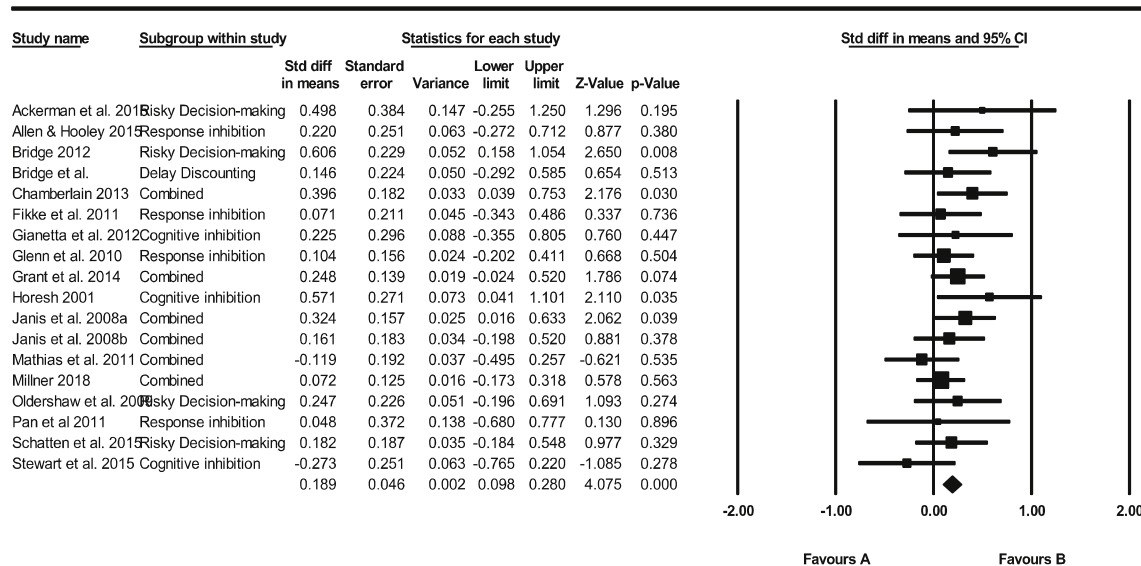
This review confirms that there are associations between multiple facets of impulsivity and self-harm or suicidal behaviors in young people. Thus, we have provided an important addition to previous meta-analyses which have found self-report measures of impulsivity and such behaviors are weakly associated (Anestis et al., 2014; Hamza et al., 2015) whereas neurocognitive measures of impulsivity and self-harm and suicidal behaviors are associated with a medium to large effect size (Liu et al., 2017).

While in several included studies the same sample showed differential deficits of decision-making, cognitive and response inhibition, our overall findings that subtype of impulsivity did not moderate the relationship is an important one. As evidence from the substance use disorder literature has previously suggested that delay discounting and response inhibition are separate domains (De Wit, 2009) and there is evidence that these facets are related to distinct neurocircuits (Fineberg et al., 2014) we had hypothesized that in suicidal populations there may be independence of these executive function deficits. The current review has not found any evidence of this. Although identifying discrete neurocognitive mechanisms and their associated neurocircuits may lead to further characterization of phenotypes of suicidal behavior and ultimately personalized interventions, at present the broader construct of impulsivity may be just as useful as a therapeutic target. Similarly dividing the broader construct of self-harm and suicidal behavior into more specific behaviors, suicide attempts and non-suicidal self-injury, did not moderate the relationship with impulsivity, which may indicate these behaviors are part of the same neurocognitive phenotype. Our finding that impulsivity differentiates between young people with self-

Table 1
Neurocognitive measures of impulsivity.

Study	N total (subjects, controls)	Age range in years (mean)	Population	Design	Outcome measure	Cognitive test <i>Self-report</i>	Findings
Ackerman et al., (2015) (Ackerman, McBee-Strayer et al., 2015)	14 SA 14 psychiatric controls	15–19 (16.9)	Community, ED F 64%	Case-control	SA <i>Recent (1 yr)</i>	CGT	CGT scores higher in SA
Allen and Hooley (2015) (Allen and Hooley, 2015)	33 NSSI 31 healthy controls	18–53 (23.7)	Community F 75%	Case-control	NSSI <i>Lifetime</i>	SST	No differences between NSSI and HCs on any dimension of the SST
Bridge et al., 2012 (Bridge, McBee-Strayer et al., 2012)	40 SA 40 psychiatric controls	13–18 (15.5)	Community F 75%	Case-control	SA <i>Recent (1 yr)</i>	IGT <i>BIS</i>	SA performed worse on IGT than controls, difference persisted once affective disorder, psychotropic use, self-report impulsivity and hostility adjusted for
Bridge et al., 2015 (Bridge et al., 2015)	40 SA 40 psychiatric controls	13–18 (15.6)	Community F 75%	Case-control	SA <i>Recent (1 yr)</i>	DD	SA were more aggressive, those on medication were less aggressive, no differences on DDQ
Chamberlain et al., (2013) (Chamberlain et al., 2013)	16 SA 288 healthy controls	18–29 (21.8)	Community F 30%	Case-control	SA <i>Lifetime</i>	CGT	CGT performance was associated with a significant incremental benefit in predicting suicidality, over clinical and demographic variables
Fikke et al., (2011) (Fikke et al., 2011)	33 high-NSSI 29 low- NSSI	14–15 (14.8)	Schools F 71%	Case-control	NSSI <i>Recent (1 yr)</i>	SST	Low-severity NSSI more impulsive than controls and high-severity NSSI
Gianetta et al. 2012 (Gianetta et al., 2012)	23 DSH 23 healthy controls	10–14 (11.6)	Schools F 30%	Case-control	DSH <i>Recent (1 year)</i>	Stroop, YSR	SI and DSH assoc. with impulsivity by self-report Cognitive measures not associated
Glenn et al. 2010 (Glenn and Klonsky, 2010)	82 NSSI 82 healthy controls	(19)	Community F 73%	Case-control	NSSI <i>Lifetime</i>	SST <i>UPPS</i>	NSSI vs. HC: no difference in Stop signal results Urgency differences greater than lack of premed. or sensation seeking
Grant et al. 2014 (Grant et al., 2014)	32 any suicidality 142 no suicidality	18–29 (21.7)	Community F 31%	Case-control	NSSI <i>Lifetime</i>	CGT <i>BIS, EIS</i>	Suicidality associated with relative impairments in decision making and cognitive flexibility
Horesh 2001 (Horesh, 2001)	37 SA 23 psychiatric controls	(15)	Inpatient F 34%	Case-control	SA <i>Current, recent</i>	CPT: TOVA <i>ICS</i>	IMP higher in suicide attempters Correlation between self-report and cog. measure low, but significant
Janis et al. 2009a (Janis and Nock, 2009)	64 NSSI 30 healthy controls	12–19 (17)	Outpatient F 80%	Case-control	NSSI <i>Lifetime</i>	IGT, CPT	No difference between self-harmers and controls
Janis et al. 2009b (Janis and Nock, 2009)	20 NSSI 20 healthy controls	18–30 (23–24)	Outpatient F100%	Case-control	NSSI <i>Recent</i>	IGT, CPT, DD <i>K-SCADS-PL</i>	No difference between self-harmers and controls
Mathias et al. 2011 (Mathias et al., 2011)	22 multiple SA 15 SA 22 psychiatric controls	13–17	Inpatients F 100%	Case-control	SA <i>Lifetime</i>	TCIP, goStop	Multiple SA > single SA > no attempts on TCIP No differences on goStop
Milner (2015) (Milner, 2015)	30 SA 34 healthy controls	18–55 (26.8)	Inpatient F 60%	Case-control	SA <i>Recent</i>	SST, DD, IST, CPT, Go-no go <i>BIS, UPPS-P</i>	No significant differences on any of the tasks
Oldershaw et al. 2009 (Oldershaw et al., 2009)	30 current DSH 24 past DSH 22 depressed controls	12–18 (15–16.5)	Outpatient Schools F 80%	Case-control	DSH <i>Current, Lifetime</i>	IGT	IMP higher in current DSH > past DSH > depressed controls > healthy controls Past DSH able to learn low risk strategy
Pan et al., (2011) (Pan et al., 2011)	57 healthy controls 15 SA 15 depressed controls	13–17 (16.2)	Outpatient F 57%	Case-control	SA <i>Lifetime</i>	Go-no go	No significant differences in any of the go-no go dimensions
Schatten et al., 2015 (Schatten et al., 2015)	14 healthy controls 48 NSSI 72 non-NSSI	18–29 (21.9)	Population F 64%	Case-control	NSSI <i>Lifetime</i>	IGT	NSSI status not associated with IGT performance either before or after social exclusion task
Stewart et al., (2015) (Stewart et al., 2015)	59 SA 101 depressed controls	13–18 (15.6)	Inpatient F 77%	Case-control	SA <i>Recent (1 yr)</i>	Grad CPT	Disinhibition moderates relationship between CSA and recent suicide attempt

Meta Analysis



Meta Analysis

Fig. 3. Forest plot of impulsivity.

Table 2

Moderators of effect.

Group	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df	p-value
Cognitive inhibition	6.000	0.139	0.119	0.014	-0.094	0.372	1.168	0.243			
Delay Discounting	4.000	-0.019	0.149	0.022	-0.310	0.273	-0.125	0.900			
Risky decision-making	9.000	0.262	0.079	0.006	0.107	0.416	3.324	0.001			
Response inhibition	8.000	0.219	0.080	0.006	0.062	0.375	2.739	0.006			
Total between									3.093	3.00	0.377
Lifetime	13.000	0.173	0.071	0.005	0.034	0.311	2.440	0.015			
Recent	14.000	0.207	0.068	0.005	0.073	0.340	3.032	0.002			
Total between									0.119	1.00	0.730
Healthy	20.000	0.193	0.053	0.003	0.090	0.296	3.663	0.000			
Psychiatric	7.000	0.177	0.160	0.026	-0.136	0.490	1.108	0.268			
Total between									0.009	1.00	0.926
Adolescent	12.000	0.192	0.092	0.008	0.011	0.372	2.082	0.037			
Adult	15.000	0.186	0.060	0.004	0.069	0.303	3.109	0.002			
Total between									0.003	1.00	0.956
Less	14.000	0.230	0.066	0.004	0.102	0.358	3.511	0.000			
Over 70% female	13.000	0.147	0.073	0.005	0.004	0.290	2.011	0.044			
Total between									0.721	1.000	0.396
Impulsive decision-making	14.000	0.173	0.065	0.004	0.045	0.300	2.657	0.008			
Inhibitory control	13.000	0.206	0.066	0.004	0.076	0.336	3.110	0.002			
Total between									0.128	1.00	0.721
NSSI	11.000	0.197	0.066	0.004	0.068	0.327	2.992	0.003			
SA	15.000	0.177	0.081	0.007	0.019	0.336	2.191	0.028			
Total between									0.036	1.00	0.849
High quality	3	0.016	0.169	0.029	-0.315	0.348	0.097	0.923			
Low quality	24	0.206	0.049	0.002	0.111	0.302	4.234	0.000			
Total within									1.159	1.00	0.282

harm and suicidal behavior and healthy controls, but not psychiatric controls must be interpreted with caution. Few studies used psychiatric control groups, such that the number of psychiatric controls in the meta-analytic sample was far fewer than healthy controls (161 vs. 1430 respectively). Thus our meta-analysis was likely underpowered to detect an effect between suicidal and self-harming young people and psychiatric controls.

4.1. Risky decision-making predicts self-harm and suicidal behaviors

Risky decision-making tasks such as the IGT and CGT, but not delay discounting tasks, differentiated young people with self-harm or suicidal behavior from controls. The majority of studies of risky decision-making used the Iowa Gambling task (IGT), which is often considered to measure multiple executive functions, such as reinforcement learning, in addition to probabilistic discounting, which may confound interpretation of our findings. Nonetheless these results are consistent with findings in adult populations (Gorlyn et al., 2013) and add to the

existing literature as other meta-analysis have not included these decision-making tasks (Liu et al., 2017).

Contrary to our hypothesis deficits of delay discounting did not differentiate young people with self-harm or suicidal behavior from controls. However, only a small number of studies (4) measured delay discounting, which suggests the analysis may have been underpowered in testing our hypothesis. Discounting is sensitive to a number of different conditions including order of magnitude (i.e. the larger the amount, the more steeply people discount), sign effect (positive outcomes discounted more than negative outcomes), duration (distant outcomes discounted more than proximal) and affective states (in 'hot' affective states persistence of current preferences overestimated) (Tucker et al., 2010). One potential model of decision-making in self-harm and suicidal behavior may involve the individual under stress valuing the smaller sooner rewards (ie. cessation of emotional pain) over the larger, later rewards that may come with continuing living. The current value of life may be suddenly decreased due to loss of social role or connection. Put alternatively the costs associated with these behaviors in the present, such as physical pain and fear, may be less than perceived costs of continued living with emotional pain. This is consistent with evidence from healthy populations that individuals in 'hot' affective states, such as in emotional crisis, are likely to overestimate the likelihood that current conditions will persist (Madden and Johnson, 2010). Under this model of self-harm and suicidal decision-making the individual may believe the immediate choice of the self-harm or suicidal act is the option with the highest utility. Other hallmarks of the suicidal crisis, including intoxication and sleeplessness have all been shown to cause steeper discounting of future gain (Tucker et al., 2010).

4.2. Deficits in inhibitory control are associated with self-harm and suicidal behavior in young people

Young people with self-harm or suicidal behavior were significantly slower in responding appropriately to stimulus in response inhibition tasks relative to controls. This finding is in keeping with current psychological models of suicidal behavior. A deficit in response inhibition, which is the motor, or behavioral component of inhibitory control may explain why some individuals engaging in self-harm and suicidal behavior describe having engaged in the act before they have had a chance to stop themselves (Skegg, 2005).

Measures of cognitive inhibition, however, did not differentiate young people with self-harm and suicidal behavior from controls, contrary to our hypothesis. Only six studies measured cognitive inhibition, which likely makes our analysis underpowered. We had hypothesized that deficits in cognitive inhibition, or the ability to override mental processes, may have particular effects on the suicidal mind, resulting in increased ideation, a predictor of behavior (Nock et al., 2010). Once an individual is in crisis they may be unable to shift attention from negative thoughts or thoughts of self-harm or suicide, which is likely to lead to increased frequency and perceived lack of control over ideas of self-harm or suicide. Suicidal ideation and behavior scales that measure frequency and control over suicidal thoughts have previously been shown to be more robust measures of suicidal ideation, relative to dichotomous descriptors (Batterham et al., 2015). Deficits of cognitive inhibition may be related to rumination, which has also been associated with these behaviors (Rogers and Joiner, 2017).

4.3. The role of state-based impulsivity is poorly understood

Only two studies used individuals who had self-harmed or made a suicide attempt within the last week to month (Horeish, 2001; Oldershaw et al., 2009) and less than half the studies recorded suicide attempts or self-harm within the previous year (Janis and Nock, 2009; Stewart et al., 2015; Ackerman et al., 2015; Bridge et al.; Bridge et al., 2015; Fikke et al., 2011; Giannetta et al., 2012). The only study that

compared current and former self-harmers, found adolescents who were current self-harmers made more high-risk choices on IGT than those with a history of self-harm, or healthy controls (Oldershaw et al., 2009). Current self-harmers were the only group who did not improve over the course of the task. This deficit of studies examining impulsivity and cognition proximally to self-harm and suicidal behavior in young people is particularly important, given the findings from Liu et al's (2017) meta-analysis that in adults the odds of impulsivity in recent (< 1 month) suicide attempters was greatly increased.

It is possible that decision-making processes are more state based than measures of inhibitory control, which would mean the methodological limitations of the literature may mask the true effect of these deficits on self-harm and suicidal behavior. Indeed previous reviews have found inhibitory control may be less impacted by stress conditions than other executive functions (Shields et al., 2016). Discounting of reward has been shown to be strongly impacted by other state variables, including both acute intoxication and chronic substance use (Bickel et al., 1999). Certainly a growing body of evidence suggests conditions of stress may significantly impact decision-making and inhibitory control in healthy individuals. It will be vital for research to get closer in time to self-harm and suicidal behaviors and measure associated state-based variables. For example, in this review few studies controlled for current or past substance use. Traditionally, measuring cognitive states has been difficult, in both clinical and research settings. Advances in technology, however, have increased both the accessibility and sophistication of neurocognitive testing, such as CanTab or Cogstat (Fray et al., 1996; Maruff et al., 2009). With these advances it may be possible to measure suicidal cognition in real-time, outside the domains of the clinical or research setting (Nock et al., 2009). Using measures that quantify state differences are likely to be more useful in understanding etiology, recognizing risk clinically and in prevention.

