HIV Associated Neurocognitive Disorder: Exploring the complexity

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A thesis submitted to fulfil requirements for the degree of
Doctor of Philosophy

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Candidate’s Statement

I, Denise Cummins, undertook this thesis as a part-time PhD student at the Susan Wakil School of Nursing and Midwifery, Sydney Nursing School, Faculty of Medicine and Health, The University of Sydney, under the supervision of Professor Donna Waters, Dr Christina Aggar and A/Professor Catherine C O’Connor.

I, Denise Cummins, was primarily responsible for developing the research proposal, design of the studies, obtaining ethics approval and the submission of scholarship applications to support the research.

I, Denise Cummins, collected, managed and analysed the data. I was primarily responsible for the interpretation of results, drafting and revising the manuscripts for submission to peer-reviewed journals, and the writing and compilation of this thesis.

I, Denise Cummins, hereby declare that this submission is my own work and that it contains no material previously published or written by another person except where acknowledged in the text. It does not contain material which has been accepted for the award of another degree.

Signed        Date        Signature

Denise Cummins   12/11/2018
ABSTRACT

Background

Human Immunodeficiency Virus (HIV) infection is now a chronic disease. People living with HIV (PLHIV) are ageing and at risk of co-morbid conditions. Regardless of HIV virological stability, 20% of PLHIV are at risk of a neurological co-morbid disease called HIV Associated Neurocognitive Disorder (HAND). HAND has three categories, asymptomatic neurocognitive impairment, mild neurocognitive disorder and HIV associated dementia each relating to varied levels of disability and affecting quality of life. The early identification and diagnosis of HAND is important, as HAND is a potentially treatable condition. Despite this, very little is known about how this complex condition is experienced by PLHIV or their caregivers and communities.

The diagnosis of HAND is multifactorial and is often achieved by the exclusion of other medical conditions which can confound the diagnosis. Additionally, PLHIV may experience mild signs and symptoms that they attribute to other causes such as morbidity associated with ageing.

Informal caregivers can make an important contribution to the diagnosis of HAND as they are often more attuned to the complexity of identifying subtle changes in cognition in PLHIV. For those PLHIV who do not have the support of an informal caregiver, professional caregivers may act as alternate observers of cognitive change through monitoring PLHIV in their own environment whilst providing care in the home.
Aim
The aim of this thesis was to explore the complexities of identifying HAND by people living with HIV, and their informal or formal (professional) caregivers. The three objectives were to:

- Explore whether people living with HIV and their informal caregivers can identify HAND.
- Explore the experience of HAND in people living with HIV.
- Explore whether community-based health care professionals can identify HAND.

Design
A pragmatic explanatory sequential design used mixed methods to elicit knowledge about the identification of HAND by PLHIV, and by their informal and professional caregivers. The thesis explored the complexities of identifying HAND through a preliminary pilot study followed by three subsequent study phases.

Method
A preliminary prospective multi-site observational study was undertaken at three HIV health clinics in Sydney, Australia to explore whether cognitive changes were being experienced by PLHIV and whether they could identify signs and symptoms of HAND. Participants in this study also identified informal caregivers who could provide additional information about witnessed changes in their cognition. Recruitment was staggered at the three sites with a one-year follow up to review the results of medical assessments.

The preliminary pilot study asked the broad initial question “Can people living with HIV and their informal caregivers identify HAND?” The results of this study informed the development of four further research questions explored through three
distinct study phases in this thesis. The Phase 1 study used an online survey with PLHIV, focusing on their experience of HAND. The survey was distributed via a peer HIV non-government organization to explore the research questions:

1. Are PLHIV aware of and/or concerned about HIV associated neurocognitive disorder?
2. Are PLHIV experiencing signs and symptoms of cognitive change and/or observing them in others?

The Phase 2 study used a cross-sectional design to conduct a file audit of patient data collected by two interdisciplinary community-based HIV specialist teams. A descriptive analysis was undertaken to explore the research question:

3. What information collected by HIV community-based teams identifies patients at risk of HAND?

Phase 3 used a Modified Delphi method, with a minimum of 80% consensus considered as agreement in any round, to answer the final research question:

4. What assessment criteria are essential to identify those at risk of HAND in the community?

Results

The preliminary pilot study recruited 165 participants (121 PLHIV and 44 caregivers) and found that a wide range of signs and symptoms of cognitive change had been experienced by 61% (73) of PLHIV over the previous 12 months. Fifty-seven per cent (25) of informal caregivers had also observed changes in cognition among those PLHIV enrolled in the study. Identification of the signs and symptoms of cognitive changes by study participants led to 16 being referred for formal testing. Four of these were subsequently diagnosed with HAND. Sixty-four per cent (77) of PLHIV
in the study did not identify the support of an informal caregiver and 41% (49) lived alone. The absence of regular observation by informal caregivers may impact on the early recognition of HAND through failure to observe changes in cognition in PLHIV over time.

In the Phase 1 study, findings from 126 eligible online surveys noted that 75% (94) of participants were aware of HAND and 59% (74) of HIV positive respondents had either experienced signs or symptoms of cognitive change in themselves or had noticed change in others. Of the 94 participants who had heard of HAND, 55% (52) responded that they were concerned and 58% (30) of them had spoken to someone about their concerns. Of these, 77% (23) stated they had a positive response when they had spoken with others (both health professionals and significant others) about their concerns, but 21% (11) had not. Importantly, the latter group stated that they would not discuss their concerns again. Thirty-nine per cent (49) thought assistance to broach the subject of HAND with others would be helpful. The results of the Phase 1 study led to a partnership with a key HIV peer organization in Sydney, Australia to develop and focus test a resource for PLHIV who have HAND and a resource for caregivers.

In Phase 2, a file audit of 262 medical records of PLHIV clearly showed that professional caregivers were not collecting and/or not documenting the type of information that might be useful for the detection of HAND. Further, incomplete patient data were noted in each file.

These results led to the Phase 3 study which utilized a modified Delphi method to gain consensus from experienced clinicians working across four community-based services. Expert clinicians with long-term experience of providing support to PLHIV
who had been diagnosed with HAND, were asked to agree on essential assessment criteria to identify those at risk of HAND in the community. More than 80% consensus was achieved by panel members on items to be included in an initial risk assessment and follow up annual monitoring tool suitable for use by community-based health professionals to regularly screen for HAND as a precursor for formal medical assessment.

**Conclusion**

The findings of this thesis indicate that the diagnosis of HAND is complex, but the observational and other experiences of PLHIV and their caregivers, whether informal or formal (professional), can offer unique insights into cognitive changes in PLHIV. This form of observational evidence is crucial to enhancing assessment and offers additional background information for clinical review, which could facilitate the early diagnosis of HAND.

PLHIV may experience social isolation, and as they age, may not have the support of an informal caregiver. Some PLHIV may be in same sex relationships where both parties may be at risk of developing HAND. For those PLHIV without the support of an informal caregiver and/or who live alone, professional caregivers can regularly undertake risk assessments to assess and monitor PLHIV who may be at risk of HAND. Professional caregivers can therefore act as an alternative to an informal caregiver, being well placed to observe changes in cognitive behavior over time.

The personal experience of PLHIV, as well as the experience of their informal and professional caregivers, can make essential and important contributions to reducing the complexity associated with identifying HAND and instigating early management
of this condition. HAND is a potentially treatable condition. Early recognition can have a positive impact on health and quality of life of PLHIV as they age.
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A/Professor Catherine C O’Connor my associate supervisor and clinical mentor. I want to express my sincere gratitude for your ongoing support. Catherine, a colleague has worked with me on several research projects and given me valuable advice over the years both personal and professional and has been a true mentor during this time which developed into a great friendship.

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No funding was received for this project.
Structure of Thesis

This thesis is presented for examination as a thesis containing published work. Of the eight chapters presented in this thesis, four contain papers that have been published in national and international peer-reviewed, indexed journals. The candidate is the principal author of all four papers. Published papers are presented in the format required by the journal; therefore, each contains an individual methods section and reference list. A complete reference list is also provided at the end of the thesis.

Chapter 1 describes a history of Human Immunodeficiency Virus (HIV) infection and offers a rationale for screening for HIV associated neurocognitive disorder (HAND) in PLHIV. A parallel history of the development of health services for HIV and HIV related cognitive impairment in Sydney, Australia is given from the personal perspective of the candidate who has worked with PLHIV throughout this time, and as a background to the studies conducted for this thesis.

Chapter 2 reviews published literature to illustrate the significance of support provided by informal and professional caregivers to PLHIV. This chapter also explores reasons why PLHIV may not have the support of an informal caregiver, and how both informal and professional caregivers may be instrumental in identifying HAND.

A methodology chapter (Chapter 3) discusses the aims and objectives of the thesis, the development of research questions and the rationale for using a mixed method approach to conduct the studies. Methods are presented in each of the published papers in Chapters 4 -7 (below), supporting the aims of the thesis:


The final chapter (Chapter 8) presents a summary of findings, discussing conclusions, recommendations and suggestions for further research directions for improving the diagnosis and treatment of HAND for PLHIV. Chapter 8 also outlines plans for the translation of the findings of this thesis into clinical practice – a major inspiration for this thesis.
# ACRONYMS AND ABBREVIATIONS

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>ANI:</td>
<td>Asymptomatic neurocognitive impairment</td>
</tr>
<tr>
<td>cART:</td>
<td>Combined antiretroviral therapy</td>
</tr>
<tr>
<td>CNS:</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CNS CPE:</td>
<td>Central nervous system penetration effectiveness rank</td>
</tr>
<tr>
<td>HAD:</td>
<td>HIV associated dementia</td>
</tr>
<tr>
<td>HAND:</td>
<td>HIV associated neurocognitive disorder</td>
</tr>
<tr>
<td>HIV:</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>LGBTI:</td>
<td>Lesbian, Gay, Bisexual, Transgender and Intersex</td>
</tr>
<tr>
<td>MND:</td>
<td>Mild neurocognitive disorder</td>
</tr>
<tr>
<td>NSW:</td>
<td>New South Wales</td>
</tr>
<tr>
<td>PLHIV:</td>
<td>People/persons living with HIV</td>
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Ethical Clearance

All studies for this thesis have been conducted in accordance with relevant HREC approvals and endorsed by the Human Research Ethics Committee of the University of Sydney, NSW, Australia.

The preliminary pilot study was approved by the Human Research Ethics Committee (HREC) of the Sydney Local Health District, NSW, Australia, Protocol number X10-0354+ HREC/10/RPAH/618 and Sydney South West HREC, Protocol number (SSA/11/LPOOL/203) [Appendix 1]. The preliminary pilot study was a collaborative project conducted across three clinical sites. The candidate undertook the literature review, liaised with staff at each clinical site, completed all data entry and analysis, and was first author on the manuscript (Chapter Four), as attested by the signatures of co-authors. Responsibility for ethical oversight was designated to site leads.

Additional approval for the following three study phases was given by the HREC of the Sydney Local Health District, NSW, Australia Protocol No X13-0314 & HREC/13/RPAH/426) and South Eastern Sydney Local Health District, NSW Australia protocol number SSA/14/RPAH/70, SSA 14/G/122 [Appendices 2-4]. The candidate was the single primary investigator for all remaining studies (Phase One – Three), completing all NEAF submissions and undertaking all associated annual reporting. Local HRECs were contacted for advice prior to submission of the National Ethics Application Forms (NEAFs) and any subsequent amendments.
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Appendix Three: Phase 2- ethics approval, participant information,
participant consent form; copy of file audit items.

Appendix Four: Phase 3- ethics approval, Delphi information sheet; participant information; participant consent (health professional and client); Health professional demographic survey; Likert scale (for initial and monitoring tools); Initial risk assessment tool, annual monitoring tool, and flow chart for HAND assessment; Pilot survey for health professional.
CHAPTER ONE

HIV associated neurocognitive disorder

Background

This chapter provides an historical overview of Human Immunodeficiency Virus (HIV), the Australian experience of the HIV epidemic from the 1980’s, and the clinical presentations and current classification criteria relating to HIV associated cognitive impairment. The purpose of this chapter is to illustrate the significance of the history of HIV and dementia in relation to the development of services for people living with HIV associated neurocognitive disorders (HAND) in Sydney NSW, Australia, as experienced by the candidate, a community HIV nurse specialist. This chapter will also summarise contemporary literature justifying reasons for screening and diagnosing HAND, and define terms used within this thesis in the context of Australian healthcare.

1.1 INTRODUCTION

The Human immunodeficiency virus (HIV) enters the central nervous system (CNS) in the first hours of infection and remains present throughout the infection (Al-Jabri, 2003). HIV can cause depletion of the immune system leading to acquired immune deficiency syndrome (AIDS) (Boasso, Shearer, & Chougnet, 2009). The history of HIV and AIDS begins in the early 1980’s when doctors in the United States of America became aware of a new illness among a small number of homosexual men (CDC, 1981; CDC, 1982). Since then, more than seventy million people have been infected, and the HIV epidemic has been the cause of death for about 35 million people globally (WHO, 2017). The burden of the epidemic varies between countries and regions, and outcomes are influenced by having access to antiretroviral drugs.
used to treat HIV since the late 1980s (Gayle & Hill, 2001; Mondal & Shitan, 2013). There are currently an estimated 36 million people living with HIV (PLHIV) globally (WHO, 2017), with around 26,444 thought to be living in Australia, and approximately 11% (2796) of these being unaware of their HIV status (Kirby Institute, 2017). For the more than 26,000 PLHIV in Australia in 2016, an estimated 89% were aware they had contracted the disease and a further estimated 86% had been prescribed antiretroviral drugs, with an expected 93% achieving viral suppression (Kirby Institute, 2017).

With HIV antiretroviral therapy having a substantial impact on morbidity and mortality, HIV infection is now seen as a chronic manageable disease (Deeks, Levin & Havlir, 2013; Degroote et al., 2013). People living with HIV are an ageing population with increasing numbers over 50 years of age and at risk of additional co-morbid conditions (Blaylock & Wortmann, 2015). Cognitive impairment is the most common CNS complication for PLHIV (Antinori et al., 2007) as the CNS acts as a reservoir for HIV, with neuronal damage occurring from the time of the initial infection (Nabha, Duong, & Timpone, 2013). As PLHIV age, they are at risk of developing neurocognitive impairment, regardless of immune system recovery and suppression of HIV viral load (Coban et al., 2017).

Many PLHIV have mild signs and symptoms of HAND but as they age, may also have other co-morbid conditions that can cause cognitive changes. The identification and diagnosis of cognitive impairment is complex and multifactorial and consequently, the diagnosis of HAND is often by exclusion (Nabha, et al., 2013). There are non-HIV related causes of cognitive impairment and other medical conditions which can confound a diagnosis of HAND, and these need to be eliminated.
in clinical assessment whilst additionally managing the person’s health in the wider context of their disease (Bloch et al., 2016).

As PLHIV are at risk of HAND as they age, it is important to recognise the signs and symptoms of HAND, to refer to early medical review for diagnosis and treatment whilst also treating other conditions that may impact cognition. HAND can significantly impact the quality of life of people living with HIV (Tozzi et al., 2004; Trepanier et al., 2005), for example, HAND may contribute to less than optimal medication adherence whereby non-adherence to antiretroviral drugs can lead to poor health (Vivithanaporn et al., 2010). Early intervention is paramount (Parsons, Braaten, Hall, & Robertson, 2006) as HAND is a potentially treatable condition by prescribing HIV antiretroviral drugs which have enhanced infiltration of the blood brain barrier (Letendre et al., 2008; Wright, 2011).

Informal caregivers may be well placed to notice subtle behavioural or cognitive changes whilst providing support to PLHIV who may not themselves notice or attribute mild cognitive changes to HAND (Blackstone et al., 2012). For those PLHIV who live alone and/or do not have the support of an informal caregiver, a professional caregiver may be in the best position to observe changes in cognition whilst providing regular clinical care and support. This is especially true for those professional caregivers who work in the community setting and are in the unique position to observe behaviour changes while the PLHIV undertakes activities of daily living, or if there are any changes in the home environment. Therefore, the personal experience of PLHIV, as well as the experience of their informal and professional caregivers, could make essential and important contributions to reducing the complexity associated with identifying HAND and instigating early management of this condition.
1.2 HUMAN IMMUNODEFICIENCY VIRUS

The human immunodeficiency virus (HIV) is a retrovirus which causes immune deficiency and leads to acquired immune deficiency syndrome (AIDS), the advanced stage of HIV infection (Sharp & Hahn, 2011; Simon, Ho, & Karim, 2006). There is no cure for HIV infection. HIV attacks the body’s immune system, specifically the CD4+ T lymphocytes, which help the immune system fight off infections (Simon, et al., 2006; Sharp & Hahn, 2011). Over time, HIV can destroy cells in the immune system, making the person susceptible to infections and other diseases such as some cancers (Moore, 2011; Simon, et al., 2006). Without treatment to maintain the immune system and reduce HIV viral load, most PLHIV will eventually become ill and die from their HIV infection (Sharp & Hahn, 2011; Simon, et al., 2006).

1.3 HIV INFECTION AND THE CENTRAL NERVOUS SYSTEM

The CNS acts as a reservoir for HIV with neuronal damage occurring both at the time of initial HIV infection and chronically, as HIV may remain latent in the brain for many years (Nabha et al., 2013; Skinner, Adewale, DeBlock, Gill & Power, 2009). Neuroimaging studies have observed reduced cortical thickness among PLHIV particularly in the premotor cortex, primary sensory, motor cortices and visual cortex (Reger, Welsh, Razani, Martin, & Boone, 2002). HIV brain changes are not restricted to the cortical areas; global reductions in white matter integrity and basal ganglia atrophy are seen. Clinically, this affects motor function, executive function, memory and visuospatial function (Reger, et al., 2002).

Dementia has become the leading cause of disability in Australians aged 65 and older and is rapidly growing into an area of major disease burden (Australian Institute of Health and Welfare, 2016). It has been noted that PLHIV may experience accelerated
ageing with dementia prevalence occurring in this population at a younger age when compared to the general community (Cohen, Seider & Navia, 2015; Letendre, 2011). HIV causes premature cognitive change (Cohen, et al., 2015; Letendre, 2011), possibly due to chronic inflammation, immune senescence, metabolic disorders and cardiovascular risk factors (Canizares et al., 2014; Soontornniyomkij et al., 2012). Additionally there is potential neurotoxicity from antiretroviral drugs (Underwood, Robertson, & Winston, 2015; Tedaldi, Minniti, & Fischer, 2015).

1.3.1 Early definitions of HIV related brain disorders

After the first reports of AIDS in the early days of the HIV epidemic it was observed that PLHIV manifested complications affecting the central and/or peripheral nervous system. Levy, Bredesen & Rosenblum (1985) reviewed a 5-year period from 1979 to 1984 and found that 124 of 315 people in their study (39%) had neurological symptoms. In 1983, Snider et al. found from 50 patients with AIDS and nervous system disease, 18 had experienced a subacute encephalitis which was attributed to cytomegalovirus infection. These authors coined the term ‘subacute encephalitis’ whereby there was evidence of progressive encephalopathy in the absence of other pathogens resulting from HIV. Around this time, Ho et al. (1985) isolated HIV in neurological tissue and cerebrospinal fluid from the autopsies of 24 of 33 patients with neurological symptoms.

Navia, Jordan and Price (1986) found that the most frequently recurring neurological complication associated with AIDS was subacute encephalitis. Motor symptoms were present in 45% of 44 participants in this study; presenting as ataxia, loss of balance, increased risk of falls and deterioration in hand writing. Headache was common, and seizures also occurred (Navia et al., 1986). Regardless of moderate deficits, such as
the presence of neurological symptoms and deficits in at least two areas (behaviour, memory and motor), study participants were still able to maintain limited independence, capable of performing activities of daily living. Progression of disease was often characterised by sudden acceleration and mental decline following a systemic illness such as aspiration pneumonia or opportunistic infection (Navia et al., 1986). With severe deficits, participants developed global cognitive impairment associated with dementia, severe disability and incontinence, with a poor prognosis of up to six months before death – usually requiring nursing care (Hilton, 1989; Navia et al., 1986). Other clinical manifestations observed among PLHIV were vague generalised complaints of withdrawal, apathy, depression, irritability and emotional lability, with some individuals reportedly losing interest in social activities and experiencing loss of emotional responsiveness (Buhrich & Cooper, 1987; Buhrich & O’Mullane, 1992).

In 1987, the term ‘AIDS Dementia Complex’ was introduced by Navia and Price (1987) to emphasise that AIDS dementia was associated with motor deficits and recognising that neurological impairments may be the early and only evidence of HIV infection. A year later the term ‘HIV encephalopathy’ was used to describe what Levy & Bresden (1988) determined was the commonest neurological complication of AIDS. As many terms were being used interchangeably to describe HIV manifestation in the CNS, the American Academy of Neurology AIDS Task Force published criteria for HIV associated dementia in 1991 to facilitate a consensus on terminology (Jannssen, Cornblad et al., 1991). The current criteria are known as the Frascati Classification Criteria and were published in 2007 (Antinori et al, 2007) and are described in Section 1.5 below.
1.4 **HIV ANTIRETROVIRAL DRUGS**

The first antiretroviral drug Zidovudine or AZT became available in 1987 (Fischl et al., 1990; Hamilton et al., 1992). At this time, there was limited evidence that AZT could reverse some types of neurological disease however, those patients withdrawn from therapy showed rapid neurological deterioration (Yarchoan et al., 1988). By the early to mid-1990’s other pharmacological agents were being developed and were being used in combinations (combined antiretroviral therapy or cART) that led to a profound improvement in HIV/AIDS progression and a decrease in morbidity and mortality related to HIV infection (Palella et al., 1998). Currently, combined formulations containing two or more HIV medications from one or more drug classes are offered as a single dose tablet from the time of HIV diagnosis.

There are now more than twenty antiretroviral drugs approved by the US Food and Drug Administration and treatment with cART now recommended for everyone with HIV. PLHIV take a combination of HIV medicines every day with initial treatment regimens generally including three HIV medicines from at least two different drug classes. The classes are: nucleoside reverse transcriptase inhibitors (NRTIs); non-nucleoside reverse transcriptase inhibitors (NNRTIs); protease inhibitors (PIs); fusion inhibitors; CCR5 antagonists; integrase inhibitors and pharmacokinetic enhancers (used to increase the effectiveness of an HIV medicine included in an HIV regimen) (US Department of Health and Human Services, 2017).

Potent antiviral drugs target multiple steps in the HIV lifecycle and inhibit HIV enzymes and proteins such as reverse transcriptase and viral protease. Treatment has resulted in virological suppression of HIV (as seen in reduced HIV viral load results), preserved immune function or restoration of immune function, and decreased risk of
opportunistic infections. Although improvements in morbidity and mortality have been profound for PLHIV, antiretroviral drugs also have side effect profiles such as lipodystrophy, pancreatitis and raised lactic acid (Gebo, 2006); increased risk of heart disease (Deeks & Phillips, 2009); metabolic syndrome (Kirk & Goetz, 2009) and; liver toxicity (Gebo, 2006).

Pre cART, the neurological prognosis of PLHIV was poor and many developed HIV associated dementia, often dying within six months of diagnosis. As more sophisticated combinations of antiretroviral drugs became available, survival time after a diagnosis of AIDS dementia complex increased from a mean of six months to 48 months (Navia et al., 1986). Improvements in survival and quality of life continue as more antiretroviral drugs are developed and the beneficial effects of these drugs are amplified when given in combination (Al-Khindi, Zakzanis, & van Gorp, 2011).

The National Institute of Mental Health and the National Institute of Neurological Diseases and Stroke conducted a study called the CNS HIV Antiretroviral Therapy Effects Research (CHARTER) study. This study was the first to explore to examine a diverse group of people from several HIV treatment centres to ascertain the frequency and severity of HAND in the US (Antinori et al., 2007; Heaton et al., 2011). The CHARTER study recruited 1555 HIV-positive people from university-associated clinics in Baltimore, New York, San Diego, Galveston, Seattle, and St. Louis. These clients underwent regular medical check-ups and measurement of their CD4+ T cell count and HIV viral load in blood. Most CHARTER participants (1205 or 77.5%) also agreed to have their HIV viral load measured in spinal fluid. All had extensive neuropsychological testing and psychiatric interviews to assess for depression and other mental illnesses (Heaton et al., 2011; Kamminga Cysique, Lu, Batchelor, &
Brew, 2013). The CHARTER study reported a significant reduction in the prevalence of motor impairments since the introduction of cART, possibly attributable to the ability of combined therapies to normalise CD4+ T cell count (Heaton et al., 2011). The study also reported that for some PLHIV, the integrity of the immune system appears to be linked to cognitive outcome, as executive function, motor function and visuospatial function was correlated with improved CD4+ T cell count in participants (Heaton et al., 2010).

1.4.1 NeuroART and CNS Penetration-Effectiveness (CPE) Rank

The term neuroART (Wright, 2011) describes a range of antiretroviral drugs which also in combination have been shown to have improved penetration in the CNS. These drugs have been identified as being more neurologically active as these drugs are able to reduce cerebrospinal HIV viral load to an undetectable level.

NeuroART drugs are known to have improved penetration across the blood brain barrier and once an individual is diagnosed with HAND they may be prescribed one of these agents as part of their medication regimen. Letendre et al. (2008) developed a ranking system for the penetration of antiretroviral drugs based on the chemical characteristics of HIV drugs, cerebrospinal fluid pharmacology and effectiveness in the CNS. Antiretroviral drugs were classified into three categories with each drug assigned a rank based on penetration (0 = lowest penetration, 0.5+ = intermediate penetration, 1+ = highest penetration) (Letendre et al., 2008). An antiretroviral drug was allocated to the lowest penetration category if concentrations of the drug were not measurable in the cerebrospinal fluid (Letendre et al., 2008). The CNS Penetration-Effectiveness (CPE) rank was then determined by summing the individual penetration ranks for each antiretroviral drug in a treatment regime. Therefore, a medication
regime score can be calculated to ascertain the CPE of all antiretroviral drugs prescribed to an individual PLHIV. As a score less than seven is deemed inadequate for effective CNS penetration, a person diagnosed with HAND would commonly have their medications adjusted to achieve a CPE of seven or greater for optimal CNS penetration (Letendre et al., 2008).

However, while some PLHIV will improve once prescribed antiretroviral drugs with higher CNS penetration, the condition of others will remain unchanged, or deteriorate (Nightingale et al., 2014). CNS neurologic complications can still occur, with 20% of PLHIV developing HAND regardless of optimal therapy and virological suppression (Coban et al., 2017). The efficacy of antiretroviral drugs in reducing HIV related cognitive impairment therefore remains unclear (Tozzi et al., 2007). Consequently, evidence for the continued use of the CPE rank in clinical practice is mixed. Some clinicians take the CPE score into consideration (particularly in patients with symptomatic CNS disease) because higher CPE scores have been associated with lower cerebrospinal fluid viral loads. However, the CPE score itself is limited by its categorical scoring, unclear weighting of each criterion (pharmacokinetic and chemical properties), and lack of consideration of toxic effects or drug interactions (Nightingale et al., 2014).

Despite mixed evidence, others have shown successful outcomes among PLHIV if signs and symptoms associated with HAND are recognised early and treated. Results from the CHARTER study showed that at least 50% of PLHIV with HAND prescribed antiretroviral medication with higher CNS penetration experienced improvement in neuropsychological performance (Letendre et al., 2004; Smurzynski et al., 2011). This can occur within twelve weeks of treatment and improvements can
continue from baseline for up to eighteen months (Gates et al., 2016; Cysique et al., 2009).

Regardless of what regimen of cART is prescribed, the single most important intervention in managing cognitive impairment in the presence of co-morbidities is to ensure that the PLHIV remains adherent to treatment in order to maintain viral suppression of HIV RNA in the plasma. Monitoring medication adherence and management through assistance with procuring prescriptions and arranging attendance at medical appointments is just one area that informal and professional caregivers can greatly assist those PLHIV experiencing changes in cognition.

1.5 THE FRASCATI CLASSIFICATION CRITERIA

Following increased access to cART in the 1990’s, diagnoses of neurological conditions such as HIV associated dementia started to decrease, however, recognition of the milder forms of cognitive impairment increased (Antinori et al., 2007). In response, the nomenclature adopted by the American Academy of Neurology Task Force on AIDS in 1991 was updated in 2007 to reflect changes in clinical presentations and acknowledge the emerging research relating to HIV cognitive impairment. The Frascati Classification Criteria (Antinori et al., 2007) proposes that the umbrella term, HIV Associated Neurocognitive Disorder, abbreviated as HAND, is now used to describe three categories of changes in cognition in PLHIV:

1. asymptomatic neurocognitive impairment (ANI);
2. mild neurocognitive disorder (MND), and;
3. HIV-associated dementia (HAD).
Each category has varying degrees of disability related to impact on daily functioning, quality of life and experience.

1.6 HIV ASSOCIATED NEUROCOGNITIVE DISORDER (HAND)

HIV associated neurocognitive disorder (HAND) refers to a spectrum of neurocognitive impairment and dysfunction, which can cause varied levels of disability in an individual. As noted above, the Frascati Classification Criteria refers to three categories of disability associated with HAND.

HIV associated neurocognitive disorder is diagnosed using neuropsychological testing, assessment of functional status and and/or radiology tests (Antinori et al., 2007). The majority of PLHIV with a diagnosis of HAND in the cART era do not present with HAD, and comprehensive neuropsychological assessment is required to recognise ANI and MND. These milder forms of HIV related neurological disorder can persist over time (milder memory problems and slowness, difficulties in concentration, planning and multitasking) and can represent substantial personal, societal and economic burden. Some authors have suggested that up to half of the participants in their studies may be affected by these milder forms of HAND (Heaton et al., 2010; Skinner et al., 2009).

In the CHARTER study described earlier (Antinori et al., 2007; Heaton et al., 2011), the prevalence of asymptomatic neurocognitive impairment (ANI) among the 1555 HIV-positive participants was 30-35% and was characterised by at least mild neurocognitive impairment in two domains (at least 1.0 standard deviation (SD) below the mean for age-education-appropriate norms). Individuals exhibited impairment in two or more ability domains such as attention, working memory,
abstract reasoning, executive function, processing speed or visuospatial processing (Antinori et al., 2007). Mild effects on everyday function was not experienced by people with a diagnosis of ANI. The CHARTER study also found that the relative risk of performance decline in those with ANI was more than five times higher compared to those with normal testing. But although those with ANI may be at greater risk of cognitive decline, it is unclear how clinically meaningful this will be (Heaton et al., 2011).

Similarly, the prevalence of mild neurocognitive disorder (MND) for PLHIV participating in the CHARTER study was 25-25% and was characterised by impairment in at least two domains (at least 1.0 SD below the mean for age-education-appropriate norms). Those with MND experienced mild negative effects on at least two types of everyday functioning (Antinori et al., 2007). This resulted in mild changes to daily function, including the ability to perform activates of daily living, work performance and social engagement (Antinori et al., 2007).

The prevalence of HIV associated dementia (HAD) in the CHARTER study was 2-3%, with moderate to severe impairments in neurocognitive functioning in multiple domains (2.0 SD or greater than demographically corrected means) (Heaton et al., 2010). Participants with HAD were therefore below average in two cognitive domains such as memory and executive function, slowed information processing, and defective attention and concentration, with marked difficulty in everyday functioning impacting on independent living and often requiring full time care (Antinori et al., 2007; Heaton et al., 2010). HAD may therefore place an increasing additional burden on resources in Australia, especially as PLHIV age. The annual cost for the care of HAD is
estimated to increase from about AU$29 million in 2009 to AU$53 Million by 2030 (Cysique, Bain, Brew & Murray, 2011).

Overall, the prevalence of HAND in HIV infected adults living in the US and based on the 2007 Frascati Classification Criteria is approximately 50-60% (Heaton et al., 2010). If not treated early, milder forms of HAND have been found to be a risk factor for developing HAD (Kamminga et al., 2013). There is also a greater chance of developing future cognitive difficulties as PLHIV age (Coban et al., 2017). Early detection is important to minimise progression of ANI and MND to HAD (Kamminga et al., 2013; Heaton et al., 2010; Lu, Brew, Siefried, Draper, & Cysique, 2014). In addition, if MND is identified and treated early, outcomes for PLHIV could be improved with reduction in symptoms, maintenance of medication adherence and independent living, and delayed disease progression (Cysique et al., 2009).

1.6.1 Signs and Symptoms of HAND

Table 1.1 outlines a range of common signs and symptoms of HAND related to the affected area of function. Cognitive changes attributable to HAND such as slowing of psychomotor skills, changes in language, memory and concentration (Barber et al., 2014; Ghate, 2012) can be mild and may be normalized by PLHIV (Antinori et al., 2007; Gisslen, Price & Nilsson, 2011; Cummins, 2014). In addition, executive function can also be affected whereby the person may experience changes in their ability to plan, organise and to solve complex or new problems (Antinori et al., 2007; Gisslen et al., 2011). Social engagement may also be affected as the person may become labile or disinhibited (Corr, personal communication, September 7, 2016).
Changes in behaviour may be attributed by the PLHIV and/or their informal caregiver to morbidity associated with ageing or other things such as being busy or stressed. Caregivers may notice changes in cognition or behaviour that the PLHIV may not, such as tiredness and irritability (Murray et al., 2015). These changes may affect the person’s ability to perform activities of daily living such as preparing meals, driving, managing finances or remembering doctor’s appointments. A person’s social relationships and the ability to retain employment, or work at a higher level, can also be affected. Negative effects on medication adherence may also impact health, wellbeing and quality of life (Osowiecki et al., 2000; Heaton et al., 2004; Letendre et al., 2008).
Table 1.1: Functional areas affected by HAND

<table>
<thead>
<tr>
<th>Area affected</th>
<th>Common Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motor skill</strong></td>
<td>Increasing fatigue&lt;br&gt;Unsteady gait&lt;br&gt;Increased clumsiness&lt;br&gt;Fine motor coordination&lt;br&gt;Slowed motor speed&lt;br&gt;Driving deficits&lt;br&gt;Difficulty typing, texting</td>
</tr>
<tr>
<td><strong>Memory</strong></td>
<td>Forgetting dates (e.g. birthdays), where placed keys, phone&lt;br&gt;Memory affecting cooking and shopping&lt;br&gt;Missing appointments and medications&lt;br&gt;Forgetting to send emails and issues for meetings</td>
</tr>
<tr>
<td><strong>Concentration</strong></td>
<td>How the person becomes receptive to stimuli and how he or she begins to process information. Problems include:&lt;br&gt;Difficult taking simple information and following directions&lt;br&gt;Difficulty keeping track of conversations&lt;br&gt;May have to re-read things&lt;br&gt;Difficulty completing activities&lt;br&gt;Difficulty following plots of movies and books&lt;br&gt;Becoming mentally fatigued easily</td>
</tr>
<tr>
<td><strong>Behavioural (social) change</strong></td>
<td>The person can experience one of two areas of behaviour change:&lt;br&gt;Apathy and listlessness&lt;br&gt;Withdrawal&lt;br&gt;Lack of motivation&lt;br&gt;Impulsivity and disinhibition: Hypomania&lt;br&gt;Change in personality&lt;br&gt;Increased agitation, aggression and irritability (e.g. stealing, swearing, over familiarity)&lt;br&gt;Emotional lability</td>
</tr>
<tr>
<td><strong>Executive function</strong></td>
<td>The person may experience difficulty in:&lt;br&gt;Initiation of a task&lt;br&gt;Planning&lt;br&gt;Problem-solving&lt;br&gt;Cognitive flexibility&lt;br&gt;Decision-making&lt;br&gt;Concept formation and abstraction&lt;br&gt;Judgment, feedback utilisation and monitoring behaviour</td>
</tr>
</tbody>
</table>

Source: Cummins, in ASHM, HIV Management in Australasia, 2017.
1.6.2 Predictors of HAND

There are several risk factors which have been shown to predict HAND and influence neurocognitive impairment in PLHIV. Non-HIV-related risk factors such as ageing and vascular risk factors such as smoking, hypertension, diabetes, hypercholesterolaemia and hyperlipidaemia should all be considered, just as they would in the non-HIV population (Letendre et al., 2009; Petoumenos et al., 2017; Rodriguez-Penny et al., 2013; Tedaldi et al., 2015; Valcour et al., 2005). Other non-HIV factors that can affect cognition and may confound the diagnosis of HAND include cardiovascular disease (Wright et al., 2010); drug and alcohol use (Fiala et al., 2005; Letendre, 2011); and hepatitis C co-infection (Schouten et al., 2012). Fewer years of education (Heaton et al., 2010) has also been shown to impact cognition.

The CHARTER study reported that cerebrospinal fluid protein concentrations of >45 mg/dL was predictive of cognitive decline in PLHIV and may be due to a disruption in the blood-brain barrier. A lower estimated glomerular filtration rate (eGFR) was also identified as a predictor of cognitive decline. The mechanism of this relationship is unclear but could reflect the presence of vascular pathology in the kidney and the brain (Heaton et al., 2010). Other (HIV-related) predictors of HAND include: past history of AIDS defining CNS disease (Fabiani, Pinto, & Bruschi, 2013); other CNS disease (Valcour, Shikuma, Watters, & Sackto, 2004); low CD4+ T cell nadir count (Ellis et al., 2011; Heaton et al., 2011); and longer duration of HIV infection (Heaton et al., 2010). Additionally, the risk of HAND increases as the CD4+ T cell count declines below 350 cells/uL and with higher plasma viral load (Bhaskaran et al., 2008).
1.7 A HISTORY OF HIV and HIV DEMENTIA IN SYDNEY, AUSTRALIA

A range of clinical reports from the beginnings of the HIV epidemic in Sydney, Australia are published and available, however, there is minimal published information relating to the parallel development of health services during this time. The candidate has worked as a nurse clinician in HIV for 25 years. The following is therefore a personal reflection and historical account of the development of services for PLHIV experiencing change in cognition over this time. This personal perspective is given both as background and context for studies conducted for this thesis, with personal verbal and written communications used to situate service developments within the historical frame.

Support services for PLHIV living in Sydney, the largest city in the state of New South Wales (NSW), Australia started to observe what was described as “unusual” presentations from the late 1980s (Personal Communication G. Cole, November 7, 2012). Community nurses and inner city mental health teams started reporting hypermania in HIV positive clients who in their view, appeared to be behaving “weirdly”. Staff were unsure whether this phenomenon was associated to HIV infection; mental health issues or; a non-described pathogenesis in the brain. Some health professionals hypothesised that presentations could be due to the (then) new anti-HIV drug Zidovudine, as little was known about long term side effects at the time (Fischl et al., 1990).

Although there was uncertainty about these unusual presentations, many staff thought they were seeing a new form of mental illness, as conventional mental health treatments did not appear to normalise symptoms in affected individuals.
We were not sure what the future of this group of patients was. Some were homeless and the two services (the homeless service and community health in Darlinghurst [inner Sydney]) co-jointly provided care for patients and many were being admitted to the local psychiatric hospital” (Personal Communication G. Cole, October 2, 2012).

By the late 1980’s and early 1990’s, the cognitive impairment associated with HIV was variously being described in the local Sydney news sources as: “… a fear of disfigurement, dread of pain and dementia, fear of abandonment by close friends, the ‘double whammy’ of breaking the news to friends and family of being gay and having a terminal illness and guilt were psychiatric symptoms common among those with HIV” (Maede, 1992, p.4).

Following a review of medical notes from a large inner-Sydney hospital specialising in the care of people with HIV, Buhrich and O’Mullane (1992) found that one in four patients had a psychiatric admission prior to being diagnosed with HIV and there was a disproportionate number of patients with AIDS being admitted to the psychiatric department. A high proportion of those were admitted for manic episodes characterised by disinhibition, loud talking and sexual promiscuity, with over half being referred from the community setting (Buhrich & O’Mullane, 1988).

Patients showed a wide range of psychiatric symptoms and differing presentations, although the most common symptoms seen in those with HIV/AIDS were anxiety and depression, delusions, hallucinations, and hypomania, both with and without evidence
of organic cerebral impairment (Buhrich & O’Mullane, 1988). Schizophrenic-like psychoses were reported in some patients showing impaired cognition, while others had features of classical mania with evidence of overactivity, overspending, grandiosity and insomnia (Buhrich & Cooper, 1987). Hypomanic symptoms, with and without evidence of cognitive impairment were also common, particularly in the later stages of the illness. However, cognitive impairment was often not recognised until the hypomania symptoms abated. A substantial number presented with delirium or AIDS dementia complex, and in those individuals, behavioural rather than cognitive disturbances predominated (Buhrich & O’Mullane, 1988).

Patients were being classified as recommended (at the time) by the United States Centre for Disease Control according to dominant psychiatric symptomatology and evidence of cognitive impairment (NSW Health, 1993; Buhrich & O’Mullane, 1988). But usual management was not appropriate for these patients, and the Diagnostic and Statistical Manual of Mental disorders –Revised (DSM3R) criteria for dementia were not useful to assess or categorise this group (Buhrich & O’Mullane, 1988).

1.7.1 Admissions to inpatient care

The emergence of HIV related dementia in the late 1980s and early 1990s placed enormous pressure on acute care or palliative care beds in Sydney hospitals. Furthermore, PLHIV with dementia often maintained physical function so did not ‘fit’ within mainstream dementia services tailored to aged persons with dementias, or meet age and other admission criteria for nursing home and hostel placements (NSW Department of Health, 1994, p.4).
The majority of persons with mild to moderate impairment were managed with the support of community-based services, volunteers and caregivers in their own home. As their physical condition deteriorated, these persons required more intensive support. Whilst an inpatient, some required one-on-one or segregated nursing care, which was both expensive and contributed to the acute and palliative care inpatient bed shortages. Others with moderate to severe AIDS dementia complex were living at home, often only partially supervised, and placing volunteer support services such as the Community Support Network (a voluntary peer support service which provided supports such as shopping, transport and cleaning) under considerable strain (Cotton & Whittaker, 1993).

During this period (early 1990s), two large area health services in Sydney were experiencing increased admissions of PLHIV with psychiatric symptoms. The Sacred Heart Hospice in Darlinghurst (managed by the NSW South Eastern Health Service) worked closely with acute care facilities (predominately St Vincent’s Hospital), to offer primary care facilities and community services to provide an integrated continuum of care for PLHIV. The hospital records note that of 73 consecutive Sacred Heart Hospice admissions of PLHIV from October 1991 to April 1992, 51% had neuropsychiatric problems ranging from adjustment reactions to active psychosis (Sacred Heart Hospice, 1993). Some HIV positive patients had been in long-term respite care at the Sacred Heart Hospice for up to a year as no other facility could accommodate them at the time as they were too young to be accepted into aged care facilities (Sacred Heart Hospice, 1993). Health services in the NSW Central Sydney Area Health Service were also affected. Between 1991 and 1994, Eversleigh Hospital in Lewisham admitted 134 people with HIV, and of these, 70 (52%) were diagnosed with HIV associated dementia (22 mild, 29 moderate and 12 severe dementia) and
seven others had brain disorders (NSW Department of Health, 1994, p4). Blockage of acute care beds was becoming a significant problem, with a back-flow of patients starting to impact two other large Sydney teaching hospitals, the Royal Prince Alfred Hospital and Concord Hospital inpatient and day stay services (NSW Department of Health, 1994, p4).

1.7.2 A model of care to reduce inpatient admissions

The NSW AIDS Bureau Report on Planning for HIV/AIDS Care and Treatment Services in New South Wales 1990-1994, recommended that people with AIDS-related neurological impairment should be managed in the least restrictive environment possible, taking into account their level of impairment, available health and community resources and the need to ensure the safety of the individual (NSW AIDS Bureau, 1990). There was ongoing discussion by the NSW Health department, clinicians and HIV positive advocates about the possibility of establishing hostel-type unit accommodation within the Sacred Heart Hospice for respite and long term care of patients with AIDS dementia complex, as the social and financial cost to the NSW health budget was becoming significant. Additionally, poor public knowledge and fear of HIV transmission was extensive within the Australian community and consequently, many services refused to accept admission of HIV positive patients.

The (then) outgoing Minister of Health, the Honorary Ron Philips who served as a Member of Parliament in the NSW Legislative Assembly from 1984 to 1999, allocated AU$2 million in one-off funding from the Mark Fitzpatrick Trust to establish more appropriate care for those with HIV related dementia. Mark Fitzpatrick had medically acquired HIV through treatment for haemophilia and had died when he was 10 years old. Several proposals were submitted to the NSW Department of
Health to establish new models of care, with the now experienced Central Sydney and South Eastern Area Health Services collaborating to develop a single proposal for a state-wide solution to provide care for affected individuals across the state of NSW (Eastern Sydney Area Health Service, 1994; NSW Department of Health, 1994).

Two key models of care were proposed: The first was to establish residential accommodation to combat the bed blockage situation at several acute inpatient facilities; and the second was to establish a community based care model. A house was procured in the inner west of Sydney (named “The Bridge”) to accommodate and provide 24 hour nursing care to those with AIDS dementia complex. Following this, the AIDS Dementia and Psychiatry HIV Team (ADAPHT) was established as a state-wide public health service for residents of NSW who had HIV-related cognitive impairment and complex needs such as mental illness, drug and alcohol dependence and other medical conditions (NSW Health, 2008). In March 1995, a single referral path was established for both services to offer an integrated program, with ADAHPT providing frontline community outreach with professional consultation, education and support throughout NSW, working with local area health services in the development of relevant resources and education. Consultation and co-case management was provided to assist with diagnosis, engagement plans or the organisation of appropriate services. All PLHIV who were referred to the outreach team were allocated a case manager.

The focus of support provided by ADAPHT has adapted over time to reflect changes in HIV presentation and outcomes for HIV associative cognitive disorder (HAND). Currently this service (ADAPHT) offers integrated HIV care including: case management for medical and psychosocial issues, neuropsychological assessment and
access to HIV supported accommodation. They also connect HIV positive prisoners to supports on discharge through the Persons in Custody program, and other HIV positive individuals who have alcohol and other drug dependence to the Alcohol and Other Drugs (AOD) Integrated Care Program. ADAPHT case managers and psychologists travel to visit individuals, regardless of where they live in NSW and “The Bridge” facility has moved to a larger property with capacity for 22 residents (NSW Health, 2008).