4.4. Impulsivity and self-harm or suicidal behavior in development

Impulsivity is associated with suicidal behavior in young people. Despite impulsive choice and behavior being a feature of normative development, deficits of inhibitory control and discounting still meaningfully differentiated groups of young people with self-harm or suicidal behavior from those without. While previous reviews have examined facets of impulsivity in development of healthy adolescents and populations of substance using young people, less is known about changing impulsivity in young people engaging in self-harm or suicidal behaviors. This analysis found the average age of the sample, either over 18 years or below, did not moderate the association between impulsivity and these behaviors. It is possible that dividing age dichotomously introduces error into the analysis. Examining age associations in meta-analysis can be problematic as each study generally reports the mean age of the sample, rather than for cases and controls. No individual studies in the current review had a study design sufficient to comment on changing impulsivity with age, which will be an important question for future research.

Half of the included studies had a sample of greater than 70% female, which suggests there may be sampling bias in the literature on impulsivity and self-harm and suicidal behavior. If sex is associated with either delayed development of inhibitory control or decision-making, the current literature may have underestimated the relationship between these behaviors and impulsivity due to sampling bias. Self-harm, with or without suicidal intent, is considered to be more prevalent in females (Skegg, 2005). Cultural difference in expression of emotion, and biological factors (ie. testosterone and aggression), have both been hypothesized to contribute to such an effect (Bresin and Schoenleber, 2015). Yet studies using broader definitions of self-harm, have shown less of a gender difference in prevalence, which suggests methodological issues in suicide research may at least in part contribute to this finding (Muehlenkamp and Gutierrez, 2004). Rippon et al. (2014) have outlined the way in which methodological error (ie.

inappropriate consideration of age and development) can confound relationships between sex and various outcomes in the neurosciences. Gender bias in sampling is particularly important to consider in the study of self-harm and suicidal behavior.

4.5. Limitations

The current review had a limited ability to look at important moderators, including other executive function deficits, and potential confounders such as substance use. This reflects the relatively small number of studies examining neurocognitive measures of impulsivity in young people with self-harm or suicidal behavior. We were only able to broadly examine the role of individual characteristics, such as age or gender, at a study level, which likely introduces bias. There were relatively few studies reporting facets of impulsivity, which likely resulted in the meta-analysis being underpowered to detect an effect. It is still not clear how to measure clinically meaningful differences in impulsive decision-making and inhibitory control. This makes it difficult to know whether the findings of this review are clinically meaningful.

5. Conclusion

The current review has demonstrated that impulsivity differentiates young people engaging in self-harm or suicidal behavior from healthy controls. This relationship exists despite the age or gender of the sample. There is limited evidence of a differential association between particular facets of impulsivity and the expression of such behaviors in young people. Deficits of response inhibition and riskier decision-making were associated with these behaviors, though deficits of cognitive inhibition and steeper delay discounting were not significantly associated. Recency of self-harm or suicidal behavior or type of behavior measured did not moderate the relationship. Future research into self-harm and suicidal behaviors and decision making should focus on state impulsivity by studying decision making processes in populations with recent self-harm or suicidal behavior. Greater understanding of trajectories of impulsive decision-making and behavior across adolescence and adulthood would increase our understanding of the contribution of this important executive function in expression of self-harm and suicidal behavior.

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Appendix A. Supplementary data

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4.2 Neurocognitive predictors of suicidal behaviour in help-seeking young people

McHugh, C.M., Iorfino, F., Crouse, J.J., Tickell, A., Nichles, A., Zmicerevska, N., Ho, N., Lee, R., Hermens, D.F., Scott, E. and Hickie, I.B., 2021. Neurocognitive functioning predicts suicidal behaviour in young people with affective disorders. *Journal of Affective Disorders*, 281, pp.289-296. DOI: [10.1016/j.jad.2020.11.077](https://doi.org/10.1016/j.jad.2020.11.077)

4.2.1 Abstract

Background

Neurocognitive impairment is recognised as a risk factor for suicidal behaviour in adults attending mental health care. The current study aims to determine whether neurocognitive deficits also predict ongoing or emergent suicidal behaviour in young people with mood and anxiety syndromes.

Methods

Participants were aged 12-30 years and presented to early intervention-focused youth mental health clinics prior to July 2018. In addition to clinical assessment, standardised neurocognitive assessment was conducted at baseline. Clinical data was extracted from subsequent visits using a standardised proforma.

Results

Of the 635 participants who met inclusion criteria (mean age 19.6 years, 59% female, average follow up 23 months), 203 (32%) reported suicidal behaviour at entry to care, while 104 (16%) participants reported suicidal behaviour during the period of subsequent mental health care. A number of neurocognitive domains differentiated those with suicidal behaviour during care from clinical controls including greater cognitive flexibility, faster processing speed, better working memory, delayed memory and visuospatial memory. Better general neurocognitive function remained a significant predictor (OR=1.85, 95% CI 1.27- 2.75) of suicidal behaviour in care, after controlling for social and clinical risk factors.

Limitations

The neurocognitive battery used was designed for use with affective and psychotic disorders and may not have detected some deficits more specific to suicidal behaviour.

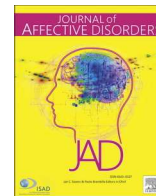
Conclusion

Contrary to expectations, better neurocognitive functioning is a predictor of ongoing or emergent suicidal behaviour in young people with affective disorders who present for care. While other sub-populations with suicidal behaviour, such as older populations or young people with psychotic disorders, tend to experience neurocognitive deficits which may limit their capacity to engage in some interventions, young people with affective disorders do not.



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Neurocognitive functioning predicts suicidal behaviour in young people with affective disorders

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ABSTRACT

Background: Neurocognitive impairment is recognised as a risk factor for suicidal behaviour in adults. The current study aims to determine whether neurocognitive deficits also predict ongoing or emergent suicidal behaviour in young people with affective disorders.

Methods: Participants were aged 12–30 years and presented to early intervention youth mental health clinics between 2008 and 2018. In addition to clinical assessment a standardised neurocognitive assessment was conducted at baseline. Clinical data was extracted from subsequent visits using a standardised proforma.

Results: Of the 635 participants who met inclusion criteria (mean age 19.6 years, 59% female, average follow up 476 days) 104 (16%) reported suicidal behaviour during care. In 5 of the 10 neurocognitive domains tested (cognitive flexibility, processing speed, working memory, verbal memory and visuospatial memory) those with suicidal behaviour during care were superior to clinical controls. Better general neurocognitive function remained a significant predictor (OR=1.94, 95% CI 1.29–2.94) of suicidal behaviour in care after controlling for other risk factors.

Limitations: The neurocognitive battery used was designed for use with affective and psychotic disorders and may not have detected some deficits more specific to suicidal behaviour.

Conclusion: Contrary to expectations, better neurocognitive functioning predicts suicidal behaviour during care in young people with affective disorders. While other populations with suicidal behaviour, such as adults with affective disorders or young people with psychotic disorders, tend to experience neurocognitive deficits which may limit their capacity to engage in some interventions, this does not appear to be the case for young people with affective disorders.

Introduction

In adults, deficits in executive function, including decision-making and problem-solving deficits, memory and attentional biases, for example overgeneralization and preferential recall of negatively valenced stimuli, are associated with the expression of suicidal behaviour independently of mental disorder (Carballo, Akamnonu et al. 2008, Iorfino, Hickie et al. 2016). As with the ageing brain (>50 yo), the developing brain (across adolescence and young adulthood) represents a period of neurocognitive vulnerability (Paus, Keshavan et al. 2008). Both periods represent important social, functional and psychological

transitions underpinned by important changes to neurobiological functioning. These periods of neurocognitive vulnerability may be particularly important to the expression of suicidal behaviour, the prevalence of which peaks in these two age ranges (Turecki and Brent 2016).

In young people specific neurocognitive functions appear to follow different developmental paths. Facets of cognitive control, such as attention and inhibitory control, increase in a linear fashion across adolescence while decision-making processes appear to follow a u-shaped curve, with increased risk taking in mid-adolescence before becoming more risk averse by young adulthood (Casey and Jones 2010, Shulman, Harden et al. 2015). While neurocognitive deficits have been

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more extensively studied in adult and older age populations with suicidal behaviour (Dombrowski 2011, Richard-Devantoy, Jollant et al. 2012), the relationship between executive function and suicidal behaviour in young people is less understood. Though studies of neurocognition in young people with mental illness have largely focused on psychotic illnesses (Allott 2019) previous work by our research group has identified distinct neurocognitive phenotypes independent of diagnosis in young people accessing mental health care (Hermens, Naismith et al. 2010, Hermens, Hodge et al. 2011). These distinct neurocognitive phenotypes predicted social and functional outcomes at follow up. (Lee, Hermens et al. 2013, Lee, Hermens et al. 2015, Crouse, Chitty et al. 2020).

The limited number of studies of neurocognition in young people with suicidal behaviour have produced mixed results. Impairments in executive functions, particularly impulsive decision-making and poorer inhibitory control, are associated with moderate effect sizes (Saffer and Klonsky 2018, McHugh, Lee et al. 2019). On the other hand greater neurocognitive function across several domains, including verbal and visuospatial memory, attention, and social cognition have also been found in population samples of adolescents with suicidal ideation (Barzilay, Calkins et al. 2019). Altered sensory and perceptual processing is another domain of cognition associated with affect regulation and symptoms such as suicidal ideation and hopelessness (Serafini, Gonda et al. 2017).

A greater understanding of the role of neurocognition in the suicidal behaviour of young people may increase understanding of the mechanisms underpinning such behaviour and thus guide the development of suicide prevention interventions in this cohort.

The current study aims to establish whether neurocognitive deficits predict suicidal behaviour in young people with affective disorders accessing mental health care. A secondary aim of this study is to understand whether the addition of neurocognitive dimensions to established social and clinical risk factors improves the predictive power of a model of suicidal behaviour. Additionally, this study will examine whether measures tapping into specific neurocognitive domains, or a general neurocognitive composite, are of greater utility in the model.

Methods

The study was approved by the University of Sydney Human Research Ethics Committee (2008/5453, 2012/1626, 2012/1631) and participants (and/or guardians) gave written informed consent for the use of routinely collected clinical data for research purposes.

Participants

Participants are drawn from a cohort of 6743 individuals aged 12–30 years old who presented to the Brain and Mind Centre's youth mental health clinics in Sydney and were recruited to a research register between June 2008 and July 2018. These clinics consist of an integrated mix of primary mental health services (*headspace*) as well as more specialised psychiatric services. Young people may be referred for care by clinicians or other services (including schools) or they may self-refer, or may attend with encouragement from family members or friends. The youth mental health clinics attract young people presenting for help with a range of psychiatric symptoms, which commonly include mood, anxiety, psychotic and obsessive-compulsive symptoms. These services use a transdiagnostic clinical staging model to guide care, which has been well described in previous publications (Iorfino, Scott et al. 2019). The staging model allows for categorisation of sub-threshold psychiatric disorders, that are either mild or non-specific (Stage 1A) or moderate (Stage 1B), as well as full-threshold psychiatric disorders (Stage 2+).

The research register did not recruit young people who met any of the following criteria; i) lacked capacity to give informed consent (as determined by a psychiatrist); ii) had a history of significant neurological disease (e.g., tumour, head trauma, epilepsy) or serious medical

illness (e.g., cancer); iii) had a history of electroconvulsive therapy in last 3 months; (iv) had a clinically evident intellectual disability and/or, (v) insufficient English language to participate in the assessment.

A subset of the cohort participated in detailed clinical (n= 2767) and neurocognitive assessments (n= 830) between 2008–2016 (Lee, Hermens et al. 2018). The current study sampled from this subset.

The inclusion criteria for the current study were that the participant; (i) was aged between 12 and 30 years old at their first presentation to the clinic; (ii) had at least one visit to the service for mental health care and iii) had a neurocognitive assessment conducted by the clinic within three months of a clinical assessment. Exclusion criteria for the current study were; (i) a primary diagnosis of a schizophrenia-spectrum disorder, neurodevelopmental disorder or substance use disorder, as determined by a psychiatrist. A flow chart that describes the current sampling is included in Supplementary Figure 1.

Data collection (baseline)

Of the 830 participants with a neurocognitive assessment 195 participants had a primary diagnoses of schizophrenia-spectrum disorder, neurodevelopmental disorder or substance use disorder and were thus excluded. Clinical symptoms were assessed by using validated measures of common mental disorders such as depression (Hamilton Depression Rating Scale) (Hamilton 1960) and psychosis (Brief Psychiatric Rating Scale) (Overall and Gorham 1962). Manic-like and psychotic-like experiences were assessed clinically by the treating psychiatrist and recorded in the clinical notes. The term 'manic-like experiences' was used to refer to affective instability and elevated energy levels that did not meet diagnostic criteria for hypomania or mania. The term 'psychotic-like experiences' included transient paranoia or perceptual disturbances that did not meet threshold for a psychotic episode. Both of these clinically defined terms could be applied if the patient self-reported the occurrence of such symptoms between visits, or the clinician observed such symptoms during the assessment. Circadian rhythm dysfunction was also clinically defined and included a range of sleep-wake cycle disturbances including initial insomnia, delayed sleep cycle and early morning wakening.

Suicidal behaviour

Suicidal behaviour was defined as any intentional self-injurious behaviour that may result in serious harm or potentially death. This included behaviours regardless of whether intent to die was present, given the often-ambiguous nature of intent, particularly in young people. Thus the term is inclusive of behaviours associated with intent to die (suicide attempts) or with no intent to die (often termed deliberate self-harm or non-suicidal self-injury) (Turecki and Brent 2016).

As part of standard clinical practice, the treating clinician conducted a risk assessment at baseline assessment and at each visit. The risk assessment includes screening for lifetime history of suicidal ideation and behaviour at first visit and suicidal ideation or behaviour between visits. This information is recorded in the clinical notes. Rather than use a standardised scale, clinicians may ask these questions in a way that allows them to be integrated into clinical assessment. The current study focused on suicidal behaviour that occurred during follow up care as the outcome variable, rather than at baseline in order to ensure the neurocognitive assessment was conducted in a currently or recently suicidal sample. Clinical controls were young people who did not engage in suicidal behaviour while in care.

Neurocognitive testing

A research neuropsychologist or supervised doctoral student administered a neurocognitive battery with the domains chosen based on relevance to common presenting syndromes in an early intervention youth mental health service, particularly affective and psychotic disorders. Measures were chosen based on sound validity and reliability, as well as overlap with the Measurement and Treatment Research to

Improve Cognition in Schizophrenia (MATRICS) initiative (Strauss, Sherman et al. 2006, Nuechterlein, Green et al. 2008, Lee, Hermens et al. 2014). Pre-morbid intelligence (IQ) was estimated on the basis of performance on the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001) or the Wide Range Achievement Test (for participants younger than 16) (Wilkinson and Robertson 2006). Other measures included: the Trail Making Test—part A (TMT A), which measured *processing speed*, and part B (TMT B; Strauss et al., 2006) which measured *cognitive flexibility*, the Rey Auditory Verbal Learning Test (RAVLT; Strauss et al., 2006) which measured *immediate verbal memory* (sum of trial 1–5, RAVLT sum) and *delayed verbal memory* (20-min delayed recall, RAVLT), respectively. The Controlled Oral Word Association Test was used to measure *verbal fluency* (COWAT FAS) (Strauss et al., 2006). Participants also completed a number of subtests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Sahakian and Owen, 1992), including Rapid Visual Processing task (RVP A), which measured *sustained attention*, the Spatial Span task (SSP maximum span length), a measure of *working memory*, the Paired Associate Learning task (PAL errors) a measure of *visuospatial learning and memory* and the Intra-Extra Dimensional task (IED errors), a measure of *set-shifting*.

Data collection (longitudinal)

Key clinical information was extracted from clinical files by a trained research psychologist using a standardised proforma at the following specified timepoints after baseline assessment; 3 months, 6 months, 12 months, 2 years, 3 years, 4 years and 5 years (Hickie, Scott et al. 2013, Iorfino, Hermens et al. 2018, Carpenter, Iorfino et al. 2020). The proforma was designed to collect information about the current episode and specific illness course characteristics between the previous timepoint and the current timepoint. If there is no clinical information available for any time point (i.e. the participant did not attend the service during that time) then that entry is left missing. A ‘time last seen’ entry was used to capture final clinical information that did not align with one of the specified follow-up time points. This ensured that for every participant data were entered for the total time they were engaged with the clinical service. As neurocognition was the primary baseline predictor for this study the clinical assessment at the timepoint nearest to the neurocognitive assessment was used as the baseline clinical assessment.

The proforma included sociodemographic and functional variables such as: age, sex, receipt of government benefits, engagement in part-time or full-time education or employment or training (to determine ‘not in education, employment or training’ (NEET) status). Functioning was measured using the clinician-rated Social Occupational Functional Assessment Scale (SOFAS), which is widely used and has good construct and predictive utility (Hilsenroth, Ackerman et al. 2000, Hay, Katsikitis et al. 2003). Clinical variables measured included; (i) mental health diagnoses (based on Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria) (American Psychiatric Association, 2013); (ii) clinical course information (hospitalisations, childhood diagnoses); and (iii) suicidal thoughts and behaviours.

Analysis

All analyses were carried out using R statistical software (R foundation). Neuropsychological variables were converted to demographically corrected standardized scores (z-scores) using the following established norms: TMT (Tombaugh, Kozak, & Rees, 1998a), RAVLT (Rickert & Senior, 1998) and COWAT FAS (Tombaugh, Kozak, & Rees, 1998b). Similarly, CANTAB z-scores, based on an internal normative database of the 3000 healthy volunteers (<http://www.camcog.com>), were calculated for each participant. Prior to analyses, outliers beyond ± 4.0 z-score for each neuropsychological variable were curtailed to values of ± 4.0 or -4.0 . There were no more than 5% of cases in any group with a z-score of beyond ± 4.0 across variables. Missing data on neurocognitive variables was uncommon, where less than 10% of a

variable was missing the mean was imputed (Supplementary table 1). A measure of general neurocognitive functioning was constructed by calculating the mean z-score across each neurocognitive variable for each participant.

Univariate analysis were carried out to determine differences in sociodemographic, clinical and neurocognitive variables between young people with suicidal behaviour in the period of follow up care relative to those without. Analysis of categorical variables were carried out using χ^2 tests and t-tests were used for continuous variables. Levels of significance were set at $p < 0.05$. The Benjamini-Hochberg procedure, or false discovery method, was used to adjust for multiple testing.

Binary logistic regression was used to investigate the relationship between sex, age, clinical and neurocognitive variables, and the outcome of interest (suicidal behaviour during care). Multiple models were constructed to test our hypothesis that neurocognitive variables would improve the model fit. Model 1 included demographic and clinical predictors only, whereas Model 2 included individual neurocognitive domains and Model 3 included a measure of general cognition instead. The entire dataset was split into a train (70%) and test dataset (30%). Repeated cross-validation was used to identify the model with the best prediction. Repeated cross-validation was carried out using the ‘caret’ package in R, with $k=10$ and 5 repeats. A receiver operator curve (ROC) was developed for each model and an area under the curve (AUC) calculated.

Multicollinearity was assessed for each model by calculating the variance inflation factor (VIF), which remained below 3 for all variables, indicating no collinearity was present.

Results

A total of 635 participants from the wider cohort had a clinical and neurocognitive assessment and therefore met eligibility criteria and were included in this study. Of these 635 participants (mean age 19.6 years, 59.2% female), 104 (16.4%) young people engaged in suicidal behaviour (SB) during care, and the remaining 531 (83.6%) young people were clinical controls (Fig. 1). The median duration of follow-up was 476 days (IQR 95.52–1115). Baseline characteristics of the sample are presented in Table 1.

History of suicidal ideation and behaviour at entry to care

Out of the 104 participants (16.4%) who reported suicidal behaviour during ongoing mental health care, 62 (9.8%) reported a history of suicidal behaviour at the baseline assessment, 55 (8.7%) reported suicidal ideation, and 42 (6.6%) reported new onset suicidal behaviour. Of those without suicidal behaviour during the period of the follow up care, 143 (22.5%) had reported a history of suicidal behaviour and 190 (30.0%) reported suicidal ideation at the baseline assessment.

Social and functional associations with suicidal behaviour

Those who reported suicidal behaviour in the follow up period were younger (17.9 years old vs. 19.9 years old, $t=5.47$, $p\text{-value} < 0.001$) and more likely to be female (79.6% vs. 55.1%, $\chi^2=234$, $p<0.001$). Clinician-rated social and occupational functioning (SOFAS; 59.17 vs. 61.41, $t=2.32$ $p\text{-value} = 0.022$) was lower in the group with suicidal behaviour, though rates of non-engagement in either part-time or full-time education or employment were lower (10.7% vs. 20 %, $\chi^2_{4.54}$ $p\text{-value} = 0.033$). Those with suicidal behaviour had fewer years of education (11.22 vs. 11.75, $t=2.24$, $p=0.027$). Sociodemographic associations with suicidal behaviour in care are available in Table 1.

Psychopathology

Although primary diagnosis at baseline was not a significant predictor (see table 1), greater depressive symptoms (15.5 vs. 11.5, $t=-5.54$, $p<0.001$), positive psychotic symptoms (11.2 vs 10.3, $p=0.05$)

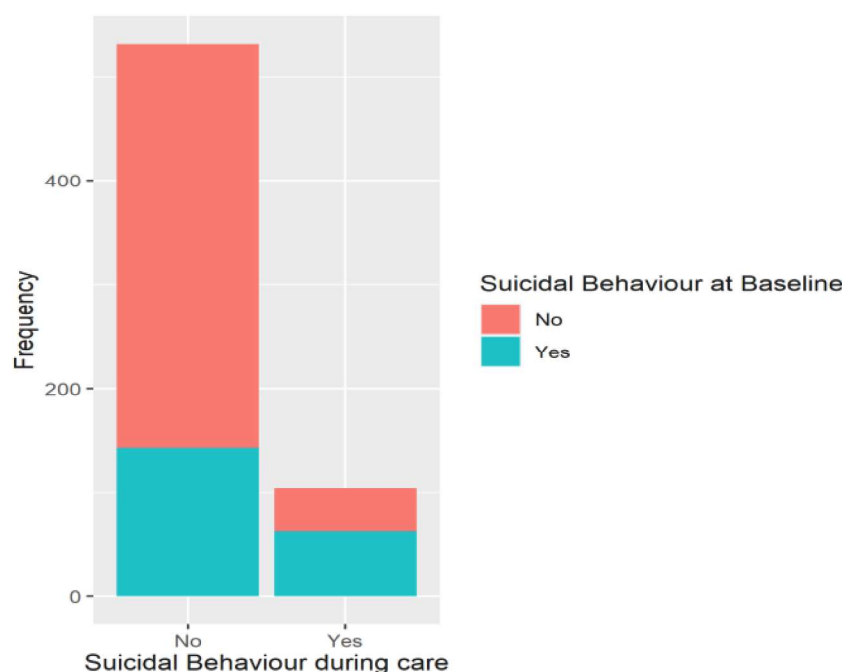


Fig. 1. Frequency of Suicidal Behaviour during care relative to baseline Suicidal Behaviour

Suicidal behaviour includes any intentional self-injurious behaviour that may result in serious harm or potentially death.

and circadian rhythm disturbance ($p=0.02$) were all significantly associated with suicidal behaviour during care. Other clinician-rated symptoms, including at-risk mental states such as psychotic-like experiences (28.2 % vs. 19.4%, $p=0.10$) and mania-like symptoms (26.2% vs. 17.5%, $p=0.11$) were more frequent in the group with suicidal behaviour, but did not reach significance. History of hospitalisation was more common in those with suicidal behaviour and approached significance (30.1% vs. 20%, $p=0.06$).

Distribution of each group (ie. with and without suicidal behaviour during care) was similar across clinical stages, with the majority of participants being in clinical stage 1B (SB 64.1% vs. without SB 61.7%). There were no significant differences between clinical stages. Differences in childhood diagnosis of mental disorder was also non-significant (10.7% vs. 14.5%, $\chi^2=0.82$, $p=0.45$). Clinical associations with suicidal behaviour in care are available in [Table 1](#).

Neurocognitive domains

Young people who had engaged in suicidal behaviour while in care were above age-adjusted population norms (indicated by a positive z-score) on a range of neurocognitive domains (see [Fig. 2](#)). Univariate analyses comparing the group with suicidal behaviour in care to those without suicidal behaviour in care identified a number of neurocognitive domains that differentiated the two groups (Supplementary Table 2).

The suicidal behaviour group was superior to population norms, and the clinical control group without suicidal behaviour, on measures of processing speed (0.222 vs. -0.067, $t=-2.71$, $p\text{-value}=0.023$), working memory (0.354 vs. 0.035, $t=-2.89$, $p\text{-value}=0.016$), delayed verbal memory (0.213 vs. -0.169, $t=-3.345$, $p\text{-value}=0.006$) and visuospatial memory (0.087 vs. -0.16, $t=-2.437$, $p\text{-value}=0.038$). Cognitive flexibility (-0.268 vs. -0.598, $t=-2.31$, $p\text{-value}=0.044$) was the only domain in which the suicidal behaviour group was impaired relative to population norm, though still less impaired than the group without suicidal behaviour during care.

The group with suicidal behaviour was also less impaired relative to clinical controls on an equally weighted composite measure of general cognition (0.058 vs. -0.175, $p=0.006$). There were no significant differences between the groups on measures of sustained attention,

immediate verbal memory, set-shifting or verbal fluency.

Logistic regression

Three alternate models were developed to test whether addition of individual (Model 2) or a composite measure of neurocognition (Model 3) would improve the prediction of the model. Sociodemographic and clinical factors that were significant in bivariate analysis were included in each logistic regression model. Each model was tuned using repeat cross validation. A receiver operator curve (ROC) was developed for each model and an area under the curve (AUC) calculated (see [Fig. 3](#)). Model three showed a slightly improved AUC (0.77) relative to model one (0.75) and model 2 (0.73). Model three had a sensitivity of 0.96, Specificity of 0.10 and positive predictive value of 0.84.

Model three identified five factors that predicted suicidal behaviour while in care (see [Table 2](#)); younger age (OR 1.18, 95% CI 1.10-1.27), female gender (OR 2.63, 95% CI 1.47- 4.76) greater depressive symptoms (OR= 1.08, 95% CI 1.03-1.12), suicidal behaviour at baseline (OR 2.49, 95% CI 1.54-4.06) and superior general cognition (OR=1.94, 95% CI 1.29- 2.94). Not being in education or employment (NEET) ($p=0.07$) and lower SOFAS score ($p=0.08$) approached significance.

Discussion

In young people accessing mental health care with mood and anxiety symptoms, suicidal behaviour during follow up care was associated with cognitive functioning above population norms on a range of tasks, including processing speed, verbal learning, working memory, delayed verbal memory and verbal fluency. Superior functioning on a range of tasks also differentiated those with suicidal behaviour in care from clinical controls (those without suicidal behaviour in care). Of note, cognitive flexibility was the one task that differentiated the two groups in which the group with suicidal behaviour was also impaired relative to the population norm (ie. a negative z-score). Superior general neurocognition remained a significant predictor of suicidal behaviour in care after controlling for known risk factors such as age, gender and history of suicidal behaviour.

While this finding was unexpected it is consistent with findings from other cohorts of young people with suicidal ideation. [Barzilay et al.](#)

Table 1
Clinical predictors of suicidal behaviour in care

Baseline variables	Total n= 635 n (%), or mean	Suicidal behaviour n= 104 (%)	No suicidal behaviour n= 531 (%)	t-test or χ^2	p-value* (adjusted)
Social and demographic					
Age	19.6	17.9	19.9	5.47	< 0.001
Female	374	82 (79.6)	292 (55.1)	23.4	<0.001
NEET	118	11 (10.7)	107 (20.0)	4.54	0.033
SOFA	61	59.17	61.41	2.32	0.021
Education, in years	11.65	11.2	11.7	2.24	0.021
Suicidal ideation and behaviour					
Suicidal ideation at baseline	243 (38.2)	54 (52.4)	189 (35.7)	9.55	0.01
Suicidal behaviour at baseline	203 (32)	61 (59.2)	142 (26.8)	40.16	0.00
Clinical features					
Depressive symptoms (HDRS score)	12.76	15.5	11.5	-5.54	<0.001
Positive psychotic symptoms (BPRS positive scale)	10.41	11.2	10.3	-2.4	0.01
Psychotic-like experiences	132 (20.8)	29 (28.2)	103 (19.4)	3.46	0.10
Mania-like experiences	120 (19.0)	27 (26.2)	93 (17.5)	3.67	0.10
Circadian disturbance	135 (21.3)	33 (32.0)	102 (19.2)	7.67	0.02
Substance use	426 (67.1)	61 (59.2)	365 (68.9)	3.56	0.10
Smoking	225 (35.4)	33 (32.0)	192 (36.2)	0.56	0.56
Primary diagnosis					
Depressive disorder	299 (47.1)	48 (46.2)	251 (47.3)	0.01	0.92
Anxiety disorder	150 (23.6)	17 (16.3)	133 (25.0)	3.18	0.07
Bipolar-spectrum disorder	104 (16.4)	23 (22.1)	81 (15.3)	2.51	0.11
Other	70 (11.0)	13 (12.5)	57 (10.7)	0.13	0.60
Clinical stage					
1A	136 (21.4)	21 (20.4)	115 (21.7)	0.04	0.93
1B	393 (61.9)	66 (64.1)	327 (61.7)	0.06	0.87
2 +	106 (16.7)	17 (16.5)	89 (16.8)	0.00	1.00
Hospitalisation	137 (21.6)	31 (30.1)	106 (20.0)	4.42	0.06
Childhood diagnosis	88 (13.9)	11 (10.7)	77 (14.5)	0.82	0.45
Medications					
Anti-depressant	331 (52.1)	58 (55.8)	273 (51.4)	χ^2 2.09	p-value 0.50
Anti-psychotic	132 (20.8)	26 (25.0)	106 (20.0)	2.77	0.41
Mood stabiliser	79 (12.4)	15 (14.4)	64 (12.1)	1.58	0.57
Stimulant	48 (7.6)	8 (7.7)	40 (7.5)	1.18	0.65

* P-value adjusted by Benjamini-Hochberg method for multiple testing. **Depressive symptoms** measured by Hamilton-Depression Rating Scale; **NEET**: not in education, employment or training; **SOFA**: Social and Occupational Functional Assessment Scale; **Positive psychotic symptoms**: measured by the Brief Psychiatric Rating Scale Positive symptom sub-scale; **Psychosis-like experiences**: attenuated or brief psychotic symptoms; **Manic-like experiences**:

hypomanic symptoms of less than four days; **Circadian disturbance**: sleep-wake cycle disturbances including initial insomnia, delayed sleep phase or early morning waking; **Clinical stage 1A**: mild or non-specific symptoms; **Stage 1B**: specific symptoms not reaching threshold for diagnosis; **Stage 2 +** refers to full-threshold psychiatric disorders.

(2019) found young people aged 11 to 21 years old with suicidal ideation had better neurocognitive performance than non-suicidal controls on a range of tests measuring attention, memory, reasoning, motor speed and social cognition. Despite better cognitive functioning young people with suicidal ideation were more functionally impaired and had greater psychopathology (Barzilay, Calkins et al. 2019). A recent review of cognition across clinical stages of psychiatric illness by Allott (2019) also found certain phenotypes of illness, particularly bipolar spectrum and anxiety disorders, may be associated with above average cognitive function early in illness course, or prior to onset of symptoms (Allott 2019). Studies of adults with affective disorders have also described distinct sensory processing profile associated with affective sub-type (ie. Irritability, anxious, or cyclothymic) and suggested sensory sensitivity can drive hyperarousal (Engel-Yeger, Muzio et al. 2016). Hyperarousal and hypervigilance are associated with anxiety and hypomanic states, which have been shown to increase some cognitive abilities, particularly related to memory, in the near term (Marin, Raymond et al. 2019). Affective state can moderate attention and memory function, with negatively valenced stimuli being preferentially encoded in distressed or negative mood states.

The neurocognitive battery used in this study was designed for early intervention services targeting mood and psychotic disorders. Tests of memory and attention used neutral stimuli, and thus may have failed to detect biases of attention and memory towards negatively valenced stimuli. Including additional measures for dimensions previously found to be associated with suicidal behaviour, such as tests of inhibitory control, impulsive decision-making or suicide-specific memory and attention biases, may have identified deficits in the group with suicidal behaviour. (Richard-Devantoy, Ding et al. 2016) Including a greater range of measures on potential mediators, such as sensory processing, may also have added to our findings. The role of state-based changes to neurocognitive functioning should also be considered. Previous work by Tickell et al. (2019) found that when measured within 48 hours of admission, attention was inversely correlated with suicidal ideation in young people in an inpatient setting (Tickell, Scott et al. 2019). The current study used a baseline neurocognitive assessment to predict suicidal behaviour in care over the next 2 years, but up to a maximum of 3.5 years. It is possible that rather than having better neurocognitive functioning as a whole, the group with suicidal behaviour display state-based, or transient, impairments in certain domains. Further exploration of the role of intraindividual variation in neurocognitive functioning and its relation to illness episodes and suicidal behaviour is needed.