Community based services have also adapted over time. The Central Sydney Area Health Service established a Clinical Nurse Consultant (CNC) position for HIV/AIDS care in 1990 to reflect the needs of the community and to support generalist community nurses who were already caring for people with AIDS dementia complex. The candidate is the current CNC and has worked in this service for 21 years. In 1996, a community based HIV allied health team was established to work in partnership with community nurses to provide holistic community services to PLHIV who lived within the Central Sydney Area Health Service boundaries. Social workers and dietitians were the first allied health disciplines to be employed and later an occupational therapist and physiotherapist joined the team. Later, an additional mental health/HIV CNC position was established to reflect the evolving needs of PLHIV in the community. Today both CNC positions provide expert HIV information, clinical care in the home, liaison with inpatient facilities, and work closely with community general practitioners. The South Eastern and Illawarra Area Health Service established a similar community HIV outreach Team in 2007. This specialist multidisciplinary team is made up of social workers, mental health and primary health nurses, a dietitian and an occupational therapist.
1.8 THE CASE FOR SCREENING FOR HAND

In the current era of combined antiretroviral therapy (cART), the majority of PLHIV with HAND do not present with HAD but with the earlier stages of cognitive impairment (ANI and MND). Identification is difficult (Elbirt et al., 2015) as these milder forms of HAND are subtle and are diagnosed only by neuropsychological testing and/or neuroimaging studies (Kamminga et al., 2013). Screening tools may therefore assist in determining which PLHIV should undergo formal neuropsychological testing, as even mild forms of HAND are associated with increased risk of morbidity and mortality in younger PLHIV (Skinner et al., 2009; Tozzi et al., 2003). Additionally, early detection is important to minimise progression of ANI and MND to HAD (Kamminga et al., 2013). With early recognition of MND there are opportunities to treat the person and some evidence that their signs and symptoms may improve (Alzheimer’s Australia, 2014; Cysique et al., 2009). For some individuals, there is a direct correlation between cognitive improvement and enhanced CD4+ T cell counts due to the early administration of antiretroviral drugs that cross the blood brain barrier (Heaton et al., 2011; Letendre, Ellis, Ances, & McCutchan, 2010). Additionally, lack of knowledge of risk factors, poor documentation of discussion during medical and patient consultations (Cummins, Trotter & Murray, 2014) and difficulty locating patient information in electronic health records (Cummins, Waters, Aggar & O’Connor, 2015) all contribute to possible delays in the early identification of risk of HAND in PLHIV.

1.8.1 Diagnostic Biomarkers

There are currently three biomarkers for HAND which may have confirmatory value in clinical practice. For PLHIV who are not currently taking cART, the CD4+ T cell
count is used. If the person is currently being treated with cART or has failed treatment, then the CD4+ T cell nadir can be used and; if the CD4+T cell count is above 200/mm³, a diagnosis of HAD is described as doubtful (Brew & Letendre, 2008; Brew & Chan, 2014). Additionally, cerebral spinal fluid protein and cerebral spinal fluid HIV RNA (above 50 copies/ml) are almost always raised in those with HAD. Other biomarkers that could be useful for exclusion diagnosis include B12, red cell folate and thyroid function (Brew & Letendre, 2008).

Currently however, there is no one clear biomarker to diagnose HIV brain disease (Abasi et al., 2016; Atluri, Kurapati, Samikkannu, & Nair, 2014; Gisslen et al., 2011) and signs and symptoms, which can be mild, may be normalized by the HIV positive individual (Antinori et al., 2007). Development of key biomarkers could be helpful in diagnosing HAND as biomarkers could predict the presence and severity of HIV brain disease and inform treatment options. Additionally, for those PLHIV who are at risk of developing other chronic diseases as they age, specific biomarkers could be helpful in separating diagnoses of co-morbid conditions which potentially confound the diagnosis of HAND including viral hepatitis and vascular disease. A reliable marker to assist in the assessment of response to antiretroviral drugs would also be useful, as inactive forms of brain disease related to HIV infection may result in PLHIV given medications unnecessarily, with additional risk of toxicity.

1.8.2 Neuropsychological testing – the Gold Standard

The current definitive test for cognitive impairment in PLHIV is neuropsychological assessment. This can confirm diagnosis, monitor the progression of disease and functional abilities, and is useful to inform clinical management. In a neuropsychological assessment, objective data is obtained via patient review,
informant review, record review, behavioural observation and objective tests of cognitive, emotional and motor function. Information is also collected on medical and social history, including educational level, pre-morbid level of functioning, age, ethnicity, and previous and current drug use (Braun et al., 2011). Neuropsychological tests include objective manipulation and inspection of responses to pictures, multiple choice tests and answers to spoken questions. The tests measure such things as: attention and concentration, learning and memory, language and communication, visual-spatial cognition and visual-motor praxis, motor and sensory function, adaptive behaviour, problem solving and executive function, reasoning and sequencing (Braun et al., 2011). Neuropsychological testing is valid and reliable with validity measures equalling those reported for neuroimaging (Meyer et al., 2001). Neuropsychological examination is the only test currently capable of predicting functional abilities, assessing neurocognitive impairment, and measuring cognitive change over time or response to treatments (Braun et al., 2011).

1.8.3 Screening tools

Early neuropsychological screening tests for HAND were designed to focus on subcortical features targeting information processing, executive function, memory and psychomotor speed. This was based on the identification of HIV staining in the subcortical and deep grey structures of the brain (Valcour, Paul, Chiao, Wendelken & Miller, 2011), possibly explaining the behavioural, motor and predominately subcortical features of HIV-related cognitive impairment (Valcour et al., 2011). Although memory deficits occur, the pattern of HAND also involves inefficient learning and problems with executive function and retrieval of information. These features are different to those seen in Alzheimer’s disease where cortical deficits are seen more with the encoding of new memories. The motor deficits observed in HIV
are not often seen in Alzheimer’s disease but are similar and may be attributed to Parkinson’s disease (Valcour et al., 2011). PLHIV may also need to be assessed for a range of other diseases that affect cognition as part of normal ageing (Valcour et al., 2011; Brew, 2016).

While several guidelines have made recommendations for screening PLHIV for cognitive impairment, recommendations of when and how often to screen are inconsistent and consensus has not yet been reached (British HIV Association, 2016; European AIDS Clinical Society, 2016). A range of reasons have been proposed for clinicians not yet routinely adopting screening (Bloch et al., 2016) including competing health issues, limited access to appropriately trained clinicians, limited knowledge of the screening tests available and the limitations of the screening tests themselves, often only able to identify the most severe form of impairment. The American Academy of Neurology recommends increased screening for those with mild cognitive impairment (Valcour et al., 2011) and The Mind Exchange Working Group (2013) recommends that all PLHIV should be screened for HAND. In a systematic review by Zipursky, et al. (2013), inconsistency of screening was noted, with only 16% of studies employing the latest 2007 Frascati HAND classification criteria as used in the CHARTER Study.

There are several screening tools currently in use, such as the HIV Dementia Scale, International HIV Dementia Scale, and the Cogstate Computerized Battery (Kamminga, Lal, Wright, Bloch, Brew, & Cysique, 2017; Muñoz-Moreno et al., 2013). However, there is currently no single tool that can be used across a full range of clinical settings (Chiao et al., 2013). While some tests must be administered by a trained clinician, others use computerised technology, requiring further clinical
interpretation. Depending on which area of the brain is affected, screening tools may be more sensitive to advanced rather than mild signs and symptoms of HAND; have limited specificity and sensitivity; or be more appropriate for non-HIV related dementias (Kamminga et al., 2017). For example, the Mini Mental State Exam is widely used for people with Alzheimer’s disease but should not be used to screen for HAND as it is not useful for identifying executive function or motor skills and has poor sensitivity to detect the subcortical neuropathology seen in HAND (Valcour et al., 2011; Kamminga et al., 2013).

It appears from the literature that the most commonly referenced HIV screening tool is the HIV Dementia Scale (HDS) which provides rapid assessment of motor skills, simple learning and attention (Kamminga et al., 2013). The HDS was validated in a predominately white male population in the pre-cART era and so is useful to assess for moderate to severe decline in cognition in this type of population (Zipursky et al., 2013). Otherwise, the performance characteristics of the HDS are modest, with acceptable sensitivity for only the most severe disease and only 70% sensitivity for detecting mild impairment (Kamminga et al., 2013; Valcour et al., 2011). Therefore, the HDS is not a useful test for screening for ANI and MND due to inadequate sensitivity and is inappropriate at a time when ANI is the most prevalent form of HAND. The International HIV Dementia Scale (IHDS) was developed for global settings after studies had shown the HDS to be less accurate in non-white populations or in those PLHIV who had mild cognitive deficits (Robinson-Papp, Elliot, & Simpson, 2009). However, pooled sensitivity of several studies demonstrates that the IHDS is only moderately useful in detecting HAND and is also not suitable for the detection of mild impairment (Zipursky et al., 2013).
The Montreal Cognitive Assessment (MCA) was designed to detect mild cognitive impairment in the older, general HIV-negative population (Ciesielska et al., 2016). While many clinicians use the MCA, it appears to be insufficiently sensitive to detect the mild neurocognitive impairment seen with HAND (Janssen, Bosch, Koopmans & Kessels, 2015; Milanini et al., 2016) and is unable to accurately monitor change over time. The MCA is therefore not suitable to detect cognitive decline in PLHIV, yet Chartier et al. (2015) note that it still has the potential to provide some clinically meaningful data. A study by Fazeli et al. (2017) further demonstrated good clinical sensitivity, supporting use of the MCA as a brief cognitive screening tool among older HIV-positive adults.

Other screening instruments to detect milder levels of neurocognitive decline are clearly needed (Lu et al., 2014). A computerized test battery, the CogState, assesses five relevant cognitive domains sensitive to the detection of HAND and general cognitive impairment. The CogState requires minimal skill for administration and scoring, but a neuropsychologist should undertake the final interpretation of scores. The CogState has been tested for validity in Australia with 254 PLHIV, age and education matched to 72 HIV negative controls (Bloch et al., 2016). Fifty-three participants and 22 of the control group underwent neuropsychological testing and Cogstate screening. Comparison of both groups resulted in a sensitivity of 76% and specificity of 71% for Cogstate screening. In the MND/HAD subgroup, the sensitivity and specificity improved dramatically to 100% and 98%, respectively. The computerized screening method is suitable for application by non-specialists and may assist with detecting patients requiring more in-depth neuropsychological testing, hence guiding the best use of resources within under-resourced settings (Bloch et al., 2016). While the CogState does not improve screening sensitivity for patients with
ANI, these individuals could be monitored longitudinally whilst controlling and treating alternate risk factors for cognitive decline (Kamminga et al., 2017). Some HIV health services and general practices with high HIV caseloads have started to adopt this model, with the overall HAND screening prevalence at one community medical practice in Sydney reported as high as 31% (Bloch et al., 2016).

Further longitudinal studies are needed to assess the validity of instruments for screening all categories of HAND. Thus far, longitudinal decline, as measured with repeat assessments of the HIV dementia scale (HDS), was reliable in the retest setting; however, similar to CogState, this technique was only able to robustly detect moderate to severe cognitive decline (Lu et al., 2014). There is also a need for screening tests that are simple for all health practitioners across a range of settings, and that can quickly and effectively monitor risk and the effects of treatment over time, whilst adhering to HAND Frascati Classification Criteria for relevant and universally standardized reporting of results. The outcome of regular screening is also important to validate the experience of PLHIV and/or their informal caregivers by offering evidence of cognitive change and prompting acceptance of diagnosis and the development of appropriate management plans.

1.8.4 Co-morbid medical conditions and HAND
Co-morbid conditions increase complexity in the diagnosis of HAND and may independently contribute to poor neuropsychological performance without actually being the cause of HAND (Kamminga et al., 2013; Nightingale et al., 2015). Risk factors for general cognitive impairment may also mimic and/or confound the signs and symptoms of HAND, therefore the accurate diagnosis of HAND relies on other co-morbid conditions and pre-existing causes of dementia or brain injury being
excluded (Antorini et al., 2007). As noted above, these may include diabetes, hepatitis C infection, hypertension (Rodriguez-Penny et al., 2013; Tedaldi et al., 2015), substance use (Elbirt et al., 2015) and cerebrovascular disease (Heaton et al., 2010; Tedaldi et al., 2015; Wright et al., 2010).

Further, decreased brain reserves in an ageing HIV seropositive population may be the result of several factors, including the synergistic effect of neuropathology related to ageing and other age-associated degenerative diseases. Age-associated comorbidity may affect physical function in HIV-infected patients and may modify the effect of ageing, for example, co-morbid conditions may appear 10 to 20 years earlier in PLHIV when compared to the general community (Oursler et al., 2011). The Veterans Aging Cohort Study compared HIV-positive veterans to HIV-negative controls and noted that PLHIV had a higher rate of co-morbidities at all ages. For those older than 60 years, the rate of co-morbidities was 63% compared to 12% for HIV–negative controls (Oursler et al., 2011). Data from an Australian study conducted by Positive Life NSW (2015) also found that for 126 PLHIV responding to a survey, 41% had HIV as a single condition, 21% self-reported one additional co-morbid condition; 14% self-reported two conditions; 10% three; 7% four and; 2% self-reported having five or six existing co-morbid conditions. In another recent study, Petoumenos et al. (2017) noted no difference in self-reported smoking rates between older PLHIV compared to HIV-negative controls, but found that recreational drug use was increased in PLHIV who also had increased risk of diabetes, neuropathy and thrombosis. The risk of heart disease was not significantly different in this study. Deeks and Philips (2009) note that for many PLHIV, HIV is no longer their primary health concern as conditions such as cardiovascular disease, diabetes, cancers, osteoporosis, cognitive impairment, liver and kidney disease and mental health issues
impact their health as they age (Oursler et al., 2011). Any screening tool must therefore be able to distinguish specific factors related to HAND among many possible competing presentations.

The Frascati Classification Criteria have significantly improved the reliable detection of neuropsychological impairment and confounding conditions (Heaton et al., 2010). The Frascati Guidelines give instruction for classifying the most common co-morbid conditions with respect to whether they should be considered *Incidental* (conditions that have little impact on HIV-related neuropsychological impairment); *Contributing* (conditions that probably affect HIV-related neuropsychological impairment to some degree); or *Confounding* (conditions that make it impossible to say whether HIV alone is causing neuropsychological impairment) (Heaton et al., 2010). As an example, neurocognitive impairment was seen in 52% (814 of 1555) of all CHARTER study participants (Heaton et al., 2010). More than half of the total participants (54.2%, n=843) were classified as having *incidental* co-morbidities and 30.4% (n=473) had *contributing* conditions. A further 15.4% (n=239) had *confounding* co-morbidities that precluded a HAND diagnosis. Among those 52% (n=814) participants with neurocognitive impairment, co-morbidities were *incidental* in 40%; *contributing* in 59% and; *confounded* in 83%. Impairment was associated with AIDS diagnosis, lower nadir CD4+ T cell, but only in the *incidental* group and was consistent with having more advanced HIV disease. When considering the entire CHARTER sample without severe co-morbidities (n= 1316) the overall number of participants diagnosed with HAND was 32.7% with ANI; 11.7% with MND; and 2.4% with HAD (Heaton et al., 2010). Predictors of HAND (exclusive of severe co-morbidities) in the CHARTER study included nadir CD4+ T cell <200, cumulative duration of cART treatment, CNS CPE score for current antiretroviral regimen,
detectable HIV in plasma (viral load), and hepatitis C sero-status (Heaton et al., 2010).

In summary, the recognition and treatment of co-factors for cognitive impairment could improve cognition in PLHIV and reduce complexity and confounding in the diagnosis of HAND. The increased longevity of PLHIV, secondary to treatment with antiretroviral drugs, and the relationship between longer HIV infection and several chronic conditions, has seen the proportion of deaths attributed to chronic non-infectious co-morbid conditions increase among this group (Peters et al., 2013). Many of the co-morbid conditions, such as diabetes and cardiovascular disease, are associated with modifiable risk factors (Klein et al., 2011) and management guidelines for HIV recommend regular risk evaluation for these conditions (Peters et al., 2013).

1.9 CONCLUSION

HIV-related neurological presentations in Australia have changed significantly since the early days of the HIV epidemic, largely due to access to antiretroviral drugs. But similar to PLHIV globally, more than 20% remain at risk of developing a subcortical neurodegenerative disease caused by HIV-1, known as HIV neurocognitive disorder (HAND) (Clifford & Ances, 2013). HAND can cause various levels of disability, impact quality of life, and is associated with increased morbidity and mortality in younger PLHIV (Skinner et al., 2009). Cognitive changes attributable to HAND can be mild and may become normalized by PLHIV, especially as they age (Gisslen et al., 2011; Cummins, 2014); these include changes in language, memory, problem solving and slowing of psychomotor skills (Barber et al., 2014; Ghate, 2012). Diagnosis is multifactorial and can be compromised by the presence of co-morbid conditions.
Early identification is important as treatment of HAND offers opportunity for improved clinical outcomes and quality of life for PLHIV (Robertson et al., 2007).

HAND can be diagnosed through neuroimaging, neuropsychological testing and cerebrospinal fluid examination but is more often diagnosed by exclusion of other causes of changes in cognition. However not all PLHIV will agree to, or have access to neuropsychological testing, therefore regular screening is important to identify which PLHIV are at risk of HAND to investigate and confirm diagnosis. For those PLHIV diagnosed with mild forms of HAND, early identification and treatment could prevent progression of neurocognitive disease. Additionally, screening can provide baseline information for monitoring the potential for future risk of cognitive decline. Screening also offers information leading to the diagnosis of other co-morbid medical conditions, which can mimic signs and symptoms of HAND. Treatment for co-morbid conditions can be commenced, whilst reassuring the PLHIV they do not have a diagnosis of HAND. Screening may also have supplementary benefit in supporting medication adherence, which can decline in PLHIV with HAND. This potentially enables PLHIV and their caregivers to develop individualised approaches for medication management, thus having a positive effect on treatment adherence and health outcomes.

People living with HIV may attribute changes in cognition to morbidity associated with ageing, other co-morbid conditions, or be unaware of their cognitive decline. Personal assessment of everyday function relies on self-insight (Chiao et al., 2013) but when impairment is moderate, insight into the self-assessment of everyday functioning can be diminished (Blackstone et al., 2012). Informal caregivers are generally in a position where they can provide evidence of cognitive changes through their observation or daily support of PLHIV. For those PLHIV who live alone and/or
do not have the support of an informal caregiver, a professional caregiver may be the only other regular contact able to observe changes in cognition whilst providing clinical care and support over time. This is especially relevant for professional caregivers who provide community based care and who are observing unique evidence of changes in the home environment, or behavioural changes while the PLHIV undertakes activities of daily living.

This chapter has provided an overview of cognitive impairment in HIV; historical and current models of care provided to PLHIV in Sydney Australia; and has made a case for improving screening for HAND. Knowledge of change in cognition, decline in daily functions, medical information including co-morbid conditions and social circumstances could provide further information to aid the diagnosis of HAND in PLHIV. Informal and professional caregivers are well placed to provide some of this information, especially as they usually offer clinical care and support to PLHIV in their home. The next chapter will discuss aspects of caregiving provided by informal and professional caregivers and explore reasons why some PLHIV may not have informal support.
CHAPTER TWO
The role of informal and professional caregivers

Background

Chapter One provided an overview of the historical aspects of cognitive impairment and HIV, classification changes resulting from the introduction of the Frascati Classification Criteria in 2007 and introduced factors that contribute to the complexity of diagnosing HAND in people living with HIV. The aim of Chapter Two is to illustrate the significance of support provided by informal and professional caregivers to people/persons living with HIV (PLHIV) through a scoping review of literature. As literature relating specifically to caregiving in the context of cognitive impairment was very limited, the review was expanded to explore who caregivers are, what types of support they provide to PLHIV, and why some PLHIV may not have the support of an informal caregiver. An argument is made that caregivers, both informal and professional, are well placed to recognise early cognitive changes in PLHIV. These changes may be mild but indicative and support the early diagnosis of HAND.

2.1 INTRODUCTION

The psychosocial and health-related consequences of HIV infection continue to impact the lives of PLHIV and the support of caregivers remains central to PLHIV continuing to maintain their quality of life. Caregivers, both informal and formal (usually health professionals), have been shown to have a positive impact on health and well-being across a range of conditions (Uchino, 2004), and for PLHIV, caregivers may also be the first to notice mild health changes and to encourage and
support attendance for early medical review (Decarlo & Folkman, 1997). PLHIV have also found the support of caregivers potentially beneficial to enhance communications and relationships with health care providers and other services, and to encourage adherence to medications (Mosack & Petroll, 2009).

2.1.1 Defining informal and professional caregiving

The terms most commonly used to describe a person who supports family members or friends are caregiver, carer or informal carer. For the purpose of this thesis, informal caregivers include: family members, friends, partners and peers (HIV positive volunteers), that is, anyone who offers unpaid support and care to a PLHIV.

Carer’s Australia is a not for profit organisation and national peak body representing Australia’s unpaid caregivers. It is estimated that Australia has over 2.7 million informal caregivers, almost 12% of the total population (Carer’s Australia, 2016). Carer’s Australia (2016 p.1) identifies informal caregivers as “people who provide unpaid care and support to family members and friends who have a disability, mental illness, chronic condition, terminal illness, an alcohol or other drug issue or who are frail aged”. Informal caregivers offer social, emotional and financial support and symptom management for the recipient of care, whilst supporting activities of daily living; and as such models of care should include caregiver participation where appropriate (Zarit & Reamy, 2013). In addition to physical and personal care such as showering and dressing, lifting, help with cooking and feeding, informal caregivers may also provide transport, medication management, organisation of social and other support services and often accompany the person to appointments (Chio et al., 2006).
The definition of family may be broad for some PLHIV. Care and support are largely perceived as the role of women – mothers, wives and daughters (Flaskerud & Tabora, 1998, Wight et al., 1998). The Australian Survey of Disability, Ageing and Carers (2015) showed that females represented 68% of primary caregivers and 56% of all caregivers. The number of female primary caregivers (134,500) aged between 55-64 years was almost double the number of male primary caregivers (70,800) (Australian Bureau of Statistics, 2015). More daughters live with and care for a frail elderly parent than do sons (Ekwall, Sivberg, & Hallberg, 2007) and women are more often the primary caregiver to unwell family members (Asuquo, Etowa, & Akpan, 2017; Bunting, 2001). Yet for some PLHIV primary caregivers may not come from the traditional female caregiving relationship. One of the aims of this literature review is to explore who caregivers for PLHIV actually are.

In contrast, professional caregivers are those who receive payment for caregiving work, often being employed by a formal service or system such as a government health service or non-government organisation (Family Caregiving Alliance, 2014). Professional caregivers often include allied health, medical, nursing and community support workers. In this thesis, the term community based health care professionals refers to any health professional or support worker providing support to PLHIV in a community setting.