Although unexpected, our findings add weight to the notion that suicidal behaviour in young people may be phenotypically different to other populations, including young people with psychotic disorders, which are known to be associated with cognitive deficits as early as age three (Khandaker, Barnett et al. 2011). Although primary diagnosis did not predict suicidal behaviour in care, specific symptom clusters (depressive, positive psychotic symptoms, circadian dysfunction) were significant predictors. Previous work in this cohort has shown that co-morbidity of symptom clusters are common, which is to be expected given the transdiagnostic nature of mental health symptoms, particularly in young people (Carpenter, Iorfino et al. 2020). While in older cohorts discrete diagnostic categories, such as major depression and bipolar disorder, are predictors of suicidal behaviour (Turecki and Brent 2016) in young people specific sub-threshold symptom clusters may be more useful in understanding risk of suicidal behaviour in the near to medium term. While clinicians or services may be hesitant to intervene to treat sub-threshold symptoms, the contribution of such symptoms to

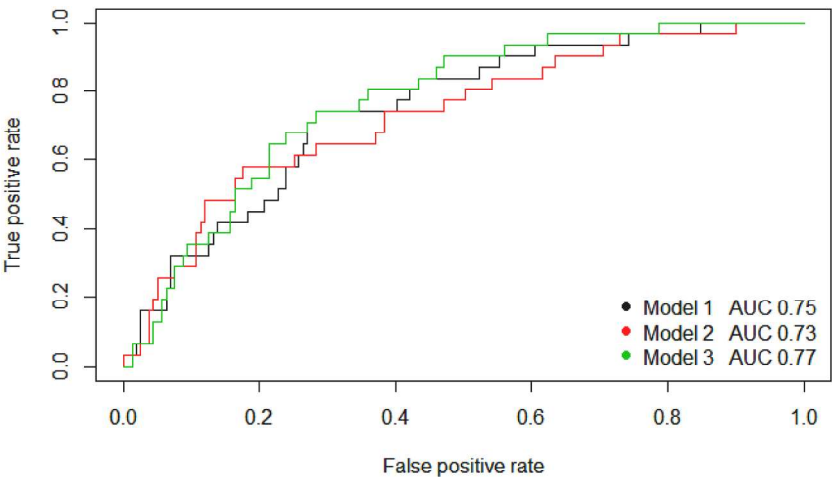
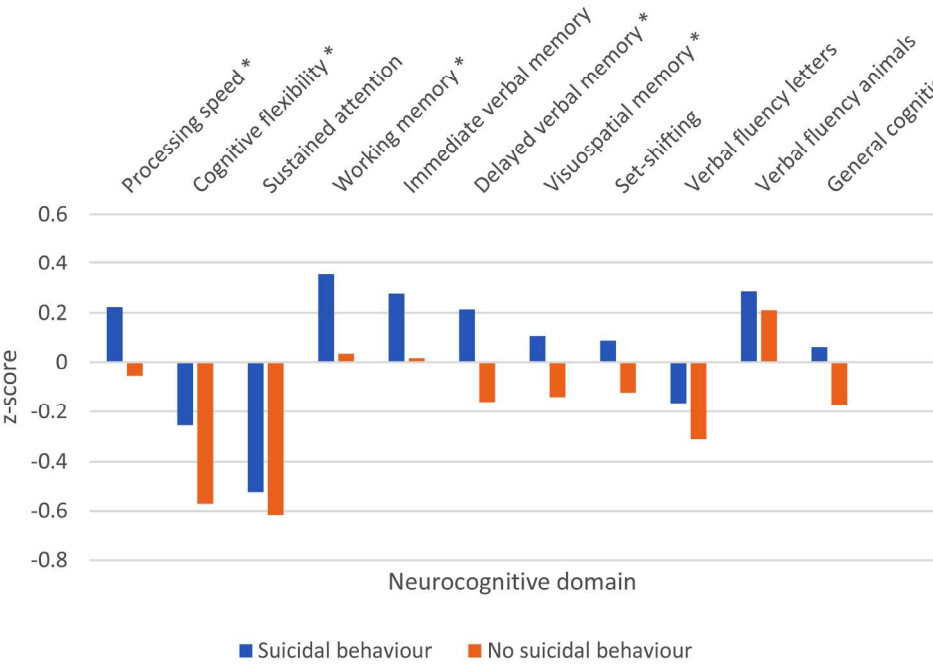


Table 2
Odds ratio of suicidal behaviour during care, by predictor variable

	OR	Confidence interval 95%	
Younger age	1.18*	1.10	1.27
Female	2.63*	1.47	4.76
SOFAS	0.98	0.95	1.0
NEET	0.50	0.23	1.03
Depression	1.08*	1.03	1.12
Suicidal behaviour at baseline	2.49*	1.54	4.06
Positive psychotic symptoms	1.03	0.94	1.12
Circadian dysfunction	1.26	0.73	2.15
General cognition	1.94*	1.29	2.94

Depressive symptoms measured by Hamilton-Depression scale score; **NEET**: not in education, employment or training; **SOFAS**: Social and Occupational Functional Assessment Scale; **Positive psychotic symptoms**: measured by the Brief Psychiatric Rating Scale Positive symptom sub-scale; **Circadian disturbance**: sleep-wake cycle disturbances including initial insomnia, delayed sleep phase or early morning waking; **General cognition**: calculated by summing the z-scores of each variable to calculate a single mean z-score across the ten variables.

Fig. 2. Neurocognitive dimensions by group, relative to population norms
*p-value <0.05, after adjusting by Benjamini-Hochberg method for multiple testing. **Predicted IQ**: Wechsler Test of Adult Reading or the Wide Range Achievement Test (for participants younger than 16); **Processing speed**: Trail Making Test—part A; **Cognitive flexibility**: Trail Making Test—part B; **Immediate verbal memory**: Rey Auditory Verbal Learning Test, sum of trial 1–5; **Delayed verbal memory**, 20-min delayed recall. **Verbal fluency**: Controlled Oral Word Association Test- letters subtest; **Sustained attention**: Rapid Visual Processing task; **Working memory**: Spatial Span task; **Visuospatial learning and memory**: Paired Associate Learning task; **Set shifting**: Intra-Extra Dimensional task; **General cognition**: calculated by summing the z-scores of each variable to calculate a single mean z-score across the ten variables.

Fig. 3. Receiver operating curve of alternate predictive models of suicidal behaviour
Model 1 includes demographic and clinical predictors only; **Model 2** includes demographic, clinical and individual neurocognitive predictors; **Model 3** includes demographic, clinical predictors and a measure of general neurocognitive functioning. Model 3 area under the curve (AUC) represents sensitivity of 0.96, specificity of 0.10, and a positive predictive value of 0.84.

suicidal behaviour in young people must be carefully considered.

Our findings are encouraging as the neurocognitive deficits that have been found in adult populations with suicidal behaviour, such as deficits of working and delayed memory, attentional tasks, processing speed and verbal fluency are not present in this younger population (Keilp, Gorlyn et al. 2013, Richard-Devantoy, Berlim et al. 2014, Richard-Devantoy, Berlim et al. 2015). This suggests neurocognitive impairments in older cohorts of suicide attempters may be the result of scarring from recurrent episodes of psychopathology or other mediating factors, rather than a predisposing or fixed deficit. Possible mediators of cognitive impairment that have previously been identified include the cumulative effect of substance use or repeated episodes of mood disorder, whether mania or depressive (Lee, Altshuler et al. 2013).

Current clinical guidelines for suicide prevention recommend a number of interventions, including means restriction, aftercare, and specific psychological therapies to target suicidal cognitions and behaviour (RANZCP 2004, Kendall, Taylor et al. 2011). Our findings of a distinct neurocognitive profile in young people with affective disorders may have implications for delivery of care. For example, deficits in

cognitive flexibility but superior memory functioning may indicate a greater ability to retain the content of structured psychological interventions, such as dialectical behavioural therapy, cognitive behavioural therapy and brief interventions like safety planning, once attentionally engaged. Impaired cognitive flexibility has also been shown to predict future social and functional impairment in this cohort, suggesting this may be an important target of intervention (Crouse, Chitty et al. 2020). While our findings concluded that including a general measure of neurocognitive functioning improved the predictive power of the model, rather than individual neurocognitive dimensions, this needs further exploration. Use of neurocognitive assessment in clinical practice has become more accessible with advances in technology though has not yet been widely adopted. The role of neurocognitive assessment in enhanced clinical characterisation and its use in treatment planning for young people requires further investigation. Similarly understanding the patient experience of enhanced clinical assessment will be important. For example, in young people in distress being given feedback that the experience of memory or attentional deficits is a symptom rather than an objective, fixed deficit may be reassuring and support recovery. Regardless, tracking trajectories of illness and neurocognitive functioning in young people and over the life course will be important in understanding mechanisms by which populations with suicidal behaviours develop cognitive impairment in order to design interventions to prevent such outcomes.

Limitations

In addition to the limitations of the neurocognitive battery used there are several other limitations that should be noted. The control group included some participants (22.5%) who had previously engaged in suicidal behaviour. Given a clinical control group was used even those without history of suicidality are at high risk of engaging in some type of suicidal behaviour on an ongoing basis. Inclusion of a healthy control group would have reduced this potential bias. The study was also conducted in a clinical setting and drop-out over time was uncontrolled thus sample attrition may have biased model estimates. There were also a number of known correlates of suicidal behaviour, such as history of childhood abuse (Pompili, Innamorati et al. 2014), that were not included in this study, which limited the ability to comprehensively explore the effect of potential confounders.

Conclusion

Suicidal behaviour in young people with affective disorders represents a different neurocognitive and clinical phenotype relative to young people with psychotic disorders or adult populations with suicidal behaviour. While a range of neurocognitive deficits may be associated with suicidal behaviour in adults, better memory function but impaired cognitive flexibility characterises neurocognition in younger people with suicidal behaviour. These findings suggest suicide prevention interventions in young people require a different approach to that of adult populations. Psychological interventions that target suicidal cognitions and behaviour may be less likely to be hampered by neurocognitive deficits in populations of young adults.

Author contributions

CM conducted planned the study design, primarily carried out the data analysis and drafting and revisions of the manuscript. FI and JJC contributed to the study design, data analysis and writing of the manuscript. JSC, AT, AN and, NZ contributed to the data collection, study design and manuscript preparation and writing. NH contributed to the data analysis and writing of the manuscript. RL, DFH, ES and IH contributed to the data collection, study design and provided supervision and overview of the manuscript preparation, interpretation of results and writing of the manuscript.

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Declaration of Competing Interest

Catherine M. McHugh, Frank Iorfino, Jacob J Crouse, Joanne S. Carpenter, Ashleigh Tickell, Alissa Nichles, Natalia Zmicerevska, Nicholas Ho, Rico Lee, Daniel F. Hermens and Sharon Naismith report no conflicts of interest. Elizabeth Scott is the clinical director of the St Vincent's Youth Mental health program. She has received honoraria for educational seminars related to the clinical management of depressive disorders supported by Servier and Eli-Lilly pharmaceuticals. She has participated in a national advisory board for the antidepressant compound Pristiq, manufactured by Pfizer. She was the National Coordinator of an antidepressant trial sponsored by Servier. Ian Hickie was an inaugural Commissioner on Australia's National Mental Health Commission (2012–18). He is the Co-Director, Health and Policy at the Brain and Mind Centre (BMC) University of Sydney. The BMC operates an early-intervention youth services at Camperdown under contract to headspace. Professor Hickie has previously led community-based and pharmaceutical industry-supported (Wyeth, Eli Lilly, Servier, Pfizer, AstraZeneca) projects focused on the identification and better management of anxiety and depression. He was a member of the Medical Advisory Panel for Medibank Private until October 2017, a Board Member of Psychosis Australia Trust and a member of Veterans Mental Health Clinical Reference group. He is the Chief Scientific Advisor to, and an equity shareholder in, Innowell. Innowell has been formed by the University of Sydney and PwC to deliver the \$30m Australian Government-funded 'Project Synergy'. Project Synergy is a three year program for the transformation of mental health services through the use of innovative technologies

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4.3 Chapter summary

Chapter 4 examined the role of neurocognition as a potential biomarker of suicidal behaviour in the developing brain. [Chapter 4.1](#) tested the hypothesis that impulsivity remains a useful predictor of suicidal behaviour and self-harm in young people, despite an increase in impulsive decision-making and behaviour being a known feature of normative adolescence and early adulthood. Measures of impulsivity were associated with a small to moderate effect on suicidal behaviour, relative to healthy controls, but not clinical controls. There was no evidence that effect was moderated by the sub-type of either impulsivity or SB (whether associated with suicidal intent or not). [Chapter 4.2](#) found the addition of a broader set of neurocognitive domains to a predictive model of SB in a clinical YMH population slightly improved performance, and that a general measure of cognition was more useful than including separate domains.

[Chapter 4](#) established that despite small sample sizes, there is emerging evidence of a unique neurocognitive profile in young people with suicidal behaviour. However, cognition as a state-based predictor of SB in young people remains relatively understudied, given the failure to measure suicidal behaviours and cognition in temporal proximity. In both studies, cognitive deficits were evident in clinical controls and, in [Chapter 4.2](#) deficits were more marked in clinical controls than in those with SB. This finding reinforces the importance of a holistic approach to reducing harms. Given such deficits are known to increase the risk of a range of outcomes, including premature mortality, chronic mental illness and persistent social and functional impairment, the final chapter of the thesis uses data linkage to examine a broader range of adverse outcomes in this cohort. [Chapter 5](#) will examine mortality outcomes, from all-causes and specific to suicide or accidental death, as well as the prevalence of emergency department and hospital admissions for suicidal behaviour, accident and injury, drug and alcohol use and physical health reasons.

Chapter 5: Mortality outcomes in young people accessing mental health care

McHugh, C., Iorfino, F., Karunaratne, N., Song, Y.S., Zmicerevska, N., Skinner, A., Scott, E. and Hickie, I.B. 2023, Premature mortality in young people accessing early intervention youth mental healthcare: data-linkage cohort study. *BJPsych Open*. 9, e76, 1–9.

5.1 Abstract

Background:

Understanding premature mortality risk from suicide and other causes in youth mental health cohorts is essential for delivering effective clinical interventions and secondary prevention strategies.

Aims:

To establish premature mortality risk in young people accessing early intervention mental health services and identify predictors of mortality.

Methods:

State-wide data registers of emergency department (ED), hospital admissions and mortality, were linked to the Brain and Mind Research Register, a longitudinal cohort of 7081 young people accessing early intervention care, between 2008 and 2020. Outcomes were mortality rates and age-standardised mortality ratios (SMR). Cox regression was used to identify predictors of all-cause mortality and deaths due to suicide or accident.

Results:

There were 60 deaths (Male 63.3%) during the study period, 25 (42%) due to suicide, 19 (32%) from accident or injury, 8 (13.3%) where cause was under investigation. All-cause SMR was 2.0 (95% CI 1.6-2.6), but higher for males (5.3, 95% CI 3.8-7.0). The mortality rate from suicide and accidental deaths was 101.56 per 100,000 person-years. Poisoning, whether intentional or accidental, was the single greatest primary cause of death (26.7%). Prior ED presentation for poisoning (HR 4.40, 95% CI 2.13-9.09) or psychiatric admission (HR 4.01, 95% CI 1.81- 8.88) were the strongest predictors of mortality.

Conclusion:

Premature mortality in young people accessing early intervention mental health services is greatly increased relative to population. Prior health service use and method of self-harm are useful predictors of future mortality. Enhanced care pathways following ED presentations should not be limited to those reporting suicidal ideation or intent.

Premature mortality in young people accessing early intervention youth mental healthcare: data-linkage cohort study

Catherine M. McHugh, Frank Iorfino, Natalia Zmicerevska, Yun Ju Christine Song, Adam Skinner, Elizabeth M. Scott and Ian B. Hickie

Background

Understanding premature mortality risk from suicide and other causes in youth mental health cohorts is essential for delivering effective clinical interventions and secondary prevention strategies.

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To establish premature mortality risk in young people accessing early intervention mental health services and identify predictors of mortality.

Method

State-wide data registers of emergency departments, hospital admissions and mortality were linked to the Brain and Mind Research Register, a longitudinal cohort of 7081 young people accessing early intervention care, between 2008 and 2020. Outcomes were mortality rates and age-standardised mortality ratios (SMR). Cox regression was used to identify predictors of all-cause mortality and deaths due to suicide or accident.