2.1.2 Supportive communities

Between the 1940s and 1950s, the term “gay” was used to describe both men and women who were attracted to the same sex. In the 1970s, women chose to use the term “lesbian” to differentiate themselves from gay men and the acronym LGB (lesbian, gay and bisexual) was introduced during the 1980s to include those who
identified as bisexual. As Australian society has become more accepting and inclusive of diversity, this acronym has expanded to include many orientations. For example, the acronym LGBTI (lesbian, gay, bisexual, transgender and/or intersex) has been used since the 1990s to describe diverse communities living around the world and has more recently been expanded to be inclusive of those identifying as lesbian, gay, bisexual, transgender, queer and questioning, intersex and intergender, anonymous and allies (LGBTQIA) (Gregg, 2017). In Australia, LGBTI people and populations are recognised in a range of Commonwealth Government policies and programs. Since 2013, there has been federal protection from both direct and indirect discrimination on the basis of sexual orientation, relationships status, gender identity, and intersex status, and individuals from these Australian communities are identified as a special needs group under the Aged Care Act 1997 (National LGBTI Health Alliance).

The National LGBTI Health Alliance acknowledges the limitations of using the LGBTI acronym; that identities are far broader than the acronym can comprise such as the wide diversity seen with gender, relationships and sexuality. The Alliance also acknowledges that the intersection of body, gender, sexuality and relationship identities and cultural identity, including indigenous identity, results in self-determined terminology not encompassed by the LGBTI acronym (National LGBTI Health Alliance). With respect to this view, the collective term LGBTI will be used in this thesis to encompass all diverse groups referred to above. The LGBTI community continue to support PLHIV in many ways and are an important part of the informal caregiver community.
2.2 INITIAL LITERATURE REVIEW

The aim of the initial literature review was to determine whether information was available about who and what types of support are offered by informal and professional caregivers to people/persons living with HIV (PLHIV) who experience changes in cognition. The significance of caregivers within this context is their potential to be able to recognise early cognitive changes in PLHIV. However, despite broad searching across several databases, initially from 1980 to 2012 and updated in 2018, literature on this topic was extremely limited. Early publications focussed on the informal and professional care of PLHIV, and not specifically on the care of those experiencing cognitive decline.

The absence of an evidence-base led firstly to a decision to explore the broader concept of caregiving within the literature, that is, who are the caregivers providing care and support to PLHIV and what are the main supports they provide? The result of the preliminary pilot study also established some basic insights and a beginning evidence-base about the care and carers of PLHIV experiencing cognitive decline (reported in Chapter 4).

2.2.1 Initial search method and keywords

As little was known about the types of support offered by informal and professional caregivers to PLHIV who experience changes in cognition, a scoping review method was chosen. Scoping reviews are used for the identification and definition of parameters for a study, and for the development of research/search questions (Armstrong, Hall, Doyle, & Waters 2011). Initially, three main keywords (HIV, dementia, caregivers) were used to search within seven databases (Medline, Embase, Pubmed, psycINFO, Cochrane Library Database, PROQUEST and CINAHL) from
the period coinciding with the beginning of the HIV epidemic internationally in 1980, through to August 2012. Studies were excluded from the review if they were written in a language other than English, were not a peer-reviewed original article, and/or the mean age of participants was below 18 years.

Despite many publications for single keyword searches, combinations of keywords yielded no results (Table 1). The term ‘aids dementia complex’ was added as this term was frequently used at the beginning of the HIV epidemic, yielding a total of eight papers, however, six of these did not fulfil the initial search criteria (two written by an anonymous author, one not in English and the remaining three focusing on patient management and caregiver needs more generally).

**Table 2.1: Initial keyword search**

<table>
<thead>
<tr>
<th>Key search terms</th>
<th>Yield</th>
<th>Search combinations and result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. HIV</td>
<td>92901</td>
<td>1 + 2 + 3 = 0</td>
</tr>
<tr>
<td>2. Dementia</td>
<td>148849</td>
<td>1 + 2 + 4 = 0</td>
</tr>
<tr>
<td>3. Caregivers</td>
<td>31019</td>
<td>1 + 3 + 4 = 0</td>
</tr>
<tr>
<td>4. AIDS dementia complex</td>
<td>3606</td>
<td>3 + 4 = 8</td>
</tr>
</tbody>
</table>

The three original keywords were then “exploded” and each database was searched using the terms: HIV associated cognitive impairment (including the terms HIV encephalitis, subacute encephalitis, HIV associated dementia, HIV dementia, AIDS dementia, AIDS dementia complex, HAND, ANI, MND and HAD) separately or in combination with keywords related to caregiving (caring, carer, informal carer, formal carer and professional care); caregiver; informal caregiver; formal caregiver; and professional caregiver. Additionally, the words: family, parent, mother, father, aunt,
uncle, brother, sister, sibling, wife, husband, partner and children (including son and daughter) were included as examples of informal caregivers and the words: nurse, doctor and allied health professional, including social worker, physiotherapist, occupational therapist and dietician as examples of professional caregivers.

Given the continuing lack of relevant literature emerging, types of support for PLHIV were then included with all caregiver search terms using the keywords: emotional support; practical support; financial support; and medication management. Each of those terms were also searched in combination with terms relating to HIV associated cognitive impairment as listed above. Using varied combinations of terms elicited no articles at all, including searching each individual informal caregiver (mother, father, brother, sister, etc.) and professional caregivers (nurse, social worker, doctor etc.) in combination with the various terms for AIDS dementia which had changed over time with new information from research and use of HIV medications (HIV encephalitis, HIV dementia, ANI, MND etc.).

Eventually after using all combinations together, only eight relevant articles could be found from a final total of 270 papers (including two from the initial search) that met the search criteria (Table 2.1). As previously, articles that were excluded were those not written in English, were not peer-reviewed, related to HIV neurology; were about the burden of care for caregivers; the stress of providing care; caregiver burnout; caring for PLHIV who were dying; caring for children with HIV, or were from a developing nations context. An updated search using the same exploded keywords and method was performed to capture any additional publications between August 2012 and May 2018. Following application of exclusion criteria as previously, this updated search resulted in four additional publications (Cummins, 2014; Hopcroft et
al., 2013; Murray et al., 2016; Terpstra et al., 2018). These four, in addition to Kelly (2010), appear to be the only studies relevant to PLHIV and/or caregiver experience of HAND in PLHIV published since the revision of the Frascati Classification Criteria in 2007.

2.2.2 Outcome of the initial review

Despite repeat testing of the significant number of keywords and search term combinations within the above databases, the initial (1980 – 2012) and updated search (2012 – 2018) revealed a total of only 12 papers published over the past 38 years that related directly to caregivers and neurocognitive function in PLHIV. The content of these final 12 papers was so varied that attempts to synthesize findings were not successful however the combined results are discussed below in 2.2.3.

As identified in Chapter 1, the introduction of the Frascati Classification Criteria in 2007 was a significant time-point for noting changes in practice in the literature (that is, pre and post introduction of HAND classification criteria). It is of note that those studies relating to professional caregiving in the period before introduction of the Frascati Classification Criteria in 2007 rarely discussed cognitive impairment but reflected the historical context of care and treatment of HIV-associated dementia at the time, focussing on stress and burnout among professional caregivers (Barbour, 1994; Lusby, 1985; Macks & Abrams, 1992; Nesbitt, Ross, Sunderland, & Shelp, 1996; Rinella & Durbin, 1988), particularly in relation to caring for PLHIV in acute and palliative care settings (Barbour, 1994; Gueritault-Chalvin, Kalichman, & Denni, 2000). For caregivers who were HIV-negative, concern about HIV exposure and fear of transmission to others was also part of the caregiving literature at this time (Brown and Powell-Cope 1991; Prachakul & Grant, 2003).
The caregiver literature also revealed discussion of HIV in many other contexts such as caregiver burden (Asuquo, Etowa, & Adejumo, 2013; Chandran et al., 2016; Lee, Li, Jiraphongsa, & Rotheram-Borus, 2010), grief and loss (Brown & Powell-Cope, 1993; Folkman, Chesney & Christopher-Richards, 1994), caregiver exhaustion (Raveis & Seigel, 1990), caregiver mental health and emotional support (Casale, Wild, Cluver, & Kuo, 2014; Flakerud, Cater & Lee, 2000; Prachakul, & Grant, 2003), personal reward (Haviland et al., 1997), caregiving in resource poor settings (Kohli et al., 2012; Majumdar, & Mazaleni, 2010), burden and fear of HIV disclosure (Baker, Sudit & Liwak, 1998), caring for children with HIV (Casale et al., 2014; Osafo, Knizek, Mugisha, & Kinyanda, 2017) and barriers to care (Liboro et al., 2018). While of great importance to the care of PLHIV, contexts of caregiving to children; personal experiences of caregiving; or caregiving in resource poor settings are not relevant to this thesis and will not be discussed further. However, what is relevant to this thesis is the notion of complexity and the repeated finding that caregiver burden and grief was multifactorial and complex (Baker et al., 1998).

2.2.3 Results: Caregivers and HIV-related cognitive impairment

The combined findings of the 12 papers included in the initial and updated review revealed that prior to antiretroviral drugs becoming available for the treatment of HIV in the early to mid-1990s, and the introduction of the Frascati Classification Criteria in 2007, discussion of cognitive symptoms in literature relating to HIV and caregiving was rare. Stajduhar (1997) describes the experience of informal caregivers caring for PLHIV dying with AIDS dementia, with the burden of caring for people with AIDS dementia complex and the development of depression in caregivers discussed by Meadows, Le Maréchal & Catalan (1999) and Flakerud & Lee (2001), respectively.
It was often the case in this early literature that the caregiver had become aware that their loved one was HIV positive, homosexual, and dying all at the same time.

Other studies published around this time examined the impact of diminishing communication between caregivers and those with AIDS dementia complex, noting that maintaining quality could enrich quality of life in PLHIV (Morrow, Allen, & Campbell, 1997). Others detail the clinical implications of the experience of cognitive decline (Morgan, Clark & Hartmann, 1988), and how PLHIV deal with the unknown future of AIDS Dementia (Kelly, 2010). A case study from Cripps, Spencer & Clark (1994) discusses the complex care needs of a person with an intellectual disability and schizophrenia also diagnosed with AIDS dementia. Hilton (1989) discussed nursing interventions for supporting informal caregivers, and caring for PLHIV with an acute diagnosis of dementia, concluding that nurses could be instrumental in the recognition of disease progression. Similarly, in a study preceding candidature, Cummins (2014) had utilised a case study approach to describe the community support offered by professional caregivers, finding that potential existed for professional caregivers to play a greater role in the context of caring for PLHIV who may be at risk of HAND. Interestingly, however, Terpstra et al. (2018) reported that there was limited discussion about HAND between PLHIV experiencing signs and symptoms of cognitive changes and professional caregivers across three sites included in their study (a community-based organization, a community-based HIV specialty hospital, and a neuropsychology clinic at a large urban hospital).

Hopcroft et al. (2013) reflected on the experiences of ageing men with HIV-related cognitive changes, noting that support from family and friends was significant as they accepted who they were regardless of cognitive change in the PLHIV. While Murray
and colleagues (2016) examined whether informal caregivers were observing signs and symptoms of decline in cognition in PLHIV, concluding that informal caregivers were instrumental in providing additional evidence of changes in cognition experienced by PLHIV.

2.3 EXPANDING THE REVIEW
The aim of the initial literature review was to determine who and what types of support are offered by informal and professional caregivers to people/persons living with HIV (PLHIV) who experience changes in cognition. As literature relating specifically to caregiving in the context of cognitive impairment was so limited, a further scoping review was undertaken to expand the topic to include caregiving for all PLHIV (regardless of their cognitive state). Using the same scoping review method, the search was re-run to include any publications about who caregivers of PLHIV are, what types of support they provide to PLHIV, and why some PLHIV may not have the support of an informal caregiver. The rationale for this second scoping review was specifically to identify which key populations provide care, and exactly what kind of supports they provide, under the assumption that caregivers may observe changes in the cognition of PLHIV whilst undertaking these roles. The expanded scoping review was intentionally broad and included all relevant publications relating to caregiving and HIV over the period 1980 – 2018. Results are qualitatively synthesized within the broader framing of the expanded search questions.

2.4 CAREGIVERS: WHO ARE THEY?
2.4.1 Informal caregivers
Because of the key populations involved, individual’s traditionally providing care and support to PLHIV have come not only from traditional family and partner networks,
but also from peer social networks and professional caregivers (Bor, Miller, & Goldman, 1993).

The impact of providing care can have significant effects on the physical and mental health of both the caregiver and the person they care for (Robles & Kiecolt-Glaser, 2003). Professional caregivers can identify informal caregivers at risk of declining health such as depression (Arai, Kumamoto, Mizuno, & Washio, 2014; Arai & Zarit, 2014; Fauth, Femia, & Zarit, 2016) and can help informal caregivers improve health and well-being by promoting self-efficacy and goal setting to focus on the caregivers own needs (Chenoweth et al., 2016; Nogales-Gonzalez, Romero-Moreno, Losada, Márquez-González, & Zarit, 2015). Prachakul and Grant (2003) reviewed the categories of caregivers of PLHIV and found these were variously described as family members (Brown & Powell–Cope, 1991), significant others, or friends and volunteers (Reynolds & Alonzo, 1998; Stajduhar & Davies, 1998). For PLHIV, the traditional definition of family can be broad, as some may not have support from traditional family members. A broad definition of family is offered by Levine (1990 p36):

“...family members are individuals who by birth, adoption, marriage or declared commitment share deep, personal connections and are mutually entitled to receive and obligated to provide support of various kinds to the extent possible, especially in times of need.”

2.4.2 Peer supports

Peer support within a health context is the provision of emotional and informational assistance by a member of the social network who has similar characteristics to the person being supported, and who has practical knowledge of specific behaviours or stressors (Dennis, 2003). Traditional support relationships for PLHIV may be
compromised for a range of reasons including being estranged from their family due to non-acceptance of lifestyle choices, or religious and cultural beliefs. In the absence of support from family members, caring networks generally expand to include lovers, life partners, friends, and volunteers from peer communities such as the LGBTI community (Ama, 2011). The LGBTI communities mobilised early in the HIV epidemic to care for PLHIV when they did not have support from traditional families (Turner & Catania, 1997). Due to ongoing discrimination related to sexual orientation or gender identity, LGBTI communities still provide much of the support for PLHIV, as these communities were disproportionately affected by HIV/AIDS (Barrett, Crameri, Lambourne, Latham & Whyte, 2015). Care provided by friends belonging to LGBTI communities is under-recognised, as is the fact that these friends may experience similar stress and depression to partners and spouses (Shiu, Muraco, & Fredriksen-Goldsen, 2016).

Homosexual and bisexual men are over-represented as caregivers for their HIV-positive peers (Turner, Catania & Gagnon, 1994). In one study of 125 caregivers of PLHIV, McCann and Wadsworth (1992) found that 77% (96) of caregivers were male and of these, 28% (21) had a health problem themselves. As such, male partners in particular may experience alienation and stigma, leading to increased depression and social isolation (Prachakul & Grant 2003; Pirraglia, 2005). While exact proportions are not given, this conclusion is supported by Munro and Edward (2008) who reported that of the twelve men in their study, some identified social isolation firstly from being homosexual, and secondly from caring for someone with HIV. As there are limited resources and services to support caregiving to PLHIV, Munro and Edward (2008) also suggest that services need to include resources for men who care for men. This is especially relevant currently, as challenges continue for ageing
2.4.3 HIV-positive caregivers

From the beginning of the HIV epidemic, much of the care provided to PLHIV was by those who were also HIV-positive. In a study of 642 caregivers of PLHIV in 1994, Wardlaw found that more than one-third were HIV positive themselves, with 96% (616) having experienced the loss of someone close to them with HIV/AIDS. One-third (211) of the caregivers also reported attending to the safety of the PLHIV because of cognitive or behavioural problems, providing medication support, enteral tube feeding for nutrition support and undertaking their household chores (Wardlaw, 1994).

HIV-positive caregivers have also reported experiencing burden, role overload and depression resulting from feelings of stigma and isolation, and grieving and adjusting to their personal losses (Pirraglia, et al., 2005), including loss of their own health and the loss of close friends (Wight, 2000). Murray et al. (2016) noted that 33% (15/44) of HIV positive caregivers in their study continued to provide support to someone with HAND whilst they themselves may be at risk of developing HAND or other medical conditions.

2.4.4 Professional caregivers

In addition, or as an alternative to traditional caregiving supports, PLHIV may rely on professional caregivers. Professional caregivers are those in paid employment who provide health care and other services to PLHIV. Nurses, for example, are well placed
to provide emotional and psychological support to PLHIV and their significant others (Firn & Norman, 1995; Govoni, 1988).

A model of care broadly relates to the provision of health services that incorporate the best evidence to provide patient-centred care (Cretin, Shortell & Keeler, 2004; Cripps et al., 1994). Current models of care for PLHIV are largely interdisciplinary and are mostly delivered in the community. An interdisciplinary approach involves professionals of different disciplines working collaboratively with a common purpose to plan care, whereas a multidisciplinary approach involves team members working independently to create discipline specific care plans with the person (Department of Human Services, 2008). Community health care services provided to PLHIV in the home setting often include case management and coordination of services (Cummins, 2014; Terpstra et al., 2018).

### 2.4.5 HIV Community Teams

To reflect the evolving needs of PLHIV in Sydney, NSW, HIV specialist community based services were established by the Central Sydney Area Health Service in 1996 and the South Eastern and Illawarra Area Health Service in 2007 (Chapter 1). Utilising a holistic model of person-centred care, these expert services continue to provide both discipline-specific clinical care and case management in partnership with PLHIV. For the purpose of this thesis, these services will be referred to throughout as *HIV community teams*.

HIV community teams use both interdisciplinary and multidisciplinary approaches. The teams consist of members from several disciplines, including primary health nurses, mental health nurses, social workers, physiotherapists, dietitians and
occupational therapists who provide a range of expertise and experience to address the needs of the PLHIV and improve their health outcomes.

The key features driving the philosophy of HIV community teams are an understanding of stigma and discrimination, cultural competence, and acceptance of diversity. The team aims to maintain a culture that promotes an environment without stigma for PLHIV and advocates for services on behalf of patients (Ojikutu et al., 2014). Members of HIV community teams are generally trained in cultural competence and aim to understand the needs of people from diverse backgrounds. HIV community teams also aim to provide services to vulnerable and hard to reach populations such as the homeless and those with mental health conditions.

2.5 CAREGIVERS: WHAT CARE DO THEY GIVE?

The Australian National HIV Strategy, released in 2010, highlighted that those PLHIV who have cognitive impairment were at greater risk of loss to follow up, disease progression and the potential for onward HIV transmission. This population is more likely to have higher support needs (Commonwealth Department of Health and Ageing, 2010), ranging through clinical, social and psychosocial care (Health Resources and Human Administration, 2014), with evolving and increasingly complex co-morbidities (Chu & Selwyn, 2011; Rodriguez-Penny et al., 2013). Maintaining access and engagement with all health services, and retaining consistent care, are crucial to maintaining health goals for PLHIV (Flores, Leblac, & Barroso, 2016).

Professional caregivers must remain responsive to the changing clinical, psychological and social needs of the person – offering a flexible and partnering
approach to care, reflecting the diversity of the person and their needs (Bainbridge, McCahman, Clifford & Tsey, 2015). Informal caregivers also have an important role to play in what has been described by O’Brien and Feeney (2018) as highly complex care. O’Brien and Feeney (2018 p18) refer to the different types of complexity related to caring for PLHIV as incorporating:

“...any set of co-occurring and interrelated medical conditions of varying severity and chronicity (medical complexity); compounded by ageing, frailty and socio-economic factors, as well as cultural, environmental and behavioural issues (situational complexity); together with systemic factors relating to access, delivery and coordination of health services (systemic complexity).”

2.5.1 Informal caregiver support

Many of the signs and symptoms of HAND are mild and it may be difficult for informal caregivers to know whether such changes are directly attributable to HAND, another health condition, or the subtle consequences of ageing. PLHIV who are experiencing signs and symptoms of HAND can have changes in memory and become forgetful. This may impact their ability to complete daily tasks, remember doctors’ appointments, maintain medication adherence and sustain employment. The psychosocial consequences of HIV infection are also far reaching and emotional support from informal caregivers can have a hugely positive impact on the person’s quality of life.

The main types of support provided by informal caregivers are practical (Ama, 2011), emotional (Kelly, Hartman, Graham, Kallen, & Giodano, 2014) and financial (Ama,
HIV-positive peers, for example, can describe the symptoms of an illness, side effects from treatments, how to manage social issues related to HIV infection (such as stigma and discrimination) and suggest personal strategies to manage situations from their own or shared experience (Dennis, 2003). Each of these contributions can act to increase social connectivity (London, Leblanc & Aneshensel, 1998), improve medication adherence and biologic outcomes (Mitchell, Robinson, Nguyen, & Knowlton, 2015; Uchino, 2004). Whilst providing this ongoing support, informal caregivers may observe changes in cognition and behaviour (Kindersley, 2013), and are therefore well placed to discuss these changes with the PLHIV and support their medical referral and treatment.

**Social and emotional support**

PLHIV generally receive emotional and psychological support from family, friends and volunteers through encouragement, keeping company, counselling and health education (Ama, 2011). Information exchange occurs during casual and social interactions, and living with another person further offers the opportunity to give and receive emotional support on a day-to-day basis (Peterson et al., 2012). Kelly et al. (2014) found that social support was a predictor of adherence to antiretroviral drugs and that higher social support scores were associated with earlier HIV diagnosis and timely access to care.

Due to stigma, discrimination, and lack of education in the early days of the HIV epidemic, many affected individuals became estranged from family or community, with caregiving peer communities largely fulfilling these emotional and social support roles. In a study from 1992, McCann and Wadsworth found that 56% (70) of friends and partners providing emotional support to a PLHIV were doing so alone, and most
of these were close friends of the PLHIV (Friedland, Renwick & McCoil, 1996). A number of peer support social networks were created around this time, including support groups, buddy systems and specialist HIV agencies (Dennis, 2003). These networks become places for socialising and bonding, enhancing wellbeing and esteem by providing an atmosphere of acceptance and self-worth (Peterson et al., 2012). de Souza (2014) found that volunteer peer support workers had a great desire to give back to the community by being role models for other PLHIV. Connecting in this way, peer supports draw on their own emotional pain and personal journey to build empathy for others (Peterson et al., 2012).

**Practical support**

Practical support includes shopping, cleaning, preparing food and cooking (Baker et al., 1998; McCann & Wadsworth 1992; Peterson et al., 2012), providing financial assistance and transportation (Folkman et al., 1994; London et al., 1998). Prior to highly active antiretroviral drugs becoming available in the early to mid-1990s, PLHIV were becoming increasingly unwell and needing intensive care and support. As symptoms worsened, informal caregivers took on more clinical roles such as keeping track of medications, giving injections, bathing, inserting catheters, enteral tube feeding and wound care (Folkman et al., 1994; McCann & Wadsworth 1992). In the late 1990s, a study by London et al. (1998) found that 90% of 642 caregivers to PLHIV in San Francisco and Los Angeles, USA were helping with activities of daily living. Interestingly, these caregivers were younger than others providing support to people with non-HIV related dementia. Further, informal caregivers were also taking care of the practical and personal needs of PLHIV who were dying at home (Folkman et al., 1994; McCann & Wadsworth, 1992). The Metlife report (2010) has more recently found that while members of the LBGTI community continue to provide
company and assistance with household chores, fixing meals, driving and financial support, the need for intimate caring support (such as daily hygiene) is required less frequently due to the overall better health of PLHIV since antiretroviral treatment has become available.