Results

There were 60 deaths (male 63.3%) during the study period, 25 (42%) due to suicide, 19 (32%) from accident or injury and eight (13.3%) where cause was under investigation. All-cause SMR was 2.0 (95% CI 1.6–2.6) but higher for males (5.3, 95% CI 3.8–7.0). The mortality rate from suicide and accidental deaths was 101.56 per

100 000 person-years. Poisoning, whether intentional or accidental, was the single greatest primary cause of death (26.7%). Prior emergency department presentation for poisoning (hazard ratio (HR) 4.40, 95% CI 2.13–9.09) and psychiatric admission (HR 4.01, 95% CI 1.81–8.88) were the strongest predictors of mortality.

Conclusion

Premature mortality in young people accessing early intervention mental health services is greatly increased relative to population. Prior health service use and method of self-harm are useful predictors of future mortality. Enhanced care pathways following emergency department presentations should not be limited to those reporting suicidal ideation or intent.

Keywords

Youth mental health; suicidal behaviour; deliberate self-harm; mortality; accident and injury.

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Longitudinal studies of cohorts accessing mental health services have found increased risk of premature mortality due to suicide, as well as deaths attributable to accident and injury, substance use and cardiometabolic disease.^{1,2} In health systems globally, an increased focus on early intervention has led to new cohorts of young people accessing mental health services. Youth mental health cohorts experience high rates of suicidal ideation, thoughts and behaviour (SITB) and non-suicidal self-harm, as well as increased rates of other risk factors associated with increased mortality across the lifetime, such as alcohol and substance use, poorer physical health and higher rates of accident and injury. Although previous register-based studies of hospital and out-patient populations have found that young people with psychiatric disorders are at increased risk of premature mortality, it is not clear whether this elevated risk is present in youth cohorts accessing community-based early intervention mental health services, who are typically considered to be at earlier stages of illness than those accessing hospital-based or out-patient mental health services.³

Suicide remains a leading cause of death of young people in the population,⁴ and many countries have reported increased demand for mental health services from young people experiencing SITB and non-suicidal self-harm. Increased demand has been evident in youth mental health services and in emergency departments, where rates of suicidal ideation and/or behaviour and non-suicidal self-harm-related presentations have been increasing.^{5–7} Given that previous suicidal behaviour remains one of the strongest risk factors

for future suicidal behaviour,^{8,9} these presentations are a compelling target of secondary intervention for health services.

Yet how clinical presentations for suicidal ideation and/or behaviour or non-suicidal self-harm relate to mortality risk from suicide and other causes varies both between and within populations. In the UK, cohort studies of adults presenting to emergency departments with self-harm, which includes both suicide attempts and self-harm without suicidal intent, have shown greatly increased risks of premature mortality from related causes of death, such as suicide or accident and injury, as well as other physical health causes relative to the general population.² Over a median of 6 years follow-up, all-cause mortality risk was elevated in males (standardised mortality ratio (SMR) 4.1, 95% CI 3.8–4.3) and females (3.2, 2.9–3.4), with accidental deaths being associated with the greatest increase in mortality risk.² Hawton et al (2020) found a similarly increased risk of premature mortality in a cohort of children and adolescents presenting to emergency departments with self-harm, also defined to include both suicide attempts and non-suicidal self-harm.¹⁰ In both cohorts, male sex was associated with almost twice the absolute risk of premature mortality. However, female sex was still associated with a greater increase in mortality risk relative to females in the general population. In both cohorts, older age at the time of presentation for non-fatal self-harm predicted greater risk of premature mortality.

A detailed understanding of cause-specific mortality risk and predictors of premature mortality within a population is essential

for delivering effective clinical and population-level interventions. Characterising health service use prior to death may also identify opportunities for targeted interventions relevant to youth mental health cohorts. For example, a history of psychiatric admission has been shown to increase risk of premature mortality from suicide and other causes, with the greatest risk of suicide occurring soon after discharge.¹¹ On the other hand, the risk of premature death from other causes, including physical health causes, increases over time. Other factors known to moderate the risk of mortality following presentations for SITB or self-harm include the method of self-harm used, a diagnosis of major mental illness or alcohol or substance use disorder, and a history of repeat presentations with self-harm.¹²

The first aim of this study was to estimate premature mortality risk in a cohort of young people accessing early intervention youth mental healthcare by determining SMRs as well as all-cause and cause-specific mortality rates. Mortality from suicide, accident or injury and other physical health causes was included. The second aim was to establish the most common primary and contributing causes of death. Finally, the study aimed to identify whether prior health service use is a useful predictor of death from suicide or accidental and injury.

Method

Participants and setting

The study used data from the Brain and Mind Research Register (BPRR), a longitudinal cohort study of 7081 young people presenting to the youth mental health clinics of the Brain and Mind Centre in the Sydney suburbs between October 2008 and October 2020.^{13,14} The early intervention clinics consist of primary mental healthcare (headspace) and more specialised mental health services, including psychiatrists and psychologists. They are accessed by young people aged 12–30 years old, presenting at early clinical stages (non-specific symptoms) through to full-threshold disorders. The study included young people aged 12–30 years to reflect the cohort of young people accessing care via headspace services.

Inclusion criteria for the BPRR were: (a) age between 12 and 30 years at first presentation to the service, and (b) attendance of at least one visit to the service. Exclusion criteria for the BPRR were: (a) medical instability or lack of capacity to give informed consent (as determined by a psychiatrist), (b) history of neurological disease (e.g. tumour, head trauma, epilepsy), (c) medical illness known to affect cognitive and brain function (e.g. cancer, electro-convulsive therapy in the past 3 months), (d) clinically evident intellectual disability, and/or (e) insufficient English to participate in the research protocol.

Data linkage

The BPRR was linked to three external databases held by the Centre for Health Record Linkage in New South Wales (NSW), Australia.^{14,15} These databases were the Register of Births, Deaths and Marriages (RBDM), the Australian Coordinating Registry Cause of Death Unit Record File (ACR-COD URF), the Emergency Department Data Collection (EDDC) and the Admitted Patient Data Collection (APDC). Gender and age were selected from the BPRR. Other exposures of interest, such as emergency department presentations and hospital admissions, were selected from the EDDC and APDC. The EDDC uses diagnostic codes primarily from Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) but also from the ICD-9-CM, ICD-10-CM and ICD-10-AM. In Australia, emergency department diagnostic codes are applied by clinicians at the point of care rather

than by professional clinical coders. Clinicians begin by entering diagnostic terms (or the presenting problem) as free text, with the closest matching SNOMED CT term then presented for selection. As a result, diagnostic codes tend to reflect presenting symptoms rather than true diagnoses.¹⁶ This has limited consequences for the aims of the current study, as psychiatric diagnoses are made formally only by specialised services, often over a number of visits. The current study aimed to capture broad categories of emergency department presentations related to outcomes of interest. Two authors (C.M.M. and N.K.) with clinical training in emergency department care and mental health independently reviewed the diagnostic terms and grouped presenting symptoms into several predetermined categories including (a) suicidal ideation, behaviour or self-harm; (b) accident and injury; (c) drug and alcohol use; (d) medical or physical illness; or (e) other. Interrater reliability was 98%. Any discrepancies between coders were resolved via consensus. Only one reason for presentation was recorded for each emergency department presentation.

This study defined suicidal behaviour and non-suicidal self-harm in clinical populations of young people as occurring along a spectrum of intent and lethality, in keeping with previous definitions by Hawton et al.¹⁰ Self-harm is used to describe an intentional act associated with an intent to harm oneself, whether or not it was associated with an intent to end one's life. This approach to combining suicidal behaviour and non-suicidal self-harm was used given that the expression (and recording) of intent associated with an act of self-harm in emergency department settings may be influenced by factors including an individual's desire to avoid restrictive interventions, therapeutic rapport and/or clinician skill. The EDDC also does not require clinicians to formally differentiate between these constructs. Given these factors, the use of the broader construct of suicidal behaviour and self-harm was considered more valid than the use of specific terms such as non-suicidal self-injury, which at present are not typically used in clinical settings in Australia and thus are not likely to be accurately recorded. Intentional self-poisoning was included as a subtype of self-harm. Suicidal behaviour refers to self-harm associated with any suicidal intent. In categorising the primary diagnostic terms associated with an emergency department presentation, the suicidal ideation, behaviour or self-harm category was applied if the terms intentional self-injury or intentional self-poisoning were used. Any self-poisoning which was specifically labelled as accidental was included in the 'accident and injury' category. Many self-poisoning presentations were not specifically labelled as intentional or accidental. In such instances, poisoning or overdose with known drugs of misuse or recreational drugs were categorised as 'drug and alcohol' presentations. Pharmaceutical drug poisoning or overdose, where patterns of misuse were not accepted to have a recreational component, were considered 'suicidal or self-harm' presentations.

Variables of interest selected from the APDC were mental health unit (psychiatric) admissions and intensive care unit (ICU) admissions. ICU refers to admissions to the general hospital ICU, not mental health admissions. ICU admissions were included as an exposure of interest given their association with high-risk suicidal behaviour and increased mortality. The total numbers of admissions and emergency department presentations per individual were counted, as well as lifetime history of each category of emergency department presentation. Childhood presentations (age <12 years) to an emergency department for any mental health reason (e.g. SITB, other psychiatric symptoms, or drug- and alcohol-related) were included in determining lifetime history of these presentation types; however, for presentations related to medical or physical illness or common injuries, lifetime history was defined as over the age of 12 years. Emergency department presentations and hospital admissions that occurred on the same date as death were excluded.

Outcome measures

The primary outcome measure was mortality from all causes and mortality due to suicide or accident. Date of death was extracted from the NSW RBDM. Underlying cause of death and contributing causes were extracted from the ACR-COD URF. The ACR-COD URF uses ICD-10 codes only. Deaths were considered suicides if coded as intentional (X60–X84) or self-inflicted but with undetermined intent (Y10–Y34), in keeping with the convention used within the suicide research literature.^{10,17} Deaths where cause had not yet been allocated an ICD code within the ACR-COD URF were included as suicide or accident deaths, as according to the ACR-COD URF a delay in cause of death being assigned indicates a coronial investigation is required to determine a specific cause of an unnatural death (i.e. suicide, accident or injury-related).¹⁸ Therefore, these deaths without an ICD code were analysed with suicide and accident or injury deaths.

Suicide deaths were further subcategorised by method, including self-injury (ICD-10 codes X70–X84, Y20–Y34) and intentional self-poisoning (X61–X69, Y11–Y19). Accidental deaths (V01–X59) were subcategorised into accidental poisoning (X40–X49), transport accidents (V01–X59) or other external causes of accidental injury (W00–X59). Contributing causes of death are presented where they are distinct from the primary cause of death and are referred to as secondary causes.

Ethics approval for the BPRR was granted by the University of Sydney Human Research Ethics Committee (2012/1626). Participants in the BPRR consented to their routinely collected clinical information being used for clinical research for a period of 5 years and to being contacted about additional research. The BPRR ethics approval (2012/1626) stipulated that additional consent would be necessary if the participant was required to return to the clinic for additional assessment for research. The current study did not require any additional assessments or further contact with participants. Ethics approval for the current study linking the BPRR to external data-sets was granted by the NSW Population and Health Services Research Ethics Committee (PHSREC) (2019/ETH12201). A waiver of consent was granted by the PHSREC as the following National Statement on Ethical Conduct in Human Research (2007) criteria were met: (a) the purposes of the study could not be met without temporary reidentification; (b) contacting participants for recontact was not practicable, given the large number of participants and that the key outcome of interest was death; and (c) there was no reason to believe participants would not have consented to the use of their routinely collected data for this study, given they had previously consented to more sensitive information being accessed, such as their individual medical records.

Analysis

Mortality rates and SMR

SMR was calculated using indirect methods of standardisation by age category (15–19, 20–24, 25–29, 30–34, 35–39, 40–45 years) and sex. The group used to determine the expected number of deaths (the denominator) was the general population of NSW in the year that marked the mid-point of the study.¹⁹ Mortality rates were calculated using the person-time method, which is the number of deaths divided by the person-years of follow-up. For calculation of the SMR, the date of the individual's first health service visit after the age of 12 years old was used to calculate years of follow-up. If the date of the individual's first youth mental health clinic visit was missing, these cases were omitted from the calculation of years of follow-up. Mortality rates for specific causes of death, including suicide, accident and injury, and those relating to

medical illness and where cause was under investigation were also calculated using this method.

Cox regression

For survival analysis, the follow-up time was calculated from the date of the last health visit (youth mental health clinic visit, emergency department presentation, mental health unit admission or ICU admission) to the date of death or the end of the study. Where the first youth mental health clinic date was missing and there was no history of other health visit types, it was not possible to accurately calculate follow-up time; thus, these individuals were not included in the Cox regression.

Cox proportional hazards regression modelling was conducted for emergency department presentations and hospital admissions, adjusted for gender. Exposure variables of interest were gender and lifetime history of emergency department presentation for suicidal ideation or behaviour, or mental health, drug and alcohol, accident and injury or medical reasons. Hospital admission variables of interest included lifetime history of mental health unit admission or ICU admission. Modelling was conducted first with all-cause mortality as the outcome and subsequently with deaths due to suicide, accident and injury, or cause under investigation as the outcome of interest. Partial residuals were plotted in order to check that proportional hazards were constant over time.

Sensitivity analysis

A sensitivity analysis was conducted to assess the effects of different constructs of self-poisoning on the prediction of mortality outcomes. In the sensitivity analysis, self-poisoning presentations were considered as distinct from other forms of self-harm. All types of self-poisoning, whether intentional, accidental or of unknown intent, were considered as one category distinct from other types of accident, injury or drug and alcohol presentations. Thus, the following categories of emergency department presentations were considered: (a) self-poisoning, (b) suicidal ideation or self-harm (without poisoning), (c) other accident and injury (excluding accidental poisoning), (d) drug and alcohol (excluding self-poisoning), (e) mental health, (f) physical illness and (g) other.

Results

Of the 7081 individuals in the cohort, 60 individuals (male $n = 38$, 63.3%) were deceased by the study end date (Table 1). Follow-up time was missing for 910 individuals (male $n = 408$, 44.8%), of whom eight individuals were deceased (mean age at death 25.9 years, s.d. 5.7).

The median duration of follow-up from first health service visit was 7.39 years (interquartile range (IQR) 3.77 years). The total person-years of follow-up from first health service visit was 50 219. Cause of death was available for 52 individuals ($M = 31$, 59.6%). The mean age at death was 27.16 years (s.d. 6.15). The median duration of follow-up time from last health service visit and end date (either death or end of study) was 36.8 months (IQR 13.5–78.3).

Mortality rates

Of the 60 individuals who died during the study period, 25 (42%) died owing to suicide; 19 deaths (32%) were due to accident or injury, eight (13%) deaths had a medical cause and eight (13%) deaths were of unknown cause (Table 2). The all-cause mortality rate in the BPRR cohort was 119.47 deaths per 100 000 person-years. All-cause SMR for the entire BPRR cohort was 2.0 (95% CI 1.6–2.6); the SMR for males was (5.3, 3.8–7.0), which was higher

Table 1 Characteristics of deaths relative to remaining BPRR cohort

		Deceased (<i>n</i> = 60)	BPRR cohort alive (<i>n</i> = 7021)	<i>t</i> -test
Age at first presentation, mean (s.d.) years		22.17 (5.03)	19.5 (4.07)	<i>P</i> < 0.001
Gender, <i>n</i> (%)	Male	38 (63.3)	3037 (43.3)	Odds ratio CI (95%) 2.34 (1.37–3.99)
	Female	21 (35)	3926 (55.9)	
First presentation type				
YMH clinic visit, <i>n</i> (%)		17 (28.3)	2876 (41.0)	0.80 (0.34–1.86)
ED presentation, <i>n</i> (%)		25 (41.7)	2800 (39.9)	1.21 (0.54–2.69)
Mental health unit admission, <i>n</i> (%)		8 (12.0)	216 (3.1)	5.0 (1.86–13.50)
Intensive care unit admission, <i>n</i> (%)		2 (3.0)	46 (0.6)	5.89 (1.22–28.5)
Unknown, <i>n</i> (%)		8 (12.0)	1083 (15.4)	

Gender does not include young people identifying as transgender; this is for privacy reasons owing to the small number (*n* = 59). First presentation type refers to the first visit date recorded on the linked BPRR-M&M (mortality and morbidity) database. YMH (youth mental health) clinic visit refers to clinic visits at the two BPRR clinic sites. Other primary care or mental health visits not recorded by the three linked data-sets may also have occurred. Unknown first visit type is the reference category for calculating odds ratios of first presentation types.

than that for females (0.91, 0.7–1.6). The highest cause-specific mortality rate was from suicide, at 49.78 per 100 000 person-years, followed by accident or injury, at 37.83 deaths per 100 000 person-years.