Not only do informal caregivers need to observe PLHIV for opportunistic infections and other health issues, they also need to observe activities of daily living to assess their safety. For example, informal caregivers of PLHIV who had a confirmed diagnosis of AIDS dementia complex stated that they needed to be extra vigilant, as PLHIV often put themselves at risk by forgetting things, not being able to drive safely, getting lost and burning food (Meadows et al., 1999). This need for constant vigilance may contribute to the social isolation of informal caregivers who may also be dealing with their own health issues, and the stigma associated with caring for a person with HIV, all while struggling to manage various appointments, medical regimens and the possible denial of cognitive decline by the PLHIV themselves (Munro & Edward, 2008).

**Medication management**

PLHIV may experience poor health outcomes secondary to impaired medication adherence (Thames et al., 2011), with symptoms of HAND potentially confounding this problem (Katz et al., 2013). Poor medication adherence has also been associated with an increased risk of antiretroviral drug resistance (Robertson et al., 2007). Informal caregivers have an important role in assisting PLHIV to maintain their health through medication management (Kelly et al., 2014). This includes supporting attendance at medical appointments (Baker et al., 1998; McCann & Wadsworth, 1992; Munro & Edward, 2008; Wacharasin & Homchampa, 2008), collecting
medications from a pharmacy or health service (Ama, 2011; Baker et al., 1998; Munro & Edward, 2008) and offering general medication adherence support (Baker et al., 1998; Miller, Bishop, Herman & Stein, 2007; Wacharasin & Homchampa, 2008).

The support of informal caregivers in the ongoing monitoring of medication has also been shown to have a positive effect on HIV viral load (Denison, Mitchell, Maragh-Bass & Knowlton, 2017). Maintaining adherence to medications maintains viral suppression and immune function, leading to a positive impact on current and future health (Kelly et al., 2014). Additionally, peer supports can facilitate the development of coping and decision making skills for medication management, as peers may have their own personal experiences and solutions to contribute (Peterson et al., 2012). ‘Buddies’ or peers assigned to support those who are newly diagnosed with HIV, can provide important early support to empower personal growth and decision-making about health choices and future care (Peterson et al., 2012).

**Support for lifestyle changes**

As previously noted, HIV is now regarded as a chronic illness (Deeks et al., 2013), and PLHIV may develop other age-related health conditions as they age (Berg, Michelson & Safren, 2007). Informal caregivers can therefore support PLHIV by promoting health and health related education (Ama, 2011), including safe sex education and personal relationship advice (Baker et al., 1998). They can encourage healthy lifestyle modifications to diet and exercise, and reduction of harms such as substance misuse, alcohol intake and smoking (Wacharasin & Homchampa, 2008). London et al. (1998) found that informal caregivers may also act as unofficial case managers, engaging and coordinating community services for the PLHIV. Informal
caregivers may also contribute by promoting self-care and independence with PLHIV (Boehmer et al., 2014; Clark et al., 2017).

2.5.2 Professional caregiver support

The needs of ageing PLHIV differ from those of the general ageing population (Foebel et al., 2016) and HIV community teams are aware that PLHIV have additional biomedical complexities related to their HIV infection and treatments (Cahill & Valadez, 2013). Combining the expert skills of a range of disciplines, HIV community teams provide clinical care, education and health promotion (Chu & Selwyn, 2011), and through a case management role, develop person-centred care plans for the management of chronic disease and ageing. Their knowledge of HIV also provides an opportunity to work with non-HIV providers and to advocate on behalf of PLHIV when required (Chu & Selwyn, 2011).

HIV community teams promote and equip PLHIV with skills to augment their self-care, and to sustain treatment regimens and health goals. To achieve these goals in partnership with the PLHIV, HIV community teams offer varied clinical services and care in the home, clinic or other setting chosen by the PLHIV (e.g. coffee shop or park for privacy reasons). Clinical care may include medication management (including organising prescriptions, medication packs, pharmacy collection, medication adherence and monitoring side effects); primary and sexual health assessment and monitoring; mental health assessment and monitoring; drug and alcohol assessment; access to dental health care; counselling and welfare support with housing and other agencies; dietetic support and nutritional advice; shopping advice and cooking classes. Physiotherapists offer individual exercise programs, group classes such as hydrotherapy and physiological support for injuries. Occupational
therapists assist with assessing the home for modifications to improve the person’s ability to live independently, set and achieve their goals for activities of daily living, energy conservation and vocational advice.

The ineffective navigation of health systems contributes to inadequate or uncoordinated care and has the potential for disengagement with care (Allen, 2014). Health professionals working within HIV community teams understand their roles and responsibilities with clear objectives to provide holistic care in partnership with the PLHIV. Whilst respecting the individual’s experience and autonomy, team members share responsibilities and promote role interdependence while recognizing of their own knowledge and expertise. The extensive communications, networking and advocating functions of the HIV community teams may enhance linkage to care and have shown potential in decreasing emergency department and hospital admissions and increases in primary health visits (Allen, 2014).

**Case management**

The standard goals of case management are that PLHIV are involved in all aspects of their care. The designated case manager develops relationships and agreements among care partners and maintains optimal communication between all involved to achieve a coordinated approach to achieving these goals in an agreed timeframe (Wagner, Sandhu, Coleman, Phillips, & Sugarman, 2014). The Case Management Society of America (CMSA, 2016 p11) defines case management as:

“…a collaborative process of assessment, planning, facilitation, care coordination, evaluation and advocacy for options and services to meet an individual’s and family’s comprehensive health needs
Crock et al. (2017) note that PLHIV are concerned about maintaining future independent living. The need for case management is therefore more likely to arise as PLHIV age and become more dependent on support to remain living independently in the community (Brennan-Ing et al., 2016). Following a diagnosis of HAND, a case manager will develop and implement a comprehensive care plan, working with the multidisciplinary team, such as family doctor, outpatient clinic staff, inpatient services, allied health, nursing staff and other informal supports (Johansson & Harkey, 2014) to help PLHIV achieve their independent living goals.

There is evidence to suggest that when a person is positively engaged with case management, their uptake of other services required to maintain health (such as social supports and medication management) are also positively influenced (New York City Department of Health, 2010). Positive experiences with case management have also been found to influence the therapeutic relationship between professional caregivers and people living with chronic conditions (Wagner et al., 2001). Regular case conferences in a case management model could improve knowledge of signs and symptoms and declining health of the individual due to additional co-morbid conditions (Agar et al, 2017). The collaborative partnership between PLHIV and their HIV community team offers opportunity for professional caregivers to detect any changes in cognitive behavior, and initiate assessment of neurocognitive impairment if indicated. This is especially pertinent if the PLHIV does not have the support of an informal caregiver who may normally notice such changes. As part of the interdisciplinary team, HIV case managers assist PLHIV to access and maintain
engagement with health services (Cahill, Mayer & Boswell, 2015; Mugavero, Amico, Horn, & Thompson, 2013) whilst promoting support for self-care (Gardner et al., 2005).

As noted in Chapter One, a goal of the NSW HIV Strategy 2012-2015 was that specialist HIV community health care services would provide support for PLHIV with complex care needs requiring enhanced care through case management, with an increased focus on managing co-morbidities. HIV community teams achieved this by working closely with mainstream services to meet future health needs; by developing focused care plans and; through monitoring changes in health such as assessing for the development of HAND.

2.6 FACTORS INFLUENCING INFORMAL CAREGIVER SUPPORT

The psychosocial impacts of HIV infection are complex and multifactorial prompting many reasons why those with HIV infection may not have the assistance of an informal caregiver. Even with informal support, the informal caregiver may not actually reside with the PLHIV, potentially further limiting their opportunities for close observation and care (Schnall, Hirshfield, Liu, Siegal, & Gradilla, 2017).

2.6.1 Stigma and discrimination

Fear of stigma and discrimination are major reasons why PLHIV do not disclose their HIV status to family, friends or society. HIV/AIDS related stigma and discrimination refers to the prejudice, negative attitudes and possible maltreatment directed towards PLHIV. The World Health Organisation (2008) cites fear of stigma and discrimination as the main reason why people are reluctant to be tested, to disclose their HIV status, or to take antiretroviral drugs to treat HIV. The consequences of
stigma include being shunned by your family, friends and wider community, poor access to health care and treatments, erosion of human rights and psychological damage (WHO, 2008).

Factors contributing to stigma include the notion that HIV infection is the result of diminished personal responsibility. Certain religious or moral beliefs may lead some to believe that the person deserves to be punished because being infected with HIV is the result of moral fault (Canavan, 2007). Further, stigma and discrimination may result from incorrect assumptions and judgements about homosexuality, substance use, commercial sex work, and promiscuity (Canavan, 2007; Ryan, Huebner, Diaz, & Sanchez, 2009).

2.6.2 HIV positive status

Although much has changed regarding the knowledge, understanding and acceptance of HIV across the globe, stigma and discrimination continue to concern people who are diagnosed with HIV. Disclosure of HIV status is a paramount concern for PLHIV and the fear of personal rejection may be high. In an early study, Crystal & Jackson (1989) found that 31% of 77 gay men diagnosed with HIV had been rejected by at least one family member; 38% (29) were abandoned by friends and; 11% (8) had lost their housing. A global study of 2035 PLHIV by Nachega et al. (2012) further illustrated that 79% (1607) of this sample feared social discrimination following disclosure of their HIV status, with 35% (712) being worried about losing their family and friends if they disclosed their status. In this study, 17% (345) reported being in a long-term sexual relationship where they had not disclosed their status to their partner.
Although families play an important role in caring for someone with HIV, not all family responses are supportive. PLHIV can experience stigma and discrimination within their home, experiencing social avoidance, or being told to conceal their HIV status (Nachega et al., 2012). Research by the International Centre for Research on Women (2006) reported that some of the consequences of HIV-related stigma among women were loss of income/livelihood, loss of marriage options, withdrawal of care giving in the home, loss of reputation and poor care within the health sector. In Australia, medical professionals continue to make judgments about the lifestyle choices of HIV positive women when they disclose their HIV status (Parr, Burkitt & Jennings, 2012). Additionally, HIV positive women may be responsible for the care of children at home, adding further complexity to accessing caregiving support for themselves (Cummins & Millar, 2004; Decarlo & Folkman, 1997) and continuing with normal daily routine even when feeling unwell (Songwathana, 2001).

In another study of 63 PLHIV, Schrimshaw & Siegel (2003) found that many participants in their study (exact numbers were not given) thought disclosure of their HIV status would be a barrier to accepting care from family and friends and also feared casual transmission of HIV to their informal caregivers. Wacharasin & Homchampa (2008) further reported that PLHIV and their family members did not want to disclose HIV status for fear of rejection, discrimination, disgust and impact on their career, including expulsion from work. In the climate of sexual negotiation, stigma about revealing HIV status clearly continues to be a major issue.

A report prepared by Parr, Burkitt and Jennings (2009) for the Australian Federation of AIDS Organisations and the National Association of People with HIV Australia, concluded that PLHIV experienced high levels of stigma with negative attitudes remaining
unchanged over the last twenty years. This study reported the results of the attitudes approximately 90 gay men. While exact numbers were not given, the study reported findings from eight focus groups with 6 to 8 participants; 14 in-depth interviews with HIV-negative men older than 35 years; and a focus group with four HIV-negative men under the age of 35 years. The study found that younger participants had little personal experience of knowing anyone with HIV and were often explicitly negative and prejudiced when discussing PLHIV (Parr, et al., 2009). Younger respondents articulated an “us and them” attitude; often refusing to openly engage with HIV positive men via the internet; associating HIV positive men as belonging to a different “club”; identifying HIV positive men as “unclean”; and likening sexual interactions with them as equivalent to playing “Russian roulette” and “poison” (Parr, Burkitt & Jennings, 2012). The report further identified that as the internet is now a more common place to meet a sexual partner than at a “gay venue”, asking questions such as “are you clean?” are commonplace on these sites. Therefore, HIV positive persons are likely to continue to experience feelings of shame and poor self-esteem into the future (Parr et al., 2009).

### 2.6.3 Culturally and linguistically diverse communities

In Australia in 2016, 21% (209/1013) of new HIV diagnoses were attributed to heterosexual contact. According to the United Nations, 17% (35) were in people born in a HIV high-prevalence country and a further 17% (35) were in people who reported heterosexual contact with a person from a HIV high-prevalence country (Kirby Institute, 2017). Between 2012 and 2016, the proportion of people with a late HIV diagnosis was higher in people born in Central America (45%), sub-Saharan Africa (43%) and Southeast Asia (43%); with the HIV risk exposure higher for heterosexual sex (47%) than for male-to-male sex (37%) (Kirby Institute, 2017).
Australia is a multicultural society that experiences a range of cultural and religious views towards HIV and/or homosexuality. The Culturally and Linguistically Diverse (CaLD) Periodic Review (2009) noted that among CaLD communities HIV related stigma is a key factor connected to late HIV diagnoses (Asante & Körner, 2011). Of 286 HIV positive people from CaLD communities included in this review, late HIV diagnoses had impacted on the ability of the person to disclose their homosexuality to family or friends, and further impacted access to treatment and health services (Asante, Körner, McMahon, Sabri, & Kippax, 2009). For nearly 61% (174) of the 286 respondents in this study, the shame of a positive result was a major concern and 43% (122) also thought that PLHIV bring shame to themselves and their families (Asante et al., 2009).

People from CaLD backgrounds may also be less likely to identify and nominate informal caregivers. In a study of 126 HIV positive participants from three clinical sites, Murray et al. (2016), noted that only 36% (45) identified an informal caregiver that could be contacted as part of the study. For the 64% (81) who did not identify an informal caregiver, reasons included not wanting to bring up their HIV status, or sexual or drug related behaviours attributed to transmission of HIV, and this was particularly the case for those from CaLD backgrounds (Murray et al., 2016).

2.6.4 Sexual orientation

For many people, disclosing their HIV status also means disclosing their homosexuality (Altman et al., 2012). Homosexuality remains misunderstood, feared and discriminated against, even though globally, heterosexual transmission of HIV is higher than homosexual transmission (Altman et al., 2012). Ryan et al. (2009) found
that a higher rate of rejection by family members was significantly related to poorer health outcomes in young homosexual, lesbian and bisexual adults. In this study of 224 participants, those who felt rejected because of their sexual orientation were 8.4 times more likely to report attempted suicide, 5.9 times more likely to report higher levels of depression, 3.4 times more likely to use illegal substances and, 3.4 times more likely to report having engaged in risky sexual activity such as unprotected sex (Ryan et al., 2009).

Human rights abuses related to sexual orientation are major social determinants of vulnerability to exposure to HIV (Beyrer et al., 2012). Individuals from the LGBTI community are subject to criminalisation for their sexual orientation in over 80 countries and homosexuality is punishable by death in others (Altman et al., 2012). The LGBTI community continue to face stigma, discrimination in housing, employment, education, health care and family life, despite legal protections (Altman et al., 2012). Thirty-eight countries in Africa criminalise same sex relationships with punishment ranging from imprisonment to death, with some also being the victims of blackmail and extortion (Pew Research Centre, 2013). Homosexuality is still framed by codes of silence and secrecy in many countries, preventing disclosure and discourse, because to speak about such things is socially unacceptable (Altman et al., 2012).

The Pew Research Centre is a not for profit organization which informs society about global issues, attitudes and trends. In the Pew Global Attitudes Report (2013), 37,653 representatives from 39 countries were asked whether homosexuality should be accepted. Many countries voted against acceptance (e.g. Nigeria 98%, Egypt 95%, Indonesia 93%, and Malaysia 80%). There is also known to be a strong relationship
between the acceptance of homosexuality and religion, but this is likely a generalisation, for example, while Brazil is a country largely regarded as accepting of homosexuals and transgender individuals, there are still frequent reports of murder among these groups due to their sexuality (Pew Research Centre, 2013).

2.6.5 Ageing

Large observational studies and results from a recent study of national registry data suggest that life expectancy for PLHIV who are receiving effective treatment in high income countries such as Australia has almost normalised to that of the population average (Marcus et al., 2016; Siddiqi, Hall, Hu, Song, 2016). More than 50% of the 25,000 PLHIV in Australia are estimated to be over 50 years of age (Murray, McDonald & Law, 2009), with the proportion of those over 55 years predicted to increase from 25.3% of all PLHIV in 2010 to 44.2% in 2020 (ACON, 2017). Moreover, the number of HIV positive gay men over 60 years of age has been increasing by 12% per year since 1995 (Jansson & Wilson 2012; Murray et al., 2009).

The National LGBTI Ageing and Aged Care Strategy (2012), recognises that “Older LGBTI Australians have lived through a time in the nation’s history when they suffered stigma, discrimination, criminalisation, family rejection and social isolation” (Department of Health and Ageing 2012, p. 4). Older persons who identify as part of the LGBTI community still rely on close peers to provide informal care and Fredriksen-Goldsen et al. (2011) have noted that of 2560 in their study, 54% (1382) were receiving care from a partner and 24% (614) from a friend. Having survived partners, friends and peers who may have succumbed in the early days of the HIV epidemic, facing increasing geographic mobility whereby support from friends or family is at a distance (Musheke, Bond & Merten, 2013), and the parallel ageing of
social networks and informal supports, PLHIV are experiencing increasingly diminishing support networks. Paddick et al. (2017) found that living alone was a predictor of HAND, therefore, ongoing engagement with HIV specialist community teams may be able to fulfil some of the roles of absent informal caregivers, including the monitoring of behavioural or cognitive change and awareness of the social circumstances of PLHIV who are increasingly becoming more isolated (Emlet, 2006).

2.7 GAPS IN KNOWLEDGE

This chapter has aimed to illustrate the significance of support provided by both informal and professional caregivers to PLHIV. There is a paucity of research pertaining specifically to caregiving in the context of HIV positive individuals diagnosed with cognitive impairment, both before and after introduction of the Frascati Classification Criteria in 2007 (Cripps et al., 1994; Cummins, 2014; Flaskerud & Lee, 2001; Hilton, 1989; Hopcroft et al., 2013; Kelly, 2010; Meadows et al., 1999; Morgan et al., 1988; Morrow et al., 1997; Murray et al., 2016; Stajduhar, 1997; Terpstra et al., 2018). However, a range of other background literature was able to offer further information about ‘who’ formal and informal caregivers might be and ‘what’ they contribute to the care of PLHIV more generally.

Early in the HIV epidemic (pre-Frascati), the signs and symptoms of neurological involvement were acute, and early studies of PLHIV related to the social context of the HIV epidemic: families dealing with HIV, disclosure of homosexuality, end of life care, informal caregivers quality of life, burden and fear of disclosure (Baker et al., 1998), caregivers health (Flaskerud & Lee, 2001; Raveis & Seigel, 1990) and, grief and loss (Brown & Powell-Cope, 1993; Folkman et al., 1994). Literature regarding
the experience of professional caregivers at the time related to stress, burnout (Barbour, 1994; Macks & Abrams, 1992; Nesbitt et al., 1996) and working with young PLHIV that were dying (Barbour, 1994).

By the time the Frascati Classification Criteria had been revised (Antinori et al., 2007), many PLHIV were experiencing milder signs and symptoms due to antiretroviral treatments but there continued to be limited published research on the experience of PLHIV and their informal caregivers regarding HAND, how they recognise signs and symptoms of HAND, and how or where they discuss their concerns with others. There is also very limited information published about professional caregiving for PLHIV with a diagnosis of HAND in the community, or how health professionals can identify PLHIV at risk of developing HAND. In the post-Frascati era, much of the published literature has pertained to the prevalence of HAND (Heaton et al., 2010; Heaton et al., 2011; Skinner et al., 2009); predictors of HAND (Antinori et al., 2007; Bhaskaran et al., 2008; Ellis et al., 2011; Fiala et al., 2005; Heaton et al., 2011; Letendre et al., 2011; Schouten et al., 2012); screening tests (Antinori et al., 2007; Valcour et al., 2011); and the treatment of HAND (Cysique et al., 2009; Heaton et al., 2010; Letendre et al., 2008; Tozzi et al., 1999; Tozzi et al., 2007). However, the significance of caregivers in this thesis, is their potential to be able to recognise early cognitive changes in PLHIV.

2.8 CONCLUSION

The experience of cognitive impairment has changed for PLHIV over time, with mild cognitive signs and symptoms possibly attributed to a range of other medical conditions, or morbidity associated with ageing, rather than consideration of HAND. In the past, PLHIV had regular and intensive health monitoring. With improved HIV
treatments, and if medically stable, PLHIV possibly only access their prescribing doctor every four to six months. Their health could significantly change between visits and further, PLHIV may be fearful of discussing their concerns about what they are experiencing with their doctor or others. For those who live alone without informal caregivers, failure to recognise cognitive decline may also significantly delay seeking medical review. HAND is a potentially treatable condition (Skinner et al., 2009), as such, early investigation and diagnosis can impact the overall health and wellbeing of PLHIV.

For those PLHIV who do not have the support of an informal caregiver, a professional caregiver based in the community may fulfil the role of an alternative caregiver, being well placed to observe cognitive and behavioural changes whilst providing care in the home environment. Furthermore, their knowledge of the past and current health history of the PLHIV can facilitate the early identification of HAND. Early screening could lead to investigation and treatment, not only improving clinical outcomes but having a positive effect on the type and timeliness of health and service interventions, and potentially preventing or reducing the need for hospital admission. Additionally, professional caregivers can assist ageing PLHIV with strategies to reduce the development of co-morbid conditions that may impact cognition, such as cardiovascular disease and diabetes.

The initial and broader scoping review has determined why PLHIV may not have caregivers, who their caregivers may be, and has identified the main supports caregivers provide. As the population of PLHIV age, the uncertainty of maintaining good health and the possibility of future ill health due to co-morbid conditions is concerning. Those PLHIV in same sex relationships may become increasingly
socially isolated without traditional supports, and a diagnosis of HAND within the relationship may impact the ability of partners to provide care for each other. Despite minimal quality evidence on the role of caregivers in recognising HAND in PLHIV, this review of published literature over the past 38 years (1980 – 2018) has shown that both informal and professional caregivers do provide practical and emotional support to PLHIV and are therefore well placed to notice mild signs and symptoms and support the early diagnosis of HAND.

However, it remains largely unknown whether PLHIV themselves, or their informal and professional caregivers, are aware of the signs and symptoms of HAND, or whether they have discussed early identification and diagnosis of HAND with others, including health professionals. In support of the early diagnosis of HAND, it is also unknown whether professional caregivers are collecting appropriate and timely medical and social information to identify which PLHIV may be at risk of developing HAND. Therefore, an additional outcome of this review was a decision to conduct a preliminary pilot study to address these gaps in the literature by firstly examining the personal experiences of PLHIV and their informal and professional caregivers to determine whether they encounter and recognise signs and symptoms of HAND. It is anticipated that findings from this and other studies undertaken for this thesis will enhance awareness of HAND for PLHIV and their informal and professional caregivers and will inform interventions for community based health professionals to identify who is at risk of HAND so that referrals can be arranged for early medical review. This is especially significant for those PLHIV who live alone and do not have the support of an informal caregiver who would normally observe changes in cognition, behaviour or the person’s environment. Additionally, for those PLHIV who
live together as a couple and both are HIV positive, both may be at risk of developing HAND and may need additional support from professional caregivers.

This chapter has outlined the results of an initial review of literature relating to the carers of PLHIV who are experiencing cognitive change. The initial review revealed an extremely limited evidence-base and therefore, an expanded review was undertaken to capture a broader scope of literature pertaining to who caregivers are for PLHIV; what types of supports they provide and reasons why PLHIV may not have the support of an informal caregiver. Both informal and professional caregivers are able to observe for signs and symptoms of cognitive change that may be indicative of HAND and their support and confidence to contribute information may lead to the early identification of HAND. Chapter Three discusses the mixed method approach to studies reported in this thesis to illicit knowledge about the identification of HAND in the context of PLHIV, their caregivers and community health care professionals.
CHAPTER THREE

Methodology and methods

Background

This chapter offers an overview of the thesis aim and objectives, and explains the methodological approach chosen to explore the research questions. The relationship between the aim, methodology, development of research questions and subsequent design of studies is described, with the study results contained as published works within this thesis (Chapters 4 – 7). A preliminary exploratory study was conducted to inform and refine research questions for three subsequent study phases utilising a mixed method sequential design. The preliminary study, Phase 1 and Phase 2 used a quantitative method, and Phase 3 a modified Delphi design.

3.1 INTRODUCTION

The candidate has worked with PLHIV in Sydney, Australia for the past 25 years. Anecdotal conversations with HIV positive patients and their informal caregivers over this time had indicated concern about cognitive changes and confusion as to whether symptoms were related to HIV or to other issues such as morbidity associated with ageing. Some individuals had expressed apprehension about the effects of HIV infection on the brain. Others reported that discussion with their medical doctor had elicited an unsatisfactory response, resulting in PLHIV feeling their concerns were not being heard or were not valid. Poor documentation of the signs and symptoms of cognitive change were also evident. This, and limited available literature specifically addressing these experiences collectively led to developing the overarching aim of
this thesis which was: to explore the complexity of this phenomenon by investigating whether the early detection and diagnosis of HAND could be facilitated by PLHIV, and/or their informal and professional caregivers from their knowledge and experience of signs and symptoms of cognitive changes.

Chapter Two has shown that since revision of the American Academy of Neurology nomenclature for HIV related cognitive impairment in 2007 (the Frascati Classification Criteria), there has been little published about the experiences of cognitive decline among informal and professional caregivers of PLHIV, or among PLHIV at risk of or living with HAND. The approach to this thesis therefore needed to be both exploratory and descriptive. To gain more insight into this largely unknown and possibly complex phenomenon, a pragmatic approach was taken to the design of an explanatory sequential study with three phases. Sequential designs transpire when one phase of data collection occurs before the next (Fetters, Curry, & Creswell, 2013; Ivankova, Creswell, & Stick, 2006) and the intent of explanatory studies is to use the results of one or more studies to help explain the results of others (Creswell & Plano Clark, 2011). Research questions relating to the aims and objectives of the study were further refined following an initial pilot study, and after each study phase and are presented in Table 3.1 and Figure 3.1 below.

The preliminary pilot study was designed to discover whether PLHIV receiving health care at three different clinics were experiencing signs and symptoms that could be related to HAND, and whether their informal caregivers had noticed and were able to offer further evidence of this by asking a broad initial research question “Can people living with HIV and their informal caregivers identify HAND?”. Following the results of the preliminary study, four further research questions were designed to specifically
ascertain the experience of PLHIV related to HAND. An online survey was conducted as the Phase 1 study, to explore two research questions “Are PLHIV aware of and/or concerned about HIV associated neurocognitive disorder?” and “Are PLHIV experiencing signs and symptoms of cognitive change and/or observing them in others?”.

The results from Phase 1 lead the candidate to further consider the situation of PLHIV who may not have the support of an informal caregiver. This raised a further question of whether HIV community teams were (or could) act as alternate caregivers to identify those PLHIV at risk of HAND in their care. Therefore, a patient file audit was conducted as the Phase 2 study to determine whether HIV community teams were collecting health information that was both sufficiently detailed, accurate and relevant to identifying PLHIV at risk of developing HAND by asking the research question “What information collected by HIV community based teams identifies patients at risk of HAND?”. The results of this Phase 2 study identified a clear need for an appropriate risk assessment process to screen for HAND in PLHIV. The Phase 3 study used a modified Delphi method with a panel of HIV health experts to reach consensus on the content of a risk assessment screening tool to be used in community settings to screen those PLHIV at risk of developing HAND. Phase 3 explored the final research question “What assessment criteria are essential to identify those at risk of HAND in the community?”. This Delphi group also recommended that content be extended to develop an accompanying annual monitoring tool.

3.2 RESEARCH PARADIGM

The philosophical framework chosen for this explanatory sequential study is based on pragmatism. Pragmatism focuses on what succeeds as the truth relating to questions
posed for the research topic (Tashakkori & Teddlie, 2003, p.713). In an attempt to solve practical problems in the real world, pragmatism accepts that there are singular and multiple realities that are open to empirical inquiry (Dewey, 1925; Creswell & Plano Clark, 2007). Pragmatism is ‘real world’ and ‘practice orientated’ and explores practical consequences to inform decisions for action and problem solving (Mackenzie & Knipe, 2006), placing high regard on the reality of human experience in action (Johnson & Onwuegbuzie, 2004). Creswell (2003, p.11) notes that the pragmatic paradigm places “the research problem as central” and applies all approaches in an attempt to understand the phenomenon; that is, to focus on the “here and now” of the research problem. The pragmatic paradigm offers a frame for the researcher to move back and forth between induction and deduction during the inquiry process (Morgan, 2007) to examine and explore evidence that consistently fits with theory and peer agreement to inform practice (Tashakkori & Teddlie, 2009).

Pragmatism is concerned with the interplay between action and knowledge, and with action and change (Goldkuhl, 2012) and aims to solve a problem by unravelling the complexity within a research question (Brannen & Halcomb, 2009). As pragmatic knowledge is constructed from people’s perspectives (Tashakkori, & Teddlie, 2009), mixed methods were chosen, with pragmatism as the underlying philosophical framework building a bridge between the quantitative and qualitative results of each study phase (Leech & Onwuegbuzie, 2009). Data were able to be considered from a multidimensional point of view with each data set informing and enhancing the others (Feilzer, 2009) allowing for a more comprehensive exploration of the experiences of PLHIV, their informal and professional caregivers.
3.3 MIXING METHODS

The concept of mixing qualitative and quantitative research methods was introduced as a means of validating study results around the 1950s (Campbell & Fiske, 1959), and further developed by Webb, Campbell, Schwartz and Sechrest (1966) who are credited with being the first to construct the term ‘triangulation’. A third paradigm emerged with Denzin (1978 p.291) defining mixed methods as “the combination of methodologies in the study of the same phenomenon”. Mixed method approaches are popular in many disciplines including nursing, health sciences and education. Integrated mixed method designs increasingly allow researchers to pursue emerging questions with fieldwork, for example, where qualitative data is used to help clarify the implication of responses to survey questions to better understand the social processes that might produce broad outcome patterns (Driscoll, Appiah-Yeboah, Salib, & Rupert, 2007).

The mixed method approach has the advantage of studying the phenomenon in different parts, examining them in relation to each other, whilst obtaining a holistic view that draws on the strengths of both approaches to explore complexity in the research (Creswell & Plano Clark, 2011). This is an approach to knowledge that endeavours to regard multiple viewpoints and perspectives (Johnson, Onwuegbuzie & Turner 2007; Creswell & Plano Clark, 2011) and allows objectives to be addressed within multiple phases to increase the breadth and depth of understanding of the subject (Johnson et al., 2007). With a more complete picture of the phenomena, findings produce a more superior insight than would be possible using each approach alone (Johnson & Onwuegbuzie, 2004). Polit and Hungler (1999) note that a mixed method approach strives to discover knowledge, insight and understanding by developing generalisations from specific lived experiences. Selected samples should
therefore produce enough data pertaining to the phenomenon to allow a rich description, enabling the researcher to make analytical generalisations to other populations and settings (Onwuegbuzie & Collins, 2007).

An explanatory sequential design using mixed method studies involves multiple phases of data collection whereby the research questions and purpose are determined by the particular sequence (Andrew & Halcomb, 2009). Sequential designs may be either exploratory (wherein qualitative data are collected first and followed by the quantitative element) or explanatory, where quantitative data are collected first and followed by the qualitative element (Creswell & Plano-Clark, 2007). Andrew and Halcomb (2009) suggest that in explanatory designs the weight is usually, but not always, afforded to the quantitative element of the study. Either way, different research strategies produce data from each phase which are analysed and scrutinised in relation to each other to inform and supplement findings (Tashakkori, & Teddlie, 2009). Therefore, the findings from each phase aim to achieve a more comprehensive understanding of the data and allow new questions to be developed (Subedi, 2016). The findings from varied data collection methods (mixed methods) are expected to converge, thereby confirming and increasing the validity of findings (Denzin, 1989).

3.3.1 Rationale for mixed method approach

To date, few studies have explored the personal experiences of PLHIV and their caregivers in relation to recognising the signs and symptoms of HAND. Information and insights from informal caregivers are essential to obtaining a holistic picture of the circumstances of PLHIV and as such, informal caregivers should be included in health consultations (with permission of the PLHIV) when available. Additionally, professional caregivers, acting as alternates to informal caregivers, should be
equipped with accurate information and knowledge to identify those PLHIV who live alone, or are without informal supports, who may be at risk of developing HAND. This information can shape the development of models of care, informed by the views and personal experience of PLHIV and their caregivers, to improve health and social strategies for PLHIV in the community into the future.

Mixed method approaches are useful for examining unexpected results in more detail (Creswell, 2009) and have been adopted for this thesis because so little previously published research is available. Data were collected sequentially, with analysis occurring separately, whilst allowing emerging data to generate questions and methods for the following phases.

3.4 AIM AND OBJECTIVES
The aim of this thesis was to explore the complexities of identifying HAND by people living with HIV, and their informal or formal (professional) caregivers. The three objectives were to:

- Explore whether people living with HIV and their informal caregivers can identify HAND.
- Explore the experience of HAND in people living with HIV.
- Explore whether community based health care professionals can identify HAND.

3.5 RESEARCH QUESTIONS and STUDY PHASES
3.5.1 Preliminary pilot study
Fundamental to the development of this thesis was an understanding of whether PLHIV and their caregivers were aware of HIV-associated cognitive decline. In the
absence of literature on this topic, it could not be assumed that in asking research questions about HAND, people living with HIV and/or their caregivers knew what they were being asked about. The preliminary study therefore acted as pilot to inform the development of four further research questions for the thesis by posing the exploratory question:

Can people living with HIV and their informal caregivers identify HAND?

### 3.5.2 Phase One

The Phase 1 study used an online survey with PLHIV, focusing on their experience HAND to explore the research questions:

1. Are PLHIV aware of and/or concerned about HIV associated neurocognitive disorder?
2. Are PLHIV experiencing signs and symptoms of cognitive change and/or observing them in others?

### 3.5.3 Phase Two

The Phase 2 study used a cross-sectional design to conduct a file audit of patient data collected by interdisciplinary specialist HIV community teams. A descriptive analysis was undertaken to explore the research question:

3. What information collected by HIV community based teams identifies patients at risk of HAND?

### 3.5.4 Phase Three

The Phase 3 study used a Modified Delphi method to answer the final research question:
4. What assessment criteria are essential to identify those at risk of HAND in the community?

The relationship between the thesis objectives, study phases, research questions and methods are outlined in Table 3.1 below. This table also lists the publications relating to the results of the pilot and three study phases, as outlined in Chapters 4 – 7. The detailed methods of each of the studies are in the related publications and are described further below.
### Table 3.1: Relationship between objectives, research questions, study methods and results

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<thead>
<tr>
<th>Objectives</th>
<th>Research Questions</th>
<th>Method</th>
<th>Published study results (Chapters 4 – 7)</th>
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| **Preliminary pilot study**  
Objective 1  
| **Phase 1**  
Objective 2  
Explore the experience of HAND in PLHIV. | 1. Are PLHIV aware of and/or concerned about HAND?  
| **Phase 2**  
Objective 3  
| **Phase 3**  
Objective 3  
3.6 METHODS

The detailed methods of each of the study phases are outlined in the published papers (Chapters 4 – 7) but are summarised below and in Figure 3.1.

3.6.1 Preliminary pilot study: prospective observational study

Anecdotal reports from PLHIV have indicated that discussion on issues relating to HAND are highly dependent on clinician knowledge and experience. The preliminary study was conducted with PLHIV attending outpatient clinics in three different geographic areas of Sydney, Australia. Those consenting to participate in the study were also asked to identify an informal caregiver that could be contacted to participate. Both groups were asked to complete a self-assessment questionnaire (a booklet) that had been previously developed by the candidate and colleague (Trotter and Cummins, 2008) to explore whether clients and caregivers had experienced or had observed any signs and symptoms of cognitive change in themselves or others over the previous 12 months. The questionnaire had 36 items grouped into four categories of behaviours: concentration, memory, motor skills and social issues, as well as information about signs and symptoms which could indicate HAND. The study was conducted from June 2012 to October 2014 to explore the exploratory research question: Can PLHIV and their informal caregivers identify HAND?

The self-assessment questionnaire was completed by 121 PLHIV and 44 informal caregivers. Participants who had self-identified cognitive behaviour changes were contacted within two weeks of receipt of the assessment. At the same time, clinical and risk data from the electronic medical record (eMR) and notes from the participant's medical file were recorded. Initially, participants were asked to discuss
any items identified from their self-assessment with their doctor during the next consultation. It soon became apparent that this discussion was not taking place as participants stated they were either “not remembering” to mention issues to the doctor, “did not think it was important” or there “was not enough time”. The researchers intervened by transcribing the list of items selected by participants and/or their nominated caregiver and placing this list in a prominent place in the clinical notes to prompt discussion at their next appointment.

Participants were able to provide free text in addition to completing the quantitatively designed survey. Informal caregivers provided additional insights and experiences relating to cognitive changes they had observed. As there were no other similar self-reflective clinical assessment tools available at the time, the researchers decided that selection of four or more items of concern would determine the need (clinical indication) for further discussion with a medical practitioner. Therefore, when clinically indicated, patients were referred for neuropsychological testing with results made available to the researchers (as per patient consent). This clinical review process did identify participants at risk, some of whom were subsequently diagnosed with HAND.

The preliminary study revealed that PLHIV and their informal caregivers are able to identify some of the signs and symptoms of HAND and indicated that discussion regarding the signs and symptoms of HAND could lead to an earlier diagnosis in some PLHIV. The quantitative data from this study offered beginning evidence to pose further questions for Phase 1.
3.6.2 Phase One: Online survey

The preliminary study had been conducted with a purposive sample of PLHIV and their informal caregivers but was not designed to answer whether changes in cognition were affecting a wider population of PLHIV. A number of other questions were also raised by the preliminary study such as: Were other PLHIV experiencing or observing signs and symptoms of cognitive change? Had PLHIV heard of the term HAND? Were PLHIV concerned about HAND and were they talking to someone about these concerns? Would resources be useful to enhance communication between PLHIV, their caregivers and doctors so that they can speak confidently and feel safe about raising their concerns?

In order to reach a larger and more diverse group of PLHIV and their informal caregivers, an online survey was collaboratively developed and distributed by a not-for-profit community-based organisation supporting people with HIV called Positive Life New South Wales (PLNSW). Distributed over a three-week period in 2015, the survey contained open and closed-ended questions designed to elicit information on the demographic background of respondents and their awareness and experience of HAND. The survey focused on four signs and symptoms of cognitive change: Being slower in your thinking than you used to be; Being more forgetful than you used to be; Finding it harder to organise things than in the past and; Being able to find pleasure in the things you used to enjoy.

Hosted on the Survey Monkey platform and accessed via the PLNSW website, the survey was also available via the PLNSW Facebook™ and Twitter™ accounts and therefore accessible to individuals living outside of NSW. Respondents could be HIV
positive or HIV negative, as some questions pertained to observing signs and symptoms of neurocognitive decline in others. One hundred and twenty-six respondents with an Australian postcode were included in the final sample (Figure 3.1). As per ethical guidelines, completion of the online survey was considered consent and all responses were anonymous. Participants were advised prior to completion of survey the names of two researchers they could contact if they had any questions or concerns. No participant contacted the researchers.

3.6.3 Phase Two: File audit

The findings from Phase 1 confirmed that a broader sample of PLHIV and their caregivers were likely aware of HAND and were concerned about it. Further, the survey results suggested that cognitive changes related to HAND were being experienced by PLHIV and were possibly being observed by others. The next question was therefore, who fulfils the role of observing changes in daily functioning or cognition when a PLHIV does not have the support of an informal caregiver, especially if the PLHIV has little personal insight into the neurological changes they may be experiencing? In the absence of an informal caregiver, professional caregivers (those who are paid to provide health care and social support) are sometimes the only other group who has regular contact with PLHIV and who may be able to observe for changes in cognitive function over time. The next research question therefore sought to understand what kind of information routinely collected by HIV community-based teams could alert or assist health professionals to identify HAND.

Phase 2 used a file audit method to collect clinical and social information from the medical records of PLHIV who were being cared for by two interdisciplinary HIV
community teams. The file audit was completed over a four-week period using an electronic spreadsheet that had been designed with relevant data labels for community team members to populate. All members returned their spreadsheet to a nominated team leader to collate, ensuring that no personal identifying characteristics remained. Data fields included demographic, social and health information, co-morbid medical conditions and specific pathology results related to clinical indicators pertaining to HAND. Newly referred patients (within the four-week period) who had not been assessed were excluded from the audit. The files of all 262 PLHIV who were currently receiving health services at home from the two HIV community teams were included in the audit (Figure 3.1). Quantitative data from the file audit were then used to build upon the explanatory sequential design, with selection of a modified Delphi method to expose essential items of assessment to identify those at risk of HAND in the community.

### 3.6.4 Phase Three: Modified Delphi Method

The main purpose of the Delphi method is to achieve consensus from a group of experts. Linstone and Turoff (1975 p.3) defined the Delphi method as “a method for structuring a group communication process so that the process is effective in allowing a group of individuals, as a whole, to deal with a complex problem”. Consensus is obtained from experts, termed ‘panel members’ through a series of structured ‘rounds’ that examine the evidence to then reach agreement about a target issue (Keeney, Haason, & McKenna, 2006). There are no universally agreed guidelines for the Delphi method (Evans, 1997), as such, flexibility can exist in the qualitative design which can be dependent on the objectives of the study. In the traditional Delphi method, content for the first round is usually obtained from a literature review
and further rounds enable a number of individuals to provide their opinion anonymously as questionnaires are sent to each individual panellist, thus avoiding dominance of one person’s opinion (Boulkedid, Abdoul, Loustau, Sibony, & Albeti, 2011; Linestone & Turoff, 1975). More recently, a modified Delphi process has been used to introduce a hybrid of techniques to Delphi rounds including face-to-face meetings, use of secondary data, or qualitative interviews with participants (Keeney et al., 2006; Diamond et al., 2014; van Vliet et al., 2016; Eubank et al., 2016).

Similarly, there is no universal approach to the selection of experts for Delphi panels, with choice of members more often related to practical logistics and the subject under investigation. The selection of the panel is important as the quality of expertise has been shown to be directly related to the quality of the results (Judd, 1972). Individuals who are primary stakeholders with first-hand knowledge of the subject area are targeted to elicit their enhanced experience and perspective (Anderson & Schneider, 1993; Jones, 1974). Although many Delphi studies comprise between 15-20 panel members (Ludwig, 1997), it is usually more important that the panel size is able to represent a collective judgement of the target issue (Delbecq, Vande Ven & Gustafson, 1975). Commitment to participate in a multi-round Delphi can be inferred by the round-by-round response rate (Keil, Tiwana & Bush, 2002) which is related to a willingness by panel members to continue and good communication skills (Adler & Ziglio, 1996).

The scoping review had raised a number of items for the Delphi panel to consider for the assessment tool. These included the monitoring of behavioural or cognitive change, and awareness of the social circumstances of PLHIV – who are increasingly
becoming more isolated (Emlet, 2006; McDonald et al., 2013). Other items included risk factors for HAND, including CD4+ T cell nadir count (Ellis et al., 2011; Heaton et al., 2011); low CD4+ cell count (Schouten et al., 2012; Heaton et al., 2011); current or past drug and alcohol use (Letendre, 2011; Elbert et al., 2015) and; hepatitis C co-infection (Schouten et al., 2012). Additional items raised through the literature review included, knowledge of other co-morbid conditions which can confound the diagnosis of HAND (Nightingale et al., 2015; Kamminga, Cysique, Lu, Batchelor, & Brew, 2013) such as diabetes (Pinhero et al., 2016), cerebrovascular disease (Heaton et al., 2011; Tedaldi, Minniti, & Fischer, 2015) and hypertension (Rodriguez-Penny et al., 2013; Tedaldi et al., 2015). Furthermore, anecdotal evidence and professional experience of the clinical experts was considered such as medication, mental health and legal issues.
Figure 3.1: Phased explanatory design and development of research questions (Adapted from Jones & Hunter, 1995)

**PRELIMINARY STUDY**

Can PLHIV and their informal caregivers identify HAND?

**PHASE 1**

1. Are PLHIV aware of and/or concerned about HIV associated neurocognitive disorder?
2. Are PLHIV experiencing signs and symptoms of cognitive change and/or observing them in others?

Survey and file audit: 121 PLHIV, 44 informal caregivers recruited.

**RESULTS**

YES, PLHIV and informal caregivers can identify HAND.

Documentation of medical consultations limited.

**OUTCOME**

The preliminary study was conducted with a small and selected cohort. This led to further exploration of whether cognitive changes were a concern for a wider HIV positive population? Are PLHIV talking to others about their concerns? Do PLHIV feel they are being listened to?

**METHOD**

Online survey: 126 responses.

**RESULTS**

YES PLHIV are concerned about HAND and outcome of discussion with others varied.

YES PLHIV are observing S&S of cognitive change.

**OUTCOME**

Develop resources to facilitate discussion with others. This led to thinking, if the PLHIV does not have support of informal caregiver can a professional caregiver act as alternative to identify those at risk of developing HAND?

**PHASE 2**

3. What information collected by HIV community based teams identifies patients at risk of HAND?

File audit of 2 teams: 262 files reviewed.

**RESULTS**

NO, file audit noted incomplete documentation in every patient file.

**OUTCOME**

This led to thinking would HIV community teams find a risk assessment tool to identify PLHIV at risk of developing HAND useful?

**PHASE 3**

4. What assessment criteria are essential to identify those at risk of HAND in the community?

Modified Delphi Method. Expert panel (n=25) from 4 community health services.

**RESULTS**

YES, > than 80% consensus reached for information initial risk assessment tool and annual monitoring tool.