The mean age at death was older for suicide deaths (27.5 years, s.d. 6.2), than accident or injury deaths (25.7 years, s.d. 5.8). The mean age of deaths from medical causes or where cause was under investigation was 28.4 (6.5) years. Deaths where cause was under investigation were most frequently associated with male gender (*n* = 7, 87.5%), followed by deaths from accident or injury (*n* = 13, 68.4%), suicide (*n* = 14, 56%) and medical causes (*n* = 4, 50%).

Cause of death

The most frequent method of suicide death was hanging, accounting for 15 (60%) deaths, followed by intentional self-poisoning with four (16%) deaths (Table 2). The most common cause of accident or injury death was poisoning, which accounted for 12 (60%) deaths, followed by motor vehicle accident with six (31.6%) deaths. Medical causes included cardiac disease, neurological causes, obesity and sepsis.

Mental illness was identified as a contributing cause in 12 (48%) suicides and four (21%) accident or injury deaths. Drug and alcohol use and poisoning were secondary causes in seven (28%) suicide deaths and three (15.8%) accidental deaths. Accident or injury was a secondary cause in three (12%) suicide deaths.

Table 2 Characteristics of deaths from suicide and accidental deaths

	Suicide (<i>n</i> = 25)	Accidental (<i>n</i> = 19)
Gender, male (%)	14 (56.0)	13 (68.4)
Age at death in years, mean (s.d.)	27.5 (6.2)	25.7 (5.8)
Time since last visit in months, mean (s.d.)	26.0 (25.7)	29.04 (21.5)
Primary cause of death		
Self-injury, <i>n</i> (%)	21 (84.0)	–
Hanging	15 (60.0)	–
Jumping from height	3 (12.0)	
Other	3 (12.0)	
Poisoning, <i>n</i> (%)	4 (16.0)	12 (60.0)
Transport accident, <i>n</i> (%)	–	6 (31.6)
Secondary causes		
Accident or injury, <i>n</i> (%)	3 (12.0)	3 (15.8)
Drug and alcohol, <i>n</i> (%)	5 (20.0)	3 (15.8)
Mental health, <i>n</i> (%)	12 (48.0)	4 (21.0)
Poisoning, <i>n</i> (%)	2 (8.0)	0
Medical, <i>n</i> (%)	0	4 (21.0)

Secondary causes are contributing causes of death other than a cause of the same type as the primary cause. Contributing causes that were related to single individuals only are not presented for privacy reasons; thus, totals may not add up. An individual could have multiple contributing causes of death.

Health care use prior to all-cause mortality

Of the 60 individuals deceased from all causes during the study period, 47 (78.3%) had at least one prior presentation to the emergency department; 23 (38.3%) had a history of an emergency department presentation related to suicidal ideation, behaviour or self-harm; 24 (40%) had presented for another mental health reason; 17 (28.3%) had presented owing to drug or alcohol use; 23 (38.3%) had presented for an accident or injury; and 37 (61.7%) had presented for a medical reason (Table 3). Thirty (50%) individuals had previously had a mental health unit admission, and 12 (20%) had been admitted to a hospital ICU in the past. Ten (16.7%) had no history of either an emergency department presentation or a hospital admission.

The health service visit types associated with the greatest risk of all-cause mortality were emergency department presentation for suicidal ideation, behaviour or self-harm (hazard ratio (HR) 2.00, 95% 1.02–3.91) and admission to a mental health unit (HR 2.79, 95% 1.34–5.79) or ICU (HR 3.80, 95% 1.81–7.98) (Table 3).

Health care use prior to death due to suicide or accident

Table 4 presents the lifetime history of each type of health service use by cause of death. The health service visit types associated with greatest risk of death due to suicide or accident were emergency department presentation for suicidal ideation, behaviour or self-harm (HR 2.46, 95% CI 1.20–5.06), emergency department presentation related to drug or alcohol use (HR 2.09, 95% CI 1.01–4.31) and mental health unit admission (HR 4.11, 95% CI 1.85–9.17) (Fig. 1). When deaths associated with medical causes were excluded, a history of ICU admission was no longer associated with increased risk of death.

The sensitivity analysis, which pooled poisonings that were intentional, accidental or where intent was unknown, found that history of presentation to the emergency department for any type of poisoning was associated with the greatest risk of death from suicide or accident (HR 4.40, 95% CI 2.13–9.09) (Fig. 2). Mental health unit admissions remained a predictor (HR 4.01, 95% CI 1.81–8.88); however, other health service use such as emergency department presentation for suicidal ideation, behaviour or self-harm, or emergency department presentation for drug and alcohol use (without poisoning), was no longer significant.

Discussion

Premature mortality in young people accessing early intervention mental healthcare is greatly increased relative to the age-matched population. Despite the earlier stage of illness, young people in

Table 3 Health service use prior to mortality (all-cause)

	All-cause mortality (<i>n</i> = 60)		BPRR cohort alive (<i>n</i> = 7021)		Hazard ratio ^a (95% CI)
	<i>n</i> (%)	No. of visits (%)	<i>n</i> (%)	No. of visits (%)	
Emergency presentations					
Total emergency department presentations	47 (78.3)	443 (100)	5343 (76.1)	38 031 (100)	
Suicidal ideation or behaviour	23 (38.3)	55 (12.4)	1076 (15.3)	2307 (6.1)	2.00 (1.02–3.91)
Mental health	24 (40)	79 (17.8)	1763 (25.1)	5937 (15.6)	0.74 (0.37–1.46)
Accident and injury	23 (38.3)	57 (12.9)	3027 (43.1)	6957 (18.3)	0.53 (0.30–0.95)
Drug and alcohol	17 (28.3)	52 (11.7)	822 (11.7)	1925 (5.1)	1.60 (0.80–3.21)
Medical	37 (61.7)	178 (40.2)	4236 (60.3)	18 836 (49.5)	0.82 (0.43–1.57)
Hospital admissions					
Total hospital admissions		708 (100)		27 927 (100)	
Mental health unit admission	30 (50)	252 (35.6)	1474 (20.9)	8683 (31.1)	2.79 (1.34–5.79)
Intensive care unit admission	12 (20)	20 (4.6)	254 (3.6)	579 (2.1)	3.80 (1.81–7.98)
No admission or presentation history	10 (16.7)		1725 (24.6)		0.31 (0.07–1.38)

n refers to the number of individuals with a lifetime history of each visit or admission type. No. of visits refers to the total number of visits in the deceased or alive cohort. Mental health unit admission includes voluntary and involuntary admissions. Intensive care unit refers to admissions to the general hospital intensive care unit, not a mental health admission. Total hospital admissions includes any hospital admission type, including non-mental health admissions. Total number of mental health admissions and intensive care unit admissions are presented. Total emergency department presentations refers to the number of individuals who had at least one emergency department presentation of any type. Each emergency department presentation was only categorised as one subtype (e.g. mental health OR medical). However, an individual could have presented multiple times for a different primary presenting reason; therefore emergency department visit subtypes do not sum to 100.

Emergency department presentations and hospital admissions exclude presentations or admissions that occurred at the time of death.

a. Hazard ratios have been adjusted for gender. Transgender young people were not included in the calculations of hazard ratios owing to the small number (*n* = 59). Hazard ratios also exclude young people where follow-up time was missing (*n* = 910).

this cohort have twice the risk of death relative to the age- and sex-matched NSW population. For males in the BPRR cohort, the elevated risk of premature death increased to five times that of age-matched males in the population. This increased mortality ratio was only slightly lower than that of adults diagnosed with psychiatric disorders in in-patient or out-patient settings in a Danish register-based study of over 7 million adults.³ Plana-Ripoli et al (2019) reported that the mortality rate ratio (MRR) was highest among young adults and peaked at around 33 years of age (MRR 7.25, 95% CI 7.06–7.44), with the gender differential (higher in males) greatest in this period also.

Suicide was the leading cause of death in this cohort of young people accessing youth mental health services, followed closely by deaths due to accident or injury. Overall rates of suicide deaths in this cohort remain much lower than in other high-risk clinical populations, such as those discharged from psychiatric hospitals, for which a meta-analysis by Chung et al (2017) estimated a rate of 484 suicides per 100 000 person-years (95% CI 422–555).²⁰ Although rates of suicide for males were double that of females in the cohort, this represented less of a gender difference than that seen in suicide rates at a population level, where rates are 3–4 times higher in males aged 15–35 years than females in the same age group.^{21,22} This is consistent with previous findings that suicide rates among psychiatric cohorts are associated with less of a gender differential than population studies.²⁰ In the current

study, greater all-cause mortality risk among males was driven by a higher frequency of accidental deaths and deaths where cause was under investigation. The distribution of gender in the BPRR cohort also indicates that previous findings suggesting that men are less likely to access mental healthcare¹⁵ are likely to apply in primary youth mental health settings.

In young people accessing early intervention youth mental healthcare, poisoning, whether intentional (suicidal) or accidental, was the single greatest primary cause of death (26.7%). When contributing causes were included, self-poisoning or substance use were primary or contributing causes in 43.3% (26/60) of all deaths. Although previous studies have identified an increased risk of death from any type of poisoning in cohorts accessing mental healthcare in adult psychiatric services or emergency departments,^{2,3} our findings confirm that such associations are present in young people accessing early intervention youth mental healthcare at earlier stages of illness. The proportion of deaths where poisoning was the primary cause also appeared to be greater in the BPRR cohort relative to other cohort studies, which report poisoning to be a primary cause in approximately 15% of deaths.¹⁷

Means restriction is one evidence-based suicide prevention intervention with particular relevance to poisoning deaths.²³ Previous reviews of means restrictions targeting pharmaceuticals, including limiting pack size and restrictions on the sale of medications, have shown efficacy in reducing risk of suicide death from

Table 4 Health service use prior to suicide and accidental death

	Suicide and accident mortality (<i>n</i> = 51)			BPRR cohort alive, <i>n</i> = 7021 (%) individuals
	Suicide, <i>n</i> = 25 (%) individuals	Accident and injury, <i>n</i> = 19 (%) individuals	Cause under investigation, <i>n</i> = 8 (%) individuals	
Emergency department presentations, all	16 (64.0)	16 (84.2)		5343 (76.1)
Suicidal ideation or behaviour	11 (44)	5 (26.3)	6 (75.0)	1076 (15.3)
Mental health	11 (44)	5 (26.3)	4 (50.0)	1763 (25.1)
Accident and injury	10 (40)	8 (42.1)	3 (37.5)	3027 (43.1)
Drug and alcohol	5 (25)	6 (24.0)	5 (62.5)	822 (11.7)
Medical	10 (40)	12 (63.2)	7 (87.5)	4236 (60.3)
Mental health admission	12 (48)	7 (36.8)	5 (62.5)	1474 (20.9)
Intensive care unit admission	2 (8)	1 (5.2)	4 (50.0)	254 (3.6)

n refers to the number of individuals with a lifetime history of each visit or admission type. Deaths due to medical causes (*n* = 8) are excluded. Denominators include young people of all genders and those where follow-up time was missing.

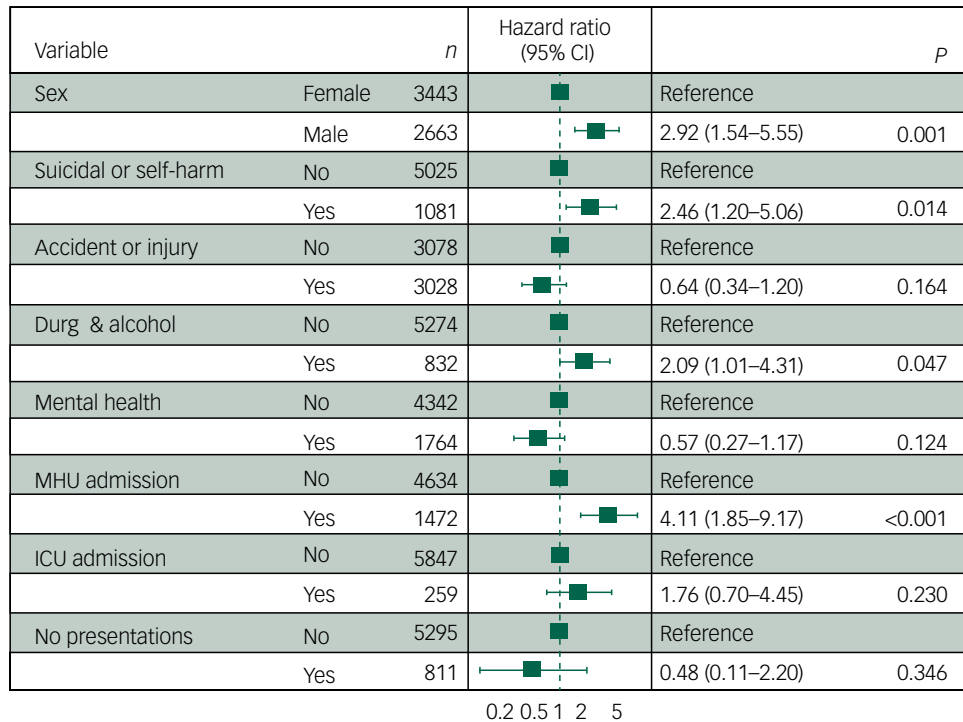


Fig. 1 Hazard ratios for health service use and suicide- or accident-related deaths. Hazard ratio refers to the risk of suicide or accidental death relative to non-deaths. Total *N* = 6106, including 43 deaths. Excludes deaths due to medical causes (*n* = 8), young people with no final visit date recorded (*n* = 910) and people who were transgender (*n* = 59). Health visit types refer to emergency department presentations, aside from those labelled as admissions. MHU admission, mental health unit hospital admission; ICU admission, intensive care unit admission.

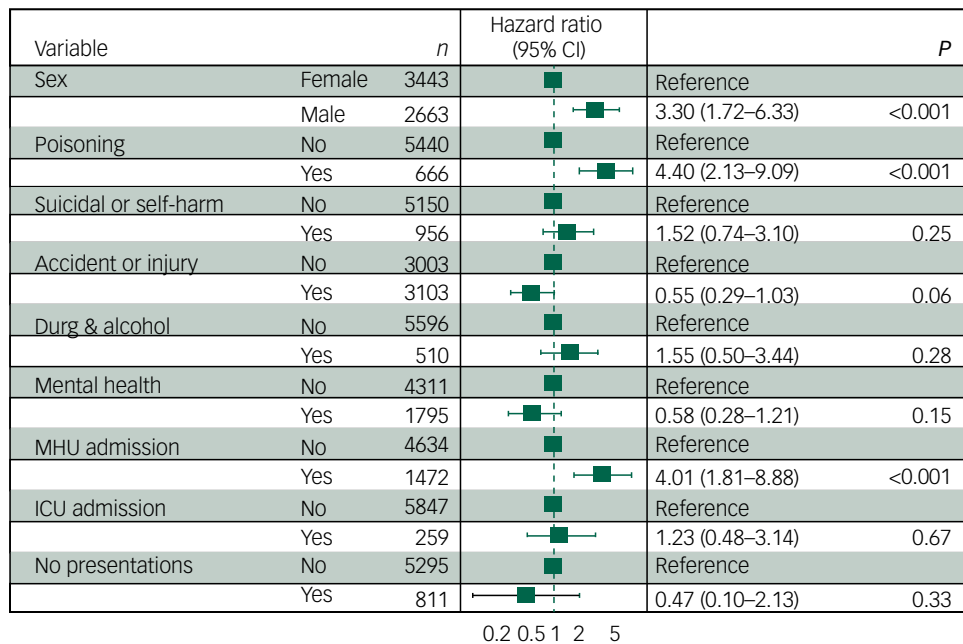


Fig. 2 Poisoning presentations and risk of suicide- or accident-related deaths (sensitivity analysis). Results are presented of a sensitivity analysis to test the effect of categorising all self-poisoning together, regardless of whether intentional or accidental; thus, the suicidal ideation or self-harm or drug and alcohol presentations here exclude any forms of self-poisoning. Total *N* = 6106, including 43 deaths. Excludes deaths due to medical causes (*n* = 8), young people with no recorded last visit date (*n* = 910) and/or those who are transgender (*n* = 59). Health visit types refer to emergency department presentations, aside from those labelled as admissions. MHU admission, mental health unit hospital admission; ICU admission, intensive care unit admission.

poisoning, as well as reduced risk of suicide death from other causes.²⁴ The effects of means restriction interventions are strongest where the target is associated with the greatest lethality. Much of the evidence on means restriction of pharmaceutical drugs relates to drugs where limitations have already been introduced, for example, barbiturates, opioids or benzodiazepines, where strict limitations on prescribing are in place. Thus, it is not clear what impact further means restrictions would have in a youth cohort. The implications of restricting access to pharmaceuticals must be carefully considered in populations accessing mental healthcare, as there are already barriers to accessing adequate treatment, of which pharmacological therapy is often a key part. It is also possible that there are other indirect relationships between access to pharmaceuticals and poisoning that need to be considered in youth mental health cohorts. For example, Chitty et al (2018) previously reported that prescription of psychotropic medication was associated with reduced risk of co-ingestion of alcohol in intentional self-poisoning and thus a reduced risk of lethality.²⁵

Prior health service use and opportunities for prevention

This study confirms that knowledge of previous health service use remains a useful predictor of all-cause mortality and deaths due to suicide and accident in young people accessing early intervention services. A meta-analysis by Franklin et al (2017) reported that prior psychiatric hospital admission was associated with an odds ratio of 3.57 (95% CI 2.81–4.53) for suicide death, relative to no history of psychiatric hospital admission.⁸ A previous Danish register-based study by Hjorthøj et al (2012) also reported an increasing risk of suicide by level of psychiatric care accessed in the previous 12 months.²⁶ Increasing relative risk (RR) was associated with accessing medication only (RR 5.8, 95% CI 5.2–6.6), out-patient treatment only (RR 8.2, 95% CI 6.1–11.0), emergency room treatment (RR 27.9, 95% CI 19.5–40.0) and, finally, psychiatric hospital admission (RR 44.3, 95% CI 36.1–54.4), relative to those with no psychiatric contact in the prior 12 months.