**OUTCOME**

Flow chart to guide clinicians and an initial risk assessment tool and annual monitoring tool to assess PLHIV for HAND developed.
Requirements for expertise for this Delphi panel included knowledge and experience with PLHIV, HAND and working in a community setting. The candidate purposefully selected experts from community-based services to maximize understanding of the underlying phenomenon. Twenty-five Delphi panel members were selected from four HIV community teams that had direct experience of providing clinical care, support and case management. Three teams were from three different locations within two local area health services in Sydney, Australia. Expert panel members from the fourth service deal with the additional complexity of offering a state-wide service with extended care to people with HAND living in regional and rural areas of NSW. All 25 participants were retained for each of three Delphi rounds (Figure 3.2).

Typically, in the Delphi method, panel members are asked to rate indicators relating to the topic (such as functional and social indicators of decline in cognition in this study) and then the ratings are compiled, summarized and distributed for review before the next round (Davies, Romano, Schmidt, Schultz, Geppert, & McDonald, 2011). Each panel member then makes a judgement to agree or disagree (using a Likert or categorical scale) for the topic under consideration and so, consensus is determined (Jones & Hunter, 1995). Responses from each round are then fed back in summarised form to panel members who are then given an opportunity to respond again to the emerging data (Boulkedid et al., 2011). The modified Delphi method selected for this study enabled panel members to contribute their expertise from a range of perspectives and to reach consensus on what observational and clinical information is important for risk assessment. The first small group meetings with each team received and rated data from the Phase 2 study (Round 1, Figure 3.2) and asked panel members how they would like the next round to take place. Due to time constraints and also to allow robust discussion, each panel member suggested that a large group meeting would be
beneficial in Round 2. At the conclusion of Round 2, the group decided that analysis of this round be distributed via email to each panel member to provide an opportunity for each panel member to independently and anonymously review the final documents (Round 3, Figure 3.2). It was decided by consensus that if there were minimal comments and over 80% consensus had been achieved, a further “round” would be unnecessary.

This ability to participate in decisions about modifications to the Delphi process, and a commitment by panel members to their patients was integral to full retention of all panel members within each round. A qualitative process was followed to iteratively develop quantitative content from the Phase 2 study which, on the recommendation of the panel of experts, would form the basis of an initial risk assessment and subsequent annual monitoring tool to be utilised by community based health professionals to assist in their identification of HAND for referral for early medical review.
Figure 3.2: Modified Delphi Method Design

Selection of experts

ROUND 1

ROUND 2

ROUND 3

Data analysis for consensus

Report results to panel

Inclusion criteria:
- Employed in community setting
- Experience providing care to PLHIV
- Experience providing care to PLHIV with HAND

- Four small group meetings (25 participants in total)
- Identify content for initial risk assessment tool
- Identify content for annual monitoring tool
- Participant score agree/disagree on 5 point Likert Scale

- Large group meeting (25 participants)
- Feedback from Round 1
- Agreement of questions for each tool
- Analysis of Round 2 data

- Redistribution of 2 tools by email to each “expert”
- Panel asked to consider Round 2 information
- Analysis of Round 3 data
3.7 SUMMARY

Techniques or methods of data collection and analysis are key to mixed method research and Creswell and Plano Clark (2007) argue that as research has an underlying worldview or assumption which guides the inquiry, the mixed method approach offers multiple world views. Structured data collection techniques (questionnaires, surveys and a file audit) used in this study led to potential strengths in quantification and reliability. Alternatively, qualitative data from the free text of surveys and from group work within the modified Delphi study brought a richer, more holistic understanding of the experience of HAND from the viewpoints of PLHIV, and their informal and professional caregivers. This is consistent with the use of an explanatory sequential design using mixed method studies in which the quantitative data and subsequent analyses provide a general understanding of the research problem, while the qualitative data and their analyses refine and explain quantitative results in greater depth (Tashakkori & Teddlie, 1998; Creswell & Plano Clarke, 2007; Creswell, 2008). The combination of quantitative and qualitative approaches provides a better understanding of the problem than either approach can achieve alone (Tashakkori & Teddlie, 2003; Creswell & Plano Clark, 2007).

A rigorous yet exploratory approach was needed to deliver the thesis argument. On a background of little or no published data, the aim was to gain a beginning understanding of the complexities of identifying HAND in PLHIV in order to facilitate their early diagnosis. The mixed method approach added strength to the design and a range of methods and tools were used for data collection in order to methodically study the phenomenon and answer research questions which likely could not be answered by designing a single approach.
3.8 CONCLUSION

This chapter has described the underpinning paradigm and design of studies for this thesis. Pragmatism is guided by knowledge to unravel the complexities of the research questions by providing insights and experiences from the multiple realities and viewpoints of PLHIV, and their informal and professional caregivers, to bring about changes in practice. The mixed method approach enabled movement back and forth between data to follow emerging ideas and allowing further exploration of the phenomenon that influenced research question development for each of three study phases. Additionally, in a pragmatic decision to exploit unexpected qualitative data from Phase 1 and free text responses from Phase 2, several themes were revealed that offered new insights to the quantitative data.

The explanatory sequential design chosen for this thesis allowed representation of varied viewpoints on the research topic using data from a preliminary study and three phases to explore the objectives of the study and enrich understanding to provide a more complete picture of the phenomenon from the specific experiences and perspectives of the participants.

The following Chapters (Four to Seven) present the published results of the four studies conducted for this thesis (described as thesis with publication). As shown in Figure 3.1, Chapter Four outlines results from the preliminary study that included a self-assessment survey conducted within a larger prospective observational design. Chapter Five addresses the results from the Phase 1 online survey while Chapter Six presents results from the Phase 2 file audit. Chapter Seven presents results from the modified Delphi Study conducted as Phase 3. Finally, Chapter Eight examines the results of each phase of the study and summarises the significance of the overall findings. Each phase has contributed to the
understanding of PLHIV and their caregiver’s experience of HAND and has identified agreed and specific content for the development of risk assessment screening tools for use by HIV community teams. The implications and suggestions for practice and future research are the focus of the final discussion. The chapter concludes with recommendations arising from the study and a proposal for future research.
CHAPTER FOUR
Identifying HAND

4.1 Overview and research question
PLHIV may be experiencing signs and symptoms of cognitive decline which could be HAND. However, the identification of early signs and symptoms of HAND by PLHIV or their informal caregivers relies on both having an understanding of what HAND is, and the appropriate information to identify it. This chapter presents findings from a prospective observational study incorporating a self-assessment questionnaire. This study was designed to explore initial concepts and ideas through an exploratory research question:

Can PLHIV and their informal caregivers identify HAND?

The preliminary pilot study was designed to give context and direction for this thesis, as minimal published literature could be located relating to the possibilities and complexities of identifying HAND in PLHIV.

4.2 Major findings
A selected sample of PLHIV and their informal caregivers were observing signs and symptoms of cognitive change and can therefore potentially contribute to the diagnosis of HAND. Twenty three of 121 (19%) HIV positive participants from this study were offered further clinical neuropsychological examination following observation of signs and symptoms of HAND, by either themselves or their caregivers. Seventy percent (16) of these 23 participants underwent standard neuropsychological testing as described in Chapter One and four were subsequently diagnosed with HAND as a result of these examinations.
4.3 Conclusion

PLHIV and their caregivers are potentially able to identify early signs and symptoms of cognitive change and are therefore important partners in clinical assessment and future care planning, including contribution to the early diagnosis of HAND.

4.4 Statement from co-authors confirming authorship contribution of the PhD candidate

Chapter Four is published as:


Reprinted with the permission of AJAN.

All authors made substantial contributions to editing and revising the manuscript.

As co-authors of the paper titled: Can patients and their caregivers boost identification of HIV associated neurocognitive disorder (HAND)? we confirm that Denise Cummins made the following contributions:

i. Concept and design of the study;

ii. Collected, managed and analysed the data;

iii. Primarily responsible for the interpretation of results;

iv. Drafting, revising and writing up of the manuscript for submission to peer-reviewed journals.

All authors read and approved the final manuscript.
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In addition to the statement above, as supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

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Title: Can patients and their caregivers boost identification of HIV Associated Neurocognitive Disorder (HAND)?

Abstract

HIV Associated Neurocognitive Disorder (HAND) may be difficult to identify as signs and symptoms (S&S) are nonspecific.

Objective: to ascertain whether people living with HIV and their caregivers using a self reflective tool could identify S&S of HAND.

Design: This study was a nurse led prospective observational multi-site study using a quantitative design.

Setting: Participants were recruited from 3 sites in Sydney Australia: an inner metropolitan HIV clinic, an inner metropolitan sexual health clinic and a suburban hospital HIV clinic.

Subjects: 121 patients and 43 caregivers who attended ambulatory clinics providing HIV care.

Main Outcome Measures: Observing usual standard of care to follow patients who had formal neuropsychological testing and diagnosis of HAND.

Results: Sixty one percent of participants and 57% of caregivers identified more than four symptoms. Sixteen had neuropsychological exams; four were diagnosed with HAND. After changes to their medication regime all of those four showed an improvement in cognition. Of the remaining 11, four results were inconclusive, with some deficits noted.

Conclusion: Patients and caregivers stated the booklet helped them to reflect on behavior changes which they could subsequently discuss with their doctor. The booklet was considered useful to identify S&S of HAND.

KEY WORDS: People living with HIV, HIV associated Neurocognitive Disorder, mild neurocognitive disorder, Caregiver

INTRODUCTION

HIV is treated with medications known as antiretroviral drugs which has had a substantial positive impact on morbidity and mortality for People Living with HIV (PLHIV) and has
resulted in life expectancy approaching population norms for those individuals who have optimal adherence to HIV medications. (Clifford and Ances 2013). Yet, despite HIV virological suppression and immune recovery, studies suggest 30% of PLHIV are affected by HIV associated Neurocognitive Disorder (HAND), (Heaton et al 2010; del Palacio et al 2012; Clifford and Ances 2013) significantly impacting quality of life (Tozzi et al 2004).

In the 1980s, the clinical features of AIDS dementia complex (ADC) were those of a sub-cortical dementia characterised by cognitive impairment, behavioural abnormalities and disturbed motor function. With the introduction of antiretroviral medications, ADC largely disappeared from clinical practice, but now milder forms of cognitive impairment are being observed. In 2007, the classification for ADC was revised, and is now known as HAND. HAND is divided into three categories, each with varying degrees of disability impacting quality of life: Asymptomatic Neurocognitive Impairment (ANI), Mild Neurocognitive Disorder (MND), which causes symptomatic disease, and HIV Associated Dementia (HAD) (Antorini et al 2007). This study focuses on the S&S associated with MND.

MND affects the person’s ability to perform activities of daily living such as preparing meals, managing finances, attending doctors’ appointments and driving. It may also affect their social relationships and the ability to retain employment or be promoted. Caregivers can have a positive effect on the health and well being of PLHIV (Gisslen et al 2011) and may be well placed to notice any changes in the PLHIV. Signs and symptoms of MND may be subtle and are potentially normalised by PLHIV and may be difficult to detect by clinicians. Individuals may start to notice mild memory problems and slowness, difficulties in concentration, planning and multitasking (Grant 2008; Heaton et al 2010; Schouten et al 2011).

A booklet was developed (Trotter and Cummins 2008) The booklet focuses on four key areas that affect cognition (memory, concentration, motor skills and social skills) for patients and
their caregivers to reflect on any changes in cognition. Using the booklet enabled the
caregiver to recognise potential signs and symptoms of MND. It should be noted that some
PLHIV may be socially isolated (McDonald et al 2013) and not have the support of a
caregiver and may have no one they can rely upon who may notice changes in their cognition
including memory, motor function and social behaviour.

There are currently no biological markers for a definitive diagnosis of HAND (Atluri et al
2014). Studies suggest predictors of HAND are: past history of AIDS defining central
nervous system disease (Fabiani et al 2013), other central nervous system disease (Valcour et
al 2004), low CD4 cell count (Schouten et al 2011), drug and alcohol use (Fiala et al 2005),
low education level (Tedaldi et al 2015), and Hepatitis C infection (Schouten et al 2012).

PLHIV with cognitive impairment have been shown to be less adherent to HIV medication
regimes. (Skinner et al 2009; Robertson et al 2010). This may lead to drug resistant HIV,
resulting in their current medication regime becoming ineffective (Skinner et al 2009;
Robertson et al 2010). Morbidity and mortality can then be affected as the person
experiences poor health outcomes secondary to impaired adherence (Thames et al 2011).

If identified and treated early, using aggressive HIV drug treatment or changing the
medication regimen may lead to improvement in previous cognitive changes related to MND
thus improving outcomes for patients (Cysique et al 2009).

In addition as PLHIV age they may be at risk of other neurologic conditions associated with
ageing such as vascular dementia and Alzheimer’s disease (del Palacio et al 2012). Thus the
complexity of neurological health for PLHIV may be on the increase. The prevalence of
MND among Sydney Australia PLHIV is unknown. There is a paucity of literature regarding
PLHIV’s experiences of and reflections on signs and symptoms, which may be predictors of HAND.

METHOD: study design, participants and study period

Aim

To consider the value of patient and caregiver use of a self-assessment booklet in leading to early medical assessment of MND.

Design

A quantitative study from a prospective observational multi-site study to evaluate the usefulness of a patient self-assessment booklet "HIV associated MND: How to recognise signs and symptoms.” (Trotter and Cummins 2008) by PLHIV and their caregivers in recognising any signs and symptoms of cognitive impairment. The study period ran over 28 months from June 2012 to October 2014.

Setting

The study was conducted at three outpatient sites within two Health Districts covering a greater part of Sydney, Australia.

Each site provides HIV specialist care: an inner city hospital based clinic, an inner city sexual health clinic and a suburban hospital based clinic. The inner city clinics are in the inner west of Sydney, which has the second highest number of HIV diagnoses in NSW, Australia. A high proportion of patients seen at these clinics are men having sex with men (NSW HIV Strategy 2012-2015). The suburban hospital HIV clinic is in the outer suburbs of Sydney and cares for a high proportion of participants from culturally and linguistically diverse (CaLD) backgrounds.
Participants

Participants were recruited whilst attending their regular multi-disciplinary consultation reviews at outpatient clinics at one of the three sites. Participants were eligible for inclusion if they were HIV positive over 18 years of age and they provided written consent at time of recruitment. Participants could nominate a caregiver to be invited to participate in the study. For the purpose of this study caregivers were considered unpaid individuals who provide practical, emotional or financial support to the person, such as partners, family members and friends. Initial recruitment was over a 4 month period in 2012.

Individuals were excluded if they were diagnosed with HIV in the last twelve months; had a preexisting identified cognitive impairment; were experiencing current social chaos or had inadequate English language skills. As depression may confound cognitive symptoms (Woods et al, 2009), patients who had current untreated depression were excluded but became eligible once their depression was treated. Current alcohol and substance use was assessed and patients with dysfunctional use were excluded from the study until substance and alcohol use was addressed.

Participants completed a demographic questionnaire and were given the booklet "HIV associated MND: How to recognise signs and symptoms” ( Trotter and Cummins 2008). The self assessment booklet was developed by a HIV Psychiatrist and HIV Clinical Nurse Consultants, informed by literature review and professional experience. It was focus group tested for readability, clarity, design, flow and acceptability. The booklet has 36 items grouped into four categories of behaviours: concentration, memory, motor skills and social issues.

Participants and caregivers were provided with the booklet and were asked to reflect on any changes experienced or observed over the last twelve months. If they noted any change in
behaviour over the previous twelve months we asked them to respond “Yes” to each relevant item. They were contacted two weeks later via telephone to provide responses to items selected from the booklet.

A file audit was attended to ascertain specific risk factors for cognitive impairment including the participants’ HIV viral load, CD4 T cell nadir and current CD4 T cell count. Current medication regimen was noted. The researchers observed the usual standard of care at medical consultations. Initially the researchers asked participants to discuss items identified in the booklet with their doctor during the next consultation. It became apparent that the discussion was not taking place as participants stated that they were either not remembering to mention issues to the doctor, did not think it was important or that there was not enough time. The researchers intervened by transcribing the list of items selected by participant and/or their nominated carer, placing the list in a prominent place in the clinical notes to promote discussion at the next appointment. This resulted in increased discussions of the items selected.

As there was no other PLHIV self-reflective booklet available at the time to use as a guide, the researchers decided selection of 4 or more items would be flagged with medical practitioner for patient discussion. Previously we relied on clinical judgement and incidental anecdotal evidence from PLHIVs to discuss issues relating to HAND.

All neuropsychological testing was conducted by a trained clinical neuropsychologist. This procedure followed the usual required battery of tests required as a neuropsychological exam. The results were made available for the researchers to ascertain which participants completed the exam and final results. The clinical review process of participants diagnosed with MND was observed for changes in treatment prescribed by their doctor and the outcome of the
treatment. Data entry was completed by one member of the team who was not involved in the recruitment process.

STATISTICAL ANALYSES

Data was analysed using SPSS (V21 IBM Corporation Armonk, NY1, USA). Analysis included presentation of descriptive statistics, Chi Square tests, Mann Whitney and Kruskall Wallis tests as indicated.

ETHICS

Ethics submission had been approved by Royal Prince Alfred Hospital Research Ethics Committee (X10-0354+ HREC/10/RPAH/618) and Liverpool Hospital Research Ethics Committee (SSA/11/LPOOL/203) Sydney Australia.

RESULTS

Of 331 people screened for enrolment in the study 165 (50%) were ineligible and 45 (14%) declined participation. At the suburban hospital site 30 people were not screened for enrolment due to limited staffing issues during study period which impacted on the overall number of participants able to be recruited at that site. Table 1 summarises the exclusion criteria of the 165 ineligible PLHIV.
Table 1: Exclusion criteria of patients excluded

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Diagnosis of HIV</td>
<td>12</td>
</tr>
<tr>
<td>Pre-existing Cognitive Impairment</td>
<td>34</td>
</tr>
<tr>
<td>Social chaos</td>
<td>16</td>
</tr>
<tr>
<td>Poor English</td>
<td>44</td>
</tr>
<tr>
<td>Drug and Alcohol Use</td>
<td>16</td>
</tr>
<tr>
<td>Current untreated depression</td>
<td>13</td>
</tr>
<tr>
<td>Declined</td>
<td>30</td>
</tr>
<tr>
<td>Total excluded</td>
<td>165</td>
</tr>
</tbody>
</table>

In total 121 participants and 43 caregivers across the 3 sites were recruited (Table 2).

Table 2: Participants and Caregivers recruited

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>121 (100%)</td>
</tr>
<tr>
<td>Number of participants who identified 4 or more S&amp;S</td>
<td>74 (61%)</td>
</tr>
<tr>
<td>Number of caregivers</td>
<td>44 (35%)</td>
</tr>
<tr>
<td>Number of caregivers who identified 4 or more S&amp;S</td>
<td>25 (57%)</td>
</tr>
</tbody>
</table>
More than one third of participants (39%) noticed some behaviour change in themselves and 28 (23%) were concerned about these changes in behaviour.

The mean age of participants was 49 years old, range 25 to 75 years. Ninety six per cent were men (116). Forty nine participants (40.5%) lived alone, 46 (38%) lived with a partner and 24 (20%) lived in shared households. Two participants lived (2%) with children.

**Depression**

Forty eight (39.7%) participants had a history of depression, which is consistent with the prevalence of depression in HIV positive populations (Grierson, et al, 2009). 32 (26.4%) were currently being treated for depression. Those with depression tended to have more symptoms selected from the booklet than those without current depression. P=0.056 Mann Whitney Test.

**HIV Information**

The median duration of HIV infection of participants was 10 years, range (0 – 29) which indicated that the participants had been infected for some time and therefore be at increased risk of developing co-morbid conditions. The CD4 T lymphocyte cell count is a marker of antiretroviral treatment responses and HIV disease progression. The participants’ median CD4 count was 590x10^7 (10 – 1720) which is within normal limits, indicating that participants have adequate immunity; CD4 nadir count is the lowest that it has ever reached and low CD4 nadir count is also a predictor of HAND, the median CD4 nadir was well below normal CD4 count at 180 x10^7 (0 – 750); median prescribed antiretroviral medications therapy was 6 years (0 – 28).

**Risk factors for non-HIV related cognitive impairment**
Many PLHIV have co-morbid conditions. A review of participants’ clinical notes revealed risk factors for non-HIV related cognitive impairment (Table 3). Of these factors, none were statistically significant.

**Table 3: Identified from clinical notes patient Risk factors for cognitive impairment**

<table>
<thead>
<tr>
<th>Current Conditions</th>
<th>Yes</th>
<th>P Mann Whitney</th>
<th>P t test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis C virus</td>
<td>10 (8.3%)</td>
<td>0.046</td>
<td>0.159</td>
</tr>
<tr>
<td>Hypertension</td>
<td>31 (25.6)</td>
<td>0.443</td>
<td>0.155</td>
</tr>
<tr>
<td>Prescribed Antihypertensive drug</td>
<td>29 (24%)</td>
<td>0.734</td>
<td>0.280</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>79 (65.3%)</td>
<td>0.803</td>
<td>0.452</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>61 (50.4%)</td>
<td>0.203</td>
<td>0.406</td>
</tr>
<tr>
<td>Sleep Apnoea</td>
<td>5 (4.1%)</td>
<td>0.498</td>
<td>0.361</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (5.8%)</td>
<td>0.078</td>
<td>0.033</td>
</tr>
<tr>
<td>Current smoker</td>
<td>38 (31.4%)</td>
<td>0.010 (Kruskal Wallis)</td>
<td>0.23 ova</td>
</tr>
</tbody>
</table>
**Antiretroviral medications**

Ninety four per cent (114) were currently taking antiretroviral medications. Of these, 30% (n=36) were on a once daily co-formulated single pill regimen, and 33 (n=40) took 3 or more pills per day.

Eleven per cent (n=13) had missed more than two doses of medications in the last month. There was a trend for a higher number of symptoms in the group who were not adhering to their medications P=0.070 Mann Whitney Test.

**Caregivers**

Seventy seven participants (64%) did not nominate a caregiver to be contacted. Six caregivers declined to be involved. The suburban hospital recruits (n=14) did not identify any caregivers. Of the caregivers identified (n=44), 82% (n=36) were male and 18% (n=8) were female. The relationship of the caregiver to the PLHIV varied: twenty-eight were male same sex partners, six were female partners of men, three were husbands of women, one was a mother, one a son, four were male friends and one was a female friend. 42% (n=15) of the caregivers identified as PLHIV. Of these, 73% (n=11) were in same sex relationships.

The most reported symptoms by both caregivers (47%) and participants (67%) was “being mentally tired at end of day” and caregivers 64% and participants 67%, “have you noticed you don’t go out socially as much as you used to?”

**Neuropsychological examination**

Twenty three (19%) participants were offered clinical neuropsychological examination from their doctor following use of the booklet, 70% (n=16) underwent the usual standard battery of tests performed in the clinical neuropsychological examination and 30% (n=7) declined
testing (Table 4). Four participants were diagnosed with MND as a result of these examinations.