The sensitivity analysis, which combined all emergency department presentations for poisoning, whether intentional or accidental, found that previous emergency department presentation for poisoning was associated with the greatest risk of death from suicide, accident or injury among all health service visit types, including admission to a mental health unit. Previous emergency department presentations for suicidal ideation, behaviour or self-harm, where self-poisoning was not the method used, were not significant as predictors of future deaths. These findings differ from those of previous UK cohort studies, which have found emergency department presentations for self-poisoning to be associated with reduced future mortality risk relative to emergency department presentations for self-injury.¹⁷ On the other hand, a cohort study by Carter et al (2005) based in Australian emergency departments found a similarly elevated risk of future mortality following emergency department presentations for poisoning.^{17,27}

Our results suggest that there may be further utility in providing targeted follow-up care after emergency department presentation for any type of poisoning, regardless of whether prior presentations were associated with suicidal intent. Assertive follow-up care following emergency department presentations for suicidal ideation or behaviour is an evidence-based suicide prevention intervention and is recommended practice in health systems across the world.²⁸ However, these interventions do not usually extend to poisonings without suicidal intent. Accidental poisonings are strongly associated with substance use.²⁹ Common treatment paradigms for drug and alcohol misuse are often based on an individual being proactive in seeking treatment.³⁰ However, suicide prevention research

has shown that assertive follow-up by services, even with brief contact interventions, can have an effect on reducing future suicidal behaviour.³¹ Given that substance use and alcohol dependence are strongly associated with mortality from suicide and accident across the lifespan, designing and testing interventions that integrate these approaches is likely to be worthwhile. For example, assertive follow-up and brief contact interventions that have a holistic, person-centred approach may be suitable for individuals at earlier stages of change, including those who are pre-contemplative about reducing drug or alcohol use. Ensuring that assessment and treatment of drug and alcohol use are wholly integrated into early intervention mental health services may increase the engagement of young people with this aspect of care. Such an approach would be supported by the development of clinical pathways and upskilling of front-line workers in assessment and treatment of high-risk drug and alcohol use behaviours.

Clinical approaches to reducing premature mortality in this cohort should be combined with population-level approaches, including the development of public policy and infrastructure. For example, in Australia, increasing rates of paracetamol overdoses among young people have led the Therapeutic Goods Administration to consider increasing restrictions on the sale of paracetamol.^{32,33} The development of public digital infrastructure at a health system level is likely to be another opportunity to increase the quality and effectiveness of care and reduce adverse outcomes such as premature mortality. For example, such infrastructure could facilitate the identification of high-risk emergency department presentations and the feasibility of delivering brief contact interventions, while preserving the clinical workforce for more intensive or in-person interventions.²³ Expanding access to other effective interventions in this clinical cohort, such as increased access to specialist mental healthcare, psychological interventions and care coordination, will also require high-quality digital infrastructure.^{34,35}

Limitations

This study had several limitations. Understanding of health service use was limited by the inclusion of only emergency department presentations and hospital admissions. Use of other health services, such as general practitioner visits or engagement with community-based mental health clinicians including psychologists or other therapists, was not measured. Greater analysis of other types of health service use, such as primary care, may have allowed for a greater understanding of engagement with services. It is important to note that the study was observational and thus not designed to test the efficacy or effectiveness of mental health services in reducing mortality outcomes. The cohort was sampled from two urban early intervention youth mental health clinics, which means young people living in rural and remote areas were not adequately represented. The study used a clinical approach to categorising emergency department visits, which may limit the external validity of our findings; however, our results were consistent with those of other research in the field.²⁴

Implications

Premature mortality in young people accessing early intervention youth mental healthcare is greatly increased relative to the age-matched population despite the early stage of illness. The elevated risk of premature mortality is especially marked for young males. Suicide was the leading cause of death in this cohort of young people accessing early intervention youth mental healthcare services, followed closely by deaths from accident or injury. Self-poisoning or substance use was a primary or contributing cause of death in almost half of deaths in this youth cohort. Previous

emergency department presentation for self-poisoning, regardless of whether it was associated with intent to self-harm, was the strongest predictor of future mortality. These findings indicate that the delivery of assertive aftercare following emergency department presentations should not be limited only to presentations identified as suicidal behaviour or self-harm. More assertive patient-centred follow-up and well-coordinated specialist care are indicated for all types of self-poisoning and drug and alcohol use presentations, given the association with increased mortality.

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Data availability

The data that support the findings of this study are available on request from the corresponding author, C.M.M., within the restrictions of the ethics approval and governance.

Author contributions

C.M.M. contributed to study design, data analysis, and drafting and editing of the manuscript. Y.S. and N.Z. contributed protocol design and revisions of the manuscript. F.I., M.R., A.S. and N.K. contributed to the study design and the analysis plan, as well as revisions of the manuscript. E.S. and I.B.H. provided supervision and contributed to the study design, as well as manuscript preparation and revisions. We thank all the young people who participated in this study, and all the staff in the Youth Mental Health Team at the Brain and Mind Centre, past and present, who contributed to this work.

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Declaration of interest

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Chapter 6: Discussion

The overall aim of this thesis was to generate new scientific understanding of suicidal behaviour in young people accessing mental health services, which may be applied in clinical services in order to reduce the impact of suicidal behaviour. While the findings of each study within this thesis have been discussed in Chapters 2 – 5, this concluding chapter will first summarise the findings of these studies in relation to the explicit aims of this thesis. Subsequent sections of this chapter will consider the broader implications of these findings, their application to youth mental health services, the limitations of the research and consider future directions.

6.1 Summary of findings

Chapter 2 addressed the first aim of this thesis, to assess the predictive performance of key risk factors used to direct clinical suicide prevention in predicting suicide deaths. **Chapter 2.1** tested the hypothesis that suicidal ideation could be used as a screening measure for later suicide. Meta-analysis was used to calculate a comprehensive set of performance measures, which highlighted the weaknesses of suicidal ideation as a screening tool given its low sensitivity and only moderate specificity for suicide death. While there were no significant differences based on the age of the sample, there were significant differences in the sensitivity and specificity between studies that sampled from the general population versus those that focused on psychiatric settings, such that SI is an even less effective screening tool in non-psychiatric samples. **Chapter 2.2** tested the hypothesis that SB was a stronger predictor of future suicide death than SI, finding that although SB was a slightly stronger predictor than SI (OR 4.06 vs. 3.06) the difference was non-significant ($p=0.14$). Suicidal behaviour, relative to SI, was associated with a greater OR in non-psychiatric settings, and a lesser OR in studies of affective disorders, relative to those with psychosis or mixed diagnoses. Taken together, **Chapter 2** concludes use of these two risk factors to direct suicide prevention may be ineffective, and that the sample and setting have an important effect on the performance of predictive models.

Chapter 3 addressed the second aim of this thesis, to explore the application of machine learning modelling to clinical suicide prevention in youth mental health services. **Chapter 3.1** synthesised findings from initial machine learning modelling studies of suicidal behaviour and concluded that despite studies reporting highly accurate performance of models, many of the same limitations apparent in earlier statistical approaches to modelling remained. The clinical utility of such ML models remained low as indicated by the low positive predictive value (PPV). Given PPV reflects the prevalence of an outcome in a population, **Chapter 3.1** concludes that future ML modelling studies

should focus on outcomes associated with a higher prevalence, such as suicidal behaviour (rather than suicide deaths) and report a comprehensive set of performance metrics in order to avoid misleading conclusions. **Chapter 3.1** also identified the need for improved data quality, with many ML studies using administrative data, which maps poorly to clinical constructs, such as clinical symptoms or diagnosis, and may limit the translation of such models into clinical interventions.

In **Chapter 3.2** these insights were applied in a longitudinal study of young people accessing YMH services, which used machine learning to develop predictive models that tested the effect of the outcome measure and sample selected. Predictive models of suicide attempts were associated with superior performance (AUC: 0.82 sensitivity: 0.72, specificity: 0.78) relative to those predicting deliberate self-harm (AUC: 0.72 sensitivity: 0.62, specificity: 0.73), however both were associated with a positive predictive value that indicated they were likely to be clinically useful (SA PPV: 0.32, DSH PPV: 0.40). Models predicting new-onset or repeat self-harm or suicidal behaviour performed poorly, however the PPV of models predicting repetition of self-harm were high enough (PPV: 0.63) to justify assertive clinical interventions. Although the outcome measured selected impacted model performance, **Chapter 3.2** found that whether an episode of self-harm or suicidal behaviour was associated with suicidal intent or not may have less predictive value than the method used to self-harm. For example, DSH via cutting (with no suicidal intent) was a more important variable in predictive models of future suicide attempts, than a history of suicide attempts by other methods, such as poisoning. Clinical symptoms of common mental disorders were the most important predictors in modelling future behaviour, with some evidence of distinct symptom profiles predicting SA versus DSH.

Having explored the role of key risk factors that are assessed by either self-report, or clinician interview, and identified opportunities and limitations of traditional statistical and novel machine learning approaches, **Chapter 4** aimed to address the third aim of this thesis, to explore the role of potential biomarkers of suicidal behaviour, specifically those identified with behavioural tasks in neurocognitive testing. In **Chapter 4.1**, a meta-analysis of 18 studies found that young people with a history of suicidal behaviour were significantly more impulsive than healthy controls, though the pooled effect size was small to moderate (SMD 0.19, 95% CI: 0.10-0.28, $p < 0.001$). Impulsivity did not differentiate between young people with suicidal behaviour and psychiatric controls, though relatively few studies included psychiatric controls. There was no evidence that sub-types of impulsivity were more useful predictors than a broader construct of impulsivity. Similarly, there was no evidence that the type of self-harm or suicidal behaviour, whether NSSI, DSH, or suicide attempt, was a moderator of effect. As the first meta-analysis examining impulsivity and SB in young people, and the first to focus on behavioural tasks rather than self-report, these findings were an important contribution to the literature. These findings should be considered with caution, however, given some sub-types of impulsivity were under-represented and only two studies assessed impulsivity measured

in close temporal proximity to suicidal behaviour (i.e. within 1-2 weeks). A number of limitations in the literature were identified including relatively few studies using psychiatric controls and evidence of a gender bias in sampling. Half of studies contained more than 70% females and those with more equal gender distribution trended towards a greater effect size.

The latter half of **Chapter 4** looked to applying these findings to a population of young people accessing early intervention youth mental health services in Australia. **Chapter 4.2** found that incorporating neurocognitive assessment into clinical assessment led to a small, but significant improvement in prediction of self-harm or suicidal behaviour at 12 months follow up. Deficits of cognitive flexibility were a key predictor of future SB. Unexpectedly, young people with SB were found to have superior cognitive functioning on a range of cognitive tests measuring executive functioning relative to clinical controls, and population norms. This finding suggests the neurocognitive profile of young people with suicidal behaviour is unique, relative to older cohorts with suicidal behaviour.

Chapter 5 addressed the final aim of this thesis, to characterise premature mortality risk in young people accessing early intervention mental health services, due to suicide and other causes, and identify health service use predictors of relevant mortality outcomes. **Chapter 5**, the first study of mortality outcomes in this clinical cohort in Australia, found despite being earlier in the course of illness young people in this cohort had a risk of premature mortality double that of the general age- matched population, which increased to five times population risk for young males in the cohort.

While suicide was the leading cause of death in this cohort, followed by accident and injury, poisoning whether intentional or accidental, was a primary or contributing causes in 43% of deaths. Health service use predictors, including prior ED presentations for SI, SB or self-harm and prior mental health unit admission were the strongest predictors of future mortality. A sensitivity analysis that tested the effect of classifying all ED presentations for poisoning together, regardless of intent, found that poisoning presentations were associated with the greatest hazard ratio for future death due to suicide or accident.

A number of key themes emerged in addressing the aims of this thesis. Firstly, the core features of suicidal behaviour and self-harm in young people accessing primary mental health services differ from that of other population or clinical cohorts. Secondly, given these differences, current suicide prevention strategies may be ineffective in reducing morbidity and mortality from self-harm and suicidal behaviour when applied to this cohort. Finally, there are a number of major opportunities to improve clinical suicide prevention presented by the digital transformation of mental health services and systems, which if implemented could improve clinical service delivery and advance suicide research.

6.2 Suicidal behaviour in youth mental health services

Young people accessing youth mental health services with suicidal behaviour represent a unique cohort with key differences to population or clinical cohorts previously reported in the literature. Firstly, the prevalence of self-harm and suicidal behaviour, and rates of repetition are higher than clinical cohorts of adults or in the population (56, 57). The elevated rates of self-harm and suicidal behaviour appear to translate to increased mortality risk, hospital admissions and emergency department presentations. This is an important finding given this cohort are generally earlier in the course of illness, and early intervention clinical services have previously been criticised for diverting resources away from cohorts considered to experience more severe forms of mental illness (46).

There is significant overlap between self-harm without suicidal intent and suicide attempts in this cohort. In [Chapter 3.2](#) all young people who reported a suicide attempt also reported engaging in non-suicidal self-harm, with 38% engaging in multiple methods of self-harm (i.e. cutting and poisoning). The risk of repetition was high regardless of whether the episode of self-harm at baseline was associated with suicidal intent. In [Chapter 4.1](#) broader definitions of self-harm, which grouped non-suicidal self-harm and suicide attempts together were as useful as stricter definitions. In [Chapter 5](#) classifying ED presentations by the method of harm (i.e. poisoning vs. injury) was more useful than classifying by intent (intentional or accidental).

Previous research has strongly argued that self-harm associated with suicidal intent and without are different phenomena and required different interventions (58, 59). While we do not argue against differentiating between these two behaviours at a population level, our findings suggest there may be less utility to doing so in clinical cohorts of young people. We also do not argue against the importance of understanding the meaning of a particular act of self-harm within the context of a therapeutic encounter between clinician and consumer. Rather our findings suggest that in this cohort determining the method used in an episode of suicidal behaviour or self-harm may offer more utility for clinical services than determining the intent associated with the act, in terms of understanding future risk.

The high burden of disease associated with self-harm and suicidal behaviour in this cohort suggests that all young people who have any history of self-harm or poisoning of any kind, should receive evidence-based suicide prevention interventions. Given the poor sensitivity and specificity of both suicidal ideation and suicidal behaviour as screening tests for future behaviour, the absence of either, during a clinical assessment, does not meaningfully rule out future suicidal behaviour. This is an important finding given current suicide prevention frameworks rely on the expression of suicidal ideation or behaviour (i.e. the presence of suicidal intent), to guide the delivery of the intervention (39).

Currently clinical service models use the expression of suicidal ideation to determine which clinical pathway is taken. For example, an individual presenting to hospital with an episode poisoning, even if almost fatal, will receive no assertive aftercare if the individual denies it was a suicide attempt (60-62). Similarly, other types of poisoning, such as those related to alcohol or recreational drugs, may be advised to engage with drug and alcohol services, but will not receive any care coordination or assertive follow up to support their engagement with treatment.

Secondly, key risk factors for suicidal behaviour at a population level appeared to be less pronounced in this clinical cohort. Research of population samples has repeatedly found males to be at greatly increased risk of suicide death relative to females, who are said to engage in self-harm more frequently but are not at increased risk of suicide death (63). Our findings are consistent with previous research showing that the association between gender and suicide death is of a lesser magnitude in cohorts of psychiatric inpatients (64) or those diagnosed psychiatric disorders (65). We found male gender associated with twice the rate of suicide death than female gender in [Chapter 5](#), and female gender associated with twice odds ratio of non-fatal suicidal behaviour relative to males in [Chapter 4.2](#).

Previous large cohort studies by Plana Ripoli et al (2019) and Hawton et al (2015) have found that in clinical populations female gender was associated with a greater increase in risk of suicide relative to risk amongst the general female population, whereas the absolute risk remained higher in males (65, 66). Our findings also suggest that in this cohort, after a history of self-harm or SB, clinical symptoms of common mental disorders were the most important predictors in modelling future suicidal and self-harm behaviour. Symptoms of depression, anxiety and substance use were all useful predictors of SB in [Chapter 3.2](#), as were ED and hospital visits in [Chapter 5](#). These findings do not necessarily mean that young people in this cohort meet criteria for full-threshold psychiatric diagnoses, and in fact in [Chapter 3.2](#) and [4.2](#) diagnosis was not a useful predictor of outcome. Chapter 4 also found cognitive factors, such as elevated impulsive decision-making and reduced cognitive flexibility, were useful predictors of SB, although it is not clear whether these factors should be considered state-based or represent a trait-like disposition.

In [Chapter 3.2](#), measures designed to capture exposure to child abuse or neglect, family or relationship conflict, and adverse life events were not useful predictors of suicidal behaviour. This was an unexpected finding as at a population level, exposure to child abuse, neglect and family violence, is the risk factor associated with the greatest attributable risk of healthy life years lost from suicide and self-inflicted harm, in both males and females (67). While our findings do not refute the association with childhood traumas and suicidal behaviour, it may suggest these factors are predictive of mental distress or illness in young people and may not differentiate those with or without suicidal behaviour in clinical settings. Our findings suggest that high-quality assessment of clinical symptoms and mental state remains crucial to suicide prevention in youth mental health services and that a transdiagnostic approach to assessment may be of most utility (68).

6.3 The role of high-quality clinical care in youth suicide prevention

Key suicide prevention strategies, at national and state levels, contain relatively brief or superficial references to clinical care or treatment. For example, the current national strategy in Australia, as well as NSW and Victorian strategies (69, 70), stipulate the need to support individuals in the community to access clinical assessment, but lack specific detail on what assessment and clinical care pathways might entail. Whole of government strategy and policy that aims to address the social determinants of ill health, reduce stress and increase resilience within the population will remain a crucial part of reducing rates of mental illness and increasing mental well-being. However, it is unclear what effect these measures are expected to have on the prevalence of self-harm or suicidal behaviours in clinical populations. Addressing these upstream factors, such as child abuse and family violence, may reduce the proportion of the population experiencing mental distress and disorders requiring clinical care, and therefore reduce rates of suicidal behaviour in clinical populations. However, our findings emphasize the importance of maintaining a focus on delivering high quality clinical care that supports recovery and is effective at reducing symptoms of mental disorders in young people (71).

Suicide prevention frameworks that are specific to health services, such as the influential Zero Suicides framework (39), guide services in implementing a systems approach to identification, assessment, and treatment of suicidal ideation or behaviour, as well as workforce development and program evaluation. The ZS framework has been associated with a significant reduction in suicide deaths when implemented in certain healthcare settings in the United States (72, 73) as well as a reduced risk of repeat suicide attempt ($RR = 0.62$; 95% CI 0.41–0.95) at 90 days follow up and an increase in time until re-presentation when implemented in Australia (74).

However, there are likely to be additional implementation considerations in YMH services. For example, under the recommendations of the Zero Suicide framework, for clients who screen positive to suicidal ideation, clinicians should use a structured suicidal ideation screening tool and full risk formulation at every subsequent visit until suicidal ideation resolves. However, in real world youth mental health services, it is not clear how these discrete symptoms should be managed in the context of other mental health symptoms or conditions. The framework also specifies the use of several structured psychotherapies specific for suicidal thoughts, including the Collaborative Assessment and Management of Suicidality (75), Dialectical behaviour therapy (DBT) (76) or Cognitive Behavioural Therapy for Suicide prevention (77). In this model suicidal ideation is the primary therapeutic target and it is not clear how this approach should be balanced with other clinical or client priorities within a patient-centered model of care. Additionally, in Australia demand for psychological therapies has been excess to workforce availability in recent years, resulting in psychological therapies being largely inaccessible for the majority of the population (78).

Evidence from large-scale implementations of other systems-based approaches to suicide prevention have been encouraging (79). For example, the National Suicide Prevention trial in Australia (80), which

involved one of two systems-based suicide prevention interventions, Alliance against Depression (81) or Lifespan (82) delivered in 11 primary health networks across Australia found the intervention increased provider knowledge of suicide and pathways to care and led to a significant reduction in suicidal ideation in participants accessing care at trial sites. However, evaluation against key outcomes, including hospital admissions for suicide attempts and suicide deaths found no effect. While overall the systems-based interventions were acceptable and well received by the community and providers, funding and resources remained a barrier to implementation. Evaluating such a complex, multicomponent intervention also proved a challenge, as many control sites had some form of suicide prevention care or adopted programs during the period of evaluation. The impact of other dynamic processes, including social and economic change, which are known impact rates of suicidal behaviour, are also particularly challenging to measure and typically are not consistent across settings or populations at any given time.

6.4 Technology-enabled clinical assessment and care

High quality care is guided by comprehensive clinical assessment that is accessible and integrated into the consumers journey of care (71). Our findings suggest that the use of comprehensive multidimensional assessment in youth mental health services (83), that captures a range of clinical symptoms, alcohol and substance use and ideally include neurocognitive assessment, is important for clinical suicide prevention. Other domains such as social and occupational functioning or physical health were not covered by this thesis but have previously been identified as central to high quality youth mental health care (84). While this recommendation may not be novel, for many clinical mental health services in Australia this remains unimplemented. The feasibility of comprehensive assessment and leveraging assessment to improve care at a service and system level (as outlined in Section 6.6) will be greatly enhanced by the increased adoption of digital tools in health care.

Digital platforms can be used to collect a comprehensive set of validated measures in a manner that enhances experience and quality of care, while reducing burden on consumers of health care and services associated with data collection and administration. Use of digital platforms enables measurement-based care, which facilitates the delivery of evidence-based interventions and the longitudinal tracking of outcomes (85). Initial digital platforms were developed by academic institutions and private organisations and more recently have become a focus of government providers. In New South Wales for example, the Ministry of Health has begun roll out of its patient-facing digital platform, HOPE, which is designed to capture patient reported outcome measures (86). Although these opportunities have been recognised by governments and health organisations they have yet to be fully realised and many existing technologies have not been implemented widely in clinical service delivery (87, 88). For example, neurocognitive factors have been proposed as potential biomarkers for a range of mental health disorders (84, 89), and relative to other proposed biomarkers, such as those identified via neuroimaging, cognitive testing has the potential to be readily accessible and rolled out in a wide range

of settings. Testing can be delivered via tablets, and even smart watches, with results of a similar validity to expensive in-person testing (90, 91). Yet neurocognitive testing remains highly inaccessible in clinical services in Australia and continues to require highly skilled professionals to carry out intensive and lengthy assessments.

Beyond assessment, optimising the use of digital platforms is also an opportunity to increase access to high quality evidence-based suicide prevention interventions. Key interventions for suicidal behaviour in young people include safety planning, access to aftercare and follow up, and means restriction.

Leveraging digital platforms and devices would increase the feasibility of delivering brief interventions, like safety planning and psychoeducation, to all young people presenting for care regardless of the setting or skill level of the clinician or service provider. Similarly, the care coordination required in aftercare programs, which aim to provide enhanced follow up, could be facilitated by hybrid models that combine digital and in-person approaches. Given clinical symptoms are important predictors of future suicidal behaviour in clinical cohorts, the longitudinal tracking of symptoms until resolution, and stepping up level of intervention when needed, could be supported by hybrid digital/in-person models of aftercare. While many interventions, such as safety planning or specific psychotherapies, are available in digital form they are not generally integrated with other platforms, including those used by providers. The integration of patient-facing platforms with existing digital health records and clinical software could improve communication of assessment and shared treatment planning (87, 88) and the value of health care delivered.

6.5 Targeting a broader range of harms

The high rates of adverse outcomes due to accident and injury, drug and alcohol use and emergency department presentations highlight the importance of taking a comprehensive approach to reducing premature mortality and morbidity in this cohort. Taken together, our findings suggest that designing interventions to address a broader construct of harm should be considered. Young people with mental health conditions are at increased risk of a range of harms, including being subject to violence and exploitation, homelessness, physical illness and chronic social and functional impairment (92). There may be shared mechanisms underpinning these harms, related to exposures such as early life trauma and socioeconomic disadvantage, substance use, untreated or inadequately treated, symptoms of mental disorders or neurocognitive vulnerabilities. Chapter 4 found some limited evidence of a distinct cognitive phenotype associated with the suicidal behaviour of young people and clinical controls which, though limited, could contribute to the increased risk of a broader range of harms in this cohort. Promisingly, other executive function deficits associated with suicidal behaviour in adults were not present, indicating an early intervention paradigm that targets secondary risk factors associated with cognitive impairments, such as substance use, may be effective. Interventions that target a broader

construct of harm and address shared mechanisms such as drug and alcohol use, would also likely increase the positive predictive value of such interventions, thus increasing the utility and value to the health system.

The current approach of having different national strategies for Suicide Prevention, Mental Health and Drugs and Alcohol may inadvertently drive fragmented responses to delivering youth mental health care (93). National strategies typically inform health planning and funding, as well as monitoring and evaluation. Developing an integrated strategy would support a systems-based approach to targeting a broader construct of the harm that includes additional harms associated with mental health disorders. Such a strategy would support the development of a shared vision across the health system, a workforce with the relevant skill and the required digital infrastructure.

6.6 Leveraging artificial intelligence for suicide prevention

Digital transformation of mental health services presents major translational research opportunity for suicide prevention. The ability to capture new forms of high-quality data in a timely manner could have an outsized impact on our understanding of psychopathology, relative to other disciplines.

Suicide research has historically been limited to the collection of clinical data at time points relatively distal to the discrete episode of suicidal behaviour or self-harm. As a result, state-dependent factors in suicidal behaviour have been entirely under researched. This is a crucial gap in the literature given suicidal ideation and associated intent is known to fluctuate in intensity over very short periods of time (94, 95). In addition to cognition, other state-dependent or behavioural factors associated with suicidal behaviour, such as sleep (96), social contact (97), and physical activity (98), may now be studied in populations with recent or current suicidal behaviour, on a larger scale than possible in the past, with data collected outside of clinical settings via smart phones, wearable devices or other digital products. The uptake of digital platforms by large health organisations, particularly government providers, and the integration of behavioural data, such as neurocognitive testing, into large data sets, will facilitate the application of artificial intelligence and computational modelling to the field (99). Collaboration between mental health clinicians and researchers, data scientists or engineers and health policymakers is paramount to ensuring the opportunities afforded by new forms of data are fully realised.

Improving the quality of data collection in clinical services is also imperative. As outlined in [Chapter 3.1](#) many ML studies thus far have relied on administrative data, which maps poorly to clinical constructs, and is likely to limit the translation of such models into clinical interventions. Suicide research has progressed since the modelling of single risk factors ([Chapter 2](#)) however the opportunities are yet to be fully realised. In this thesis there was some limited evidence that more detailed definitions of clinical constructs impact the performance of models. In [Chapter 2.2](#) there was evidence of a threshold effect in suicidal ideation. Measures that included greater detail allowed for a third category of analysis, that of

‘suicidal threats’, which was associated with greater risk than passive suicidal ideation. Similarly, in [Chapter 2.2](#) studies that differentiated between groups who had experienced suicidal ideation without behaviour, and those with both, found that suicidal behaviour was associated with twice the risk relative to a group with suicidal ideation and no history of behaviour. In [Chapter 3.2](#), the use of validated self-report and clinician rated measures improved the predictive performance of models, relative to a previous study from our group that used the same method of analysis but relied on data extracted from a retrospective audit of clinician notes (100).

While at present there is insufficient evidence that discrete categories of suicidal ideation, suicidal behaviour, and self-harm, should be used to direct interventions within clinical services, this may change as the quality of data collected improves. The collection of data that maps to clinical constructs is likely to lead to predictive models of greater utility to clinical services and health planners (101). Improving the availability and quality of large health datasets from clinical services also increases opportunities for international collaboration in mental health research. Larger datasets and open data approaches may increase the feasibility of cross-national research that can enhance our understanding of country-level factors, for example cultural factors or the effect of health system differences.

6.7 Limitations

While the limitations of the studies included in this thesis have been discussed within each chapter, there are a number of limitations relevant to the thesis as a whole to acknowledge. Firstly, the studies draw on observational data from real-world clinical settings. While using data drawn from a clinical cohort was central in addressing the aims of this thesis, observational data from clinical settings may have limitations, such as sampling bias and generalisability. The cohort of clients accessing clinical services like headspace can change over time, for reasons not measured in clinical research. For example, health-system factors such as workforce shortages or the development of new clinical services, may alter the characteristics of consumers accessing a service. Other potential sampling biases have been identified in previous work published by our group, which reported that select sub- cohorts of the BPRR (n= 7081), including the neurobiological cohort from which [Chapter 4.2](#) is drawn from, may have been biased towards sampling young people with more severe clinical presentations (50, 51). In [Chapter 4.2](#) young people with primary diagnoses of psychosis, schizophreniform or neurodevelopmental disorder, were excluded in order to focus primarily on mood and affective presentations. Excluding these presentations, which are often considered of greater severity, may have reduced this bias, however understanding how these potential biases impact generalisability is complex. Later studies of the thesis, such as [Chapter 5](#), used the entire BPRR cohort linked to hospital and emergency department data sets to counter this.

Another factor limiting the generalisability of findings from studies described in [Chapter 3.2](#), [4.2](#) and [5](#), is the urban setting. The BMC youth clinics, and the additional sites included in the ‘Transitions’ cohort in Melbourne, provide early intervention mental services to young people in major urban capitals. As a result, important groups of young people known to be at elevated risk of suicidal behaviour, such as those living in rural or regional areas, are not adequately represented. While these *headspace* branded clinics have relatively high rates of engagement with some demographic groups of young people at increased risk of suicidal behaviour, such as LGBTQI young people, other groups such as Aboriginal and Torres Strait islander young people, have typically been less likely to engage with headspace (102).

6.8 Conclusion

Young people accessing youth mental health (YMH) services with suicidal behaviour represent a unique cohort and differ from young people in population samples, or clinical cohorts of adults, previously reported in the suicide research literature. In early intervention YMH services the 12-month prevalence of self-harm and suicidal behaviour is high (42%) with rates of repetition at 12-month follow up of 54%. In contrast to population samples, in this cohort there is a significant overlap between non-suicidal self-harm and suicide behaviour, in terms of co-occurrence, methods used and risk of repetition. This strongly suggests differentiating between types of self-harm based on intent (e.g., non-suicidal or suicidal) in YMH clinical settings is likely to be less useful and valid than previously suggested in studies based on population cohorts. The increased burden of disease associated with self-harm and suicidal behaviour translates into significantly elevated mortality risk, which is a particularly important finding given young people accessing YMH services are generally earlier in the course of illness. Elevated mortality risk was attributable to increased rates of suicide death, as well as higher rates of death due to poisoning, drug and alcohol use. Predictive modelling of suicidal behaviour, whether using statistical approaches such as regression, or novel machine learning algorithms, perform poorly in terms of sensitivity, specificity and positive predictive value, a result of the low base rate (i.e. prevalence) of suicide deaths. Predictive modelling of outcomes with a higher prevalence rate, for example episodes of self-harm or suicidal behaviour, is associated with a higher PPV, however still below the threshold considered acceptable for interventions other than those with few associated harms. These findings suggest that developing strategies and designing interventions to address a broader construct of harm should be considered.

Systems-based approaches to suicide prevention that rely on the detection of suicidal ideation to direct the delivery of interventions are likely to be ineffective given the poor sensitivity of SI for future suicide death. Rather than a risk stratification approach to suicide prevention in youth mental health services, all young people accessing mental health services should receive evidence-based suicide prevention interventions that are cost-effective and where the benefits outweigh the risk of potential harms (e.g. safety planning) (34).

High quality clinical assessment guided by transdiagnostic frameworks that capture a range of clinical symptoms, drug and alcohol use, cognition, as well as functioning and recovery, is a core component of clinical suicide prevention. Rather than assessment with the aim of predicting outcomes related to suicidal behaviour, the aim of such comprehensive clinical assessment is to guide the delivery of person-centered, evidence-based care, relevant to the individual's presentation. Leveraging the digital transformation of mental health services to develop system-wide approaches to assessment and delivery of interventions presents a major opportunity in suicide prevention. The optimal use of digital platforms and devices can increase the quality of clinical care, by improving access and consistency of interventions and capture new forms of high-quality data that can be used to further knowledge of

suicidal behaviour and improve the effectiveness of interventions (78).

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