**Table 4: Neuropsychological Exam Results**

<table>
<thead>
<tr>
<th>Number of Neuropsychological exam (n=16)</th>
<th>Results of Neuropsychological exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (31%)</td>
<td>Inconclusive, ongoing monitoring recommended</td>
</tr>
<tr>
<td>7(44%)</td>
<td>Within normal limits (1 depression, 1 sleep apnoea)</td>
</tr>
<tr>
<td>4 (25%)</td>
<td>MND diagnoses (medication regimen optimised, subsequent improved cognition noted)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

MND can have a detrimental impact on the health and well-being of PLHIV. As part of the HAND spectrum, MND may be difficult to identify because key signs and symptoms are nonspecific. Signs and symptoms of MND may be subtle and often the PLHIV and their caregivers may believe signs and symptoms are attributable other issues such as ageing, stress and/or lifestyle factors.

There were no previous studies regarding PLHIV and/or Caregivers’ self-reflection of signs and symptoms of cognition to guide us. The researches chose the identification of 4 or more symptoms by either participants or caregivers as a cue to monitor subsequent investigations and current standard of care. The 61% of participants and 57% of caregivers who identified 4
or more symptoms supported adoption of using the booklet to reflect on changes in the participants behaviour.

Caregivers are well placed to notice changes in cognitive behaviour (Glissen et al 2011). Many stated that they welcomed being involved in the study and that using the booklet to help reflect on the PLHIVs behaviour enabled them to start a discussion regarding behaviours they had noticed but did not know how to raise with the person. In addition some of the caregivers also identified as PLHIV and this may impact on future support if they as the caregiver also become ill or cognitively impaired.

Many of the participants live alone and did not identify caregivers who may be well placed to notice any changes in cognitive behaviour. At one site, none of the participants identified a caregiver. A majority of these participants were MSM who were married to women. Their lifestyle did not include HIV culture of gay men in Australia, perhaps best illustrated by one participant “We don’t talk about the HIV much, and I sure don’t want to mention this”. The clinician needs to be more vigilant in asking PLHIV without identified carers about cognition. The combination of PLHIV reflecting regularly on their behaviour and staff with a therapeutic relationship with the PLHIV, including knowing their social situation may combine to improve identification of impairment (as PLHIV may underrate signs and symptoms). As this population age they may become isolated socially (McDonald et al 2013) and the relationship with their clinician may become very important for asking questions about cognition. Discussion of cognition and memory should be incorporated and normalised into an annual review of HIV care, and may result in early detection (Wright and Watson 2012). This may reduce fear and apprehension of results from neuropsychological testing and enhanced discussion of signs and symptoms (Several participants declined testing due to fear of the outcome and being labelled cognitively impaired).
Regular reflection by the PLHIV and their caregiver may assist in early interventions for HAND screening and diagnosis. Many of the participants had long standing HIV which may place them at risk of developing HAND even though their HIV was well managed (Antorini et al 2007). The average age of participants was 49 years and as they age they may be at risk of developing co-morbidities such as heart disease which may affect cognitive impairment and may need to be closely monitored for signs and symptoms of cognitive impairment. The greatest co morbidity risk factors for cognitive impairment identified in the participants were vascular risk factors, such as: current nicotine smoking (31%), those with hypercholesterolaemia (65%), hyperlipidaemia (50%), or hypertension (25%). (Table 3) These figures point to the need to monitor patients and develop strategies to improve management of co morbidities such as smoking cessation. In addition successful management of co morbidities may help improve HAND outcomes (Wright and Watson 2012).

The signs and symptoms of depression may confound MND diagnosis so it is important to screen the PLHIV for this (Grierson et al 2009). Forty per cent of participants in this study had a previous history of depression, 26% were currently being treated for depression and 9% identified signs and symptoms of depression, and so were excluded from the study until reviewed by their doctor. The group who were currently being treated for depression were non-significantly more likely to have S & S of cognitive impairment (p=0.056). Many PLHIV were excluded from this study due to current untreated depression, substance use issues and language difficulties. Early detection and treatment of depression, providing assistance with depression and substance issues and developing resources in different languages would support improvement of rates of PLHIV being identified with and treated for MND.

Ninety four per cent of the participants were prescribed antiretroviral medications. Of these 33% were taking more than 3 antiretroviral drugs. The researchers did not enquire about
other medications. Pill burden may be a factor in adherence (Skinner et al 2009; Robertson et al 2010). Eleven per cent had missed > 2 doses of medications in the last month. This group had a non-significantly higher number of items from the booklet (P=0.070). There is a potential for a closed feedback loop whereby the patient with adherence problems may, as a result of the poor adherence, suffer further cognitive decline, leading to further impairment of adherence.

This study enabled some people who would otherwise been missed to be identified and referred for neuropsychological assessment. Using this booklet the PLHIV was able to reflect and use the booklet to report to clinicians, leading to neuropsychological testing. Several had their treatments changed and had improvements in cognition when subsequently reviewed (Table 4). Thirty per cent of PLHIV offered neuropsychological testing declined. Nurses are well placed to explore the reasons for declining and facilitating understanding of the improved outcomes formal testing could facilitate. The therapeutic relationship between patient and nurse may promote an open conversation, allowing the nurse to provide information to the PLHIV enabling further assessment and investigations.

Initially participants did not divulge items they had noticed from the booklet with their doctor as they did not think it was important, forgot or ran out of time. Nurses are well placed to discuss this with patients prior to their appointment with their doctor, to ask if the person has noticed any recent changes in cognitive symptoms or behaviours. Information from this discussion can be documented and brought to the attention of the doctor prior to the consultation. Nurses can use the booklet to initiate discussion and with regular questioning normalize the issue with the patient. Scheduled annual review of the patient would also be of benefit, utilising the initial documentation as a baseline for noticing changes in behavior and cognition.
LIMITATIONS/CHALLENGES

There were several challenges during this study.

There was no HIV negative matched comparison group for this study. This study was designed to follow the patient through their usual standard of care at the clinic they attended. Future studies could include a comparison group.

As there was no validated self reflective tool available we relied on professional judgement and incidental anecdotal evidence from PLHIVs to discuss issues relating to HAND. We decided to flag if four or more items from the booklet were selected.

Exclusion of people who did not speak English well excluded many possible study participants. Translation of the resource into community languages would assist in recruitment of this group in future.

IMPLICATIONS FOR PRACTICE

Nurses providing care and support to PLHIV should be aware of HAND and what questions to ask, and should explore further patients’ experience. A booklet exists which can be used by clinicians, patients and their carers to start a conversation about any signs and symptoms the PLHIV may be experiencing - assisting the PLHIV to reflect on recent changes in behaviour such as memory and concentration problems which could affect their quality of life.

Reflection of change may prompt further exploration by their doctor of cognitive decline. Early recognition and treatment may have a positive impact on the health and well being of the patient by reducing signs and symptoms and restoring independence.

As PLHIVs age and are at risk of developing other diseases of the brain, a HAND diagnosis should be considered in a neurological setting.
CONCLUSION

PLHIV are experiencing signs and symptoms of cognitive impairment which can affect their quality of life. HAND is a diagnosis of exclusion and PLHIV and their caregivers can have a major part in recognising signs and symptoms. Self-reflection is very important, as is reflection from caregivers.

Acknowledgements

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Much appreciation to all the participants and caregivers involved in the study.
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CHAPTER FIVE  
Experience of HAND

5.1 Overview and research questions

The preliminary pilot study indicated that some PLHIV are experiencing changes in cognition, are recognising these, and are concerned about HAND. An anonymous online survey was designed as Phase 1 of this thesis to give context to the experience of a broader population of PLHIV regarding HAND. The survey included questions about how PLHIV communicate with others about HAND. The results are presented here in the context of examining the research questions:

1. Are PLHIV aware of and/or concerned about HIV associated neurocognitive disorder?

2. Are PLHIV experiencing signs and symptoms of cognitive change and/or observing them in others?

5.2 Major findings

A total of 163 survey responses were completed. Thirty-seven were excluded (28 international responses and 9 duplicate responses), leaving 126 surveys for the final analysis. Of 126 eligible responses to the survey from PLHIV across Australia, 94 (75%) had heard of HAND and 74 (59%) had noticed symptoms of HAND in themselves and in others. Results showed that of the 94 respondents who had heard of HAND, 52 (55%) were concerned about it, and of these, 48 (92%) were anxious to talk about the subject. Yet of the 30 respondents who had spoken to someone about their concerns, 23 (77%) had received a positive response and stated that they felt they had been listened to.
Forty-nine (39%) of respondents indicated that they would like further guidance to initiate discussion about HAND with their doctor, caregiver or other PLHIV. The only statistically significant finding from this study was that those who had noticed a decrease in their ability to organise things in their daily lives had been diagnosed with HIV approximately five years longer, on average (17.4 years, SD 9.99 years), than those who responded ‘No’ to this symptom (11.9 years, SD 10.13 years, p = 0.033).

5.3 Conclusion

Further to the literature related to stigma and discrimination discussed in Chapter 2, the results of this study clearly show that responses to questions or discussion about HAND can impact on the willingness of PLHIV to seek further help for medical review and/or acceptance of other supports. Raising the awareness of HAND may reduce concerns and encourage engagement in open conversation with others for the benefit of PLHIV and their informal and professional caregivers. PLHIV also identified that the development of additional resources to facilitate communication with caregivers would be helpful.

5.4 Statement from co-authors confirming authorship contribution of the PhD candidate

Chapter Five is published as:


All authors made substantial contributions to editing and revising the manuscript.

As co-authors of the paper titled: “Voices from Australia– concerns about HIV associated neurocognitive disorder” we confirm that Denise Cummins made the following contributions:

i. Concept and design of the study;
ii. Collected, managed and analysed the data;
iii. Primarily responsible for the interpretation of results;
iv. Drafting, revising and writing up of the manuscript for submission to peer-reviewed journals.

All authors read and approved the final manuscript.

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In addition to the statement above as supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

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<tr>
<th>Name</th>
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<tr>
<td>Professor Donna Waters</td>
<td></td>
<td>06.08.2018</td>
</tr>
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TITLE: Voices from Australia—concerns about HIV associated neurocognitive disorder

Abstract

This study aimed to determine whether people living with HIV (PLHIV) are concerned about HIV associated neurocognitive disorder (HAND) and would find information and resources for HAND beneficial. An online survey focusing on the experience of HAND was distributed via the website of Positive Life New South Wales: a peak peer-support non-government organization in Australia.

Of 126 respondents, 94 (74%) had heard of HAND, 52/94 (55%) had experienced concerns and of these, 48/52 (92%) felt anxiety about discussing the subject. Of those who had experienced concerns, 30/52 (58%) had spoken to someone about these concerns and 23/30 (77%) had received a positive response. Across the entire sample, 74 (59%) had noticed symptoms of cognitive decline in themselves and/or others. Respondents who noted a decrease in their ability to organize were on average five years older than those who had not noticed a decline (p=0.012, effect size -.54). Forty-nine (39%) indicated that they would like guidance to initiate discussion about HAND with their doctor, caregiver or other PLHIV.

The survey findings suggest that increasing awareness of HAND among PLHIV and their caregivers, and providing resources to facilitate discussion about HAND may assist to reduce concerns among PLHIV and enhance the effectiveness of clinical review.

Key words

People living with HIV, HIV Associated neurocognitive disorder, caregivers, stigma
Background

Due to the success of HIV treatments, people living with HIV (PLHIV) are now an ageing population (Deeks, Lewin, & Havlir, 2013). In addition to being at similar risk of developing dementias as the general ageing population, ageing PLHIV have an increased risk of neurocognitive co-morbidities such as HIV associated neurocognitive disorder (HAND) (Rodriguez-Penney et al., 2013; Hopcroft et al., 2013). HAND is an umbrella term used to describe a subcortical neurodegenerative disease caused by HIV-1 infection that may affect more than 30% of PLHIV (Antinori et al., 2007; Clifford & Ances, 2013). Older PLHIV, routinely defined as older than 50 years of age (Kirk & Goetz, 2009), have a three-fold risk of HAND when compared to younger peers (Valcour et al., 2004), resulting in experience of cognitive and neurological decline during mid-life (Cohen, Seider, & Navia, 2015). Awareness, knowledge and experience of HAND is varied, and little is known about the perspectives of PLHIV towards HAND (Hopcroft et al., 2013; Moore et al., 2015).

Cognitive impairment is associated with poor quality of life and may impact upon skills needed to perform activities of daily living (Cody & Vance, 2016; Tozzi et al., 2003). HAND can impact a range of cognitive domains, including motor skills, psychosocial, memory, concentration and executive function (Clifford & Ances, 2013). Moore et al. (2015) found that for PLHIV with HAND, cognitive performance was inversely related to the amount of time spent engaged in passive leisure activities, with neurocognitive impairment being linked to passivity and decreased participation in cognitively stimulating activities (Fazeli et al., 2014). Conversely, engagement in physical, mental and social activities have been associated with improved cognitive outcomes and a lower prevalence of HAND (Tan et al., 2013).
While dementia primarily affects individuals over 65 years, HAND impacts a much younger population of PLHIV (Pascal et al., 2016). A diagnosis of HAND can create fear about loss of independence and mental capacity, and is associated with delay in help seeking (Gagnon, 2015; Chambers et al., 2015). Those with HAND may experience increased social isolation, with some PLHIV already living alone due to an age related decrease in social participation and shrinking social networks (Rueda, Law, & Rourke, 2014). Further, the symptoms of HAND may also affect medication adherence, with a resulting impact on general health (Katz et al., 2013; Vance, 2013). The recognition and diagnosis of HAND in PLHIV is therefore important, particularly as HAND is associated with an increased risk of morbidity and mortality (Skinner, Adewale, DeBlock, Gill, & Power, 2009) and there is potential to minimise the impact of HAND if treated early (Cysique et al., 2009).

The purpose of this exploratory study was to gain an understanding of the knowledge of HAND among PLHIV. The aims were to investigate if PLHIV in Australia 1) had knowledge of and were concerned about HAND; 2) had noticed any signs and symptoms of cognitive decline in themselves or others; 3) had discussed HAND with either a professional or informal caregiver; 4) whether knowledge of and concern about HAND were associated with age and the duration of HIV diagnosis; and 5) whether PLHIV thought resources for HAND would be helpful. It was anticipated that the results could be used to inform clinical care and the development of relevant resources for PLHIV and their caregivers.

**Method**

An online survey was designed with and distributed by Positive Life New South Wales (PLNSW); a non-profit community-based organization supporting people with HIV living in New South Wales (NSW), Australia. The PLNSW organization aims to eliminate
the stigma, discrimination and isolation of PLHIV, and advocates with government and non-
government organizations on behalf of this group (Positive Life, NSW). Although a state-
based organization, PLNSW has national and international reach through internet and social 
media networks.

**Survey development and distribution**

The online survey was developed by two of the study authors, both of whom have extensive 
clinical experience with PLHIV. The survey contained both open-ended and closed questions 
designed to elicit information on the demographic background of the respondent and their 
awareness and experience of HAND. Closed question response options were ‘Yes’, ‘No’ or 
‘Don’t know’ with embedded logical branching, while open-ended questions provided 
respondents with unlimited free text space to discuss their experience of HAND. The content 
of the survey focused on four signs and symptoms of cognitive change: slowed thinking, 
increased forgetfulness, decreased organisational skills and decreased pleasure in activities. 
The survey was piloted for readability, face validity and appropriate language with HIV 
positive volunteers.

The researchers anticipated that awareness of HAND was likely to be varied and that concern 
and anxiety may be higher in older age groups for whom the signs and symptoms of HAND 
may be of longer duration or more obvious. As PLNSW applies standard age groupings 
across all investigations and reports, older age was defined in this survey as those over 45 
years. The analysis explored associations between age, duration of HIV infection, and signs 
and symptoms that could be indicators of HAND. The words ‘concern’ and ‘anxiety’ were 
purposefully not defined in the survey so that participants could answer questions about these 
emotions from their own perspective. The study was approved by the Human Research Ethics 
Committee (HREC) of the Sydney Local Health District, NSW, Australia and endorsed by
the HREC of the University of Sydney. Consent was implied by online submission of the survey.

The survey was distributed via the PLNSW website over a three-week period from August to September 2015. Access to the survey, hosted on the Survey Monkey platform, was also available via the PLNSW Facebook and Twitter accounts. Respondents were informed that participation was voluntary and results would remain anonymous. Only respondents with an Australian postcode were included in the final sample due to possible cultural and health service differences between countries.

**Data Analysis**

Responses entered into the Survey Monkey platform were downloaded for analysis into IBM SPSS Statistics (SPSS Version 21, IBM Corporation Armonk, NYI, USA). Demographic and other variables related to HIV and HAND are reported as number and percentage, or mean and standard deviation, as appropriate. Duration of HIV was analysed using Analysis of Variance (ANOVA) or independent groups t test following confirmation of normality through a histogram and Q-Q plot. Differences in categorical variables were analysed using Chi Square tests of independence. Adjusted Standardised Residuals (ASRs) were used to further interpret significant Chi Square test results (Field, 2013).

For all analyses, a p value of <0.05 was considered statistically significant. As an indicator of the practical or clinical significance of differences in HIV duration and cognitive decline, effect sizes (Cohen’s D) are reported. A 0.50 (medium) criterion was chosen as a benchmark against which to assess the effect sizes in this study, as this is conventionally the effect size at which a trained observer can detect a difference (Norman, Sloan, & Wyrwich, 2003). There
has been no adjustment for multiple testing in this exploratory study as measures to control for the Type I error rate (such as Bonferonni adjustment) are conservative and may fail to reveal potentially important early findings.

Results

A total of 163 survey responses were received over the three-week period the survey was open online. Thirty-seven responses were excluded (n=28 international responses and n=9 duplicate responses), leaving 126 surveys for the final analysis. Table 1 outlines the socio-demographic profile of respondents and notes a broad sample with the majority being English speaking males born in Australia and identifying as homosexual.

<Table 1 here>

Awareness of HAND

Seventy-five percent of respondents (n=94) had heard of HAND and results in Table 2 are based on the responses of these 94. The remaining 32 (25%) respondents who did not know about HAND did not respond to questions about concerns or anxiety, nor identified having spoken to others about it.

<Table 2 here>

Of the 94 respondents who had heard of HAND, 52 (55%) reported concerns. Of these 52, the highest percentage (n=38, 73%) were in the 45-64 age range, 48 (92%) reported feeling anxious about discussing the subject and 30 (58%) had already spoken to someone about their concerns. Of these 30, the majority (n=23, 77%) felt they had been listened to, usually identifying their HIV medical specialist. Seven (23%) respondents had a negative response, with 5 of these 7 (71%) stating they would not discuss their concerns again.
Those respondents who had heard of HAND (n=94) had been living with HIV for a longer period of time (mean 16.5 years, SD 10.00) than those 32 who indicated no knowledge of HAND (12.3 years, SD 10.62, p = 0.047, Cohen’s d 0.40). There was no statistically significant difference in the duration of HIV infection among those 52 people who expressed concern about HAND (mean duration 16.0 years, SD 9.12) and those 42 who did not (mean duration 17.1 years, SD 11.08, p>.05, Cohen’s d -.10).

**Experience of cognitive impairment**

When asked about which signs and symptoms of cognitive impairment 126 respondents had noticed in themselves or in their HIV positive friends, 74 (59%) reported that they were finding it harder to organise things; 68 (54%) had experienced or observed slowed thinking; 65 (52%) noted increased forgetfulness; and 47 (37%) reported having less pleasure with activities. Fifty-three respondents (42%) reported that other people had noticed changes in their cognition and 30 (24%) had noticed some cognitive changes in their friends who were living with HIV.

Respondents expressed varying levels of comfort in discussing cognitive changes with others. Just over one-third of respondents (n=49, 39%) indicated that they would be able to discuss cognitive changes with their friends. A further 49 (39%) responded that they would like more information on how to broach the subject of changes in cognition observed in themselves or in others.

**Cognitive change and duration of HIV infection**

The study focused on four signs and symptoms of cognitive change (slowed thinking, increased forgetfulness, decreased organisational skills, decreased pleasure in activities). The duration (in years) of HIV for those who responded ‘Yes’, ‘No’ or ‘Don’t know’ to each of
the signs and symptoms was compared using one-way ANOVA (Table 3). The only statistically significant finding was in the reported ability of respondents to organise things (p = 0.033). Post hoc testing indicated that those who responded ‘Yes’ to this symptom had been diagnosed with HIV approximately five years longer (17.4 years, SD 9.99) than those who responded ‘No’ (11.9 years, SD 10.13, p = 0.012, effect size 0.54). Although not statistically significant, medium effect sizes were also evident for differences in HIV duration between those who responded ‘No’ and ‘Don’t know’ to experiencing slower thinking (0.51) and for those who reported being more forgetful (0.50).

Cohen et al. (2015) has noted that some PLHIV may begin to experience signs and symptoms of HAND in their mid 40’s. The experience of the four cognitive signs and symptoms explored in this study were compared between three age ranges (18 – 44, 45 – 64, >64 years). There were no statistically significant associations between age and respondents’ experience of these four signs and symptoms of changes in cognition. There were also no statistically significant differences between the occupational status of the respondent (full time, part time work, or student) and three of the signs and symptoms of cognitive change. However, a statistically significant result was found for the association between occupational status and respondents’ experience of being more forgetful (p=0.016). The adjusted standardised residuals (ASR) indicated that 33 of 47 (70.2%) people on a government benefit had noticed becoming more forgetful (ASR 3.2), whereas this was the case for only 20 of 55 (36.4%) of people who were working full time (ASR -3.0).

Themes from open ended questions

In addition to the 52 (55%) closed question responses indicating concern about HAND, 62 (49%) specific responses were also made to the open-ended survey question ’What are your
concerns about HAND?’ and a further 30 (24%) of all survey respondents also chose to provide additional final comments. Several consistent themes were identified from the two opportunities to provide comment to the open-ended questions. Collectively, comments outlined fear of a HAND diagnosis (n=27, 29%); fear of losing mental capacity (n=26, 28%); general fear for the future (n=12, 13%); and fear of loss of independence (employment and becoming a burden on others) n=9 (10%).

Examples of respondents’ comments include:

Some family and friends have "heard" me when I bring up my sense that I am in early cognitive decline, but most doctors just look at you; say little, or dismiss it as not being all that bad. This makes me feel dismissed; like I'm over-exaggerating it all.

I am worried about …memory issues, concentration, multiple tasking issues, short attention span. All of these affect my day to day living issues as well as ability to work well in employment.

I don't want to end up in a human waste facility, "rest home", ignored, and by some staff treated badly and by other staff.

Of the total 126 respondents, 8 (9%) disclosed they had a current diagnosis of HAND and some (n=5, 5%,) expressed concern that they would not notice further cognitive decline. As the examples below illustrate, there was a genuine expression of fear of future consequences.

I don't want to die lying in my own body waste, I don't want to be some brain dead vegetable that people are scared of or laugh at.

I would rather go before any long term, visibly embarrassing traits develop.... I just don't want my family seeing me like that.
Discussion

People living with HIV are ageing and are at risk of developing HIV associated neurocognitive disorder (Rodriguez-Penny et al., 2013; Hopcroft et al., 2013). If diagnosed and treated early, the adverse impacts of HAND can be minimised (Alzheimer’s Australia, 2014; Cysique et al., 2009). This explorative study utilised an online survey to gain an understanding of the knowledge of HAND among PLHIV. Overall, respondents did know about HAND, had concerns about it, and some had experienced signs and symptoms which may be related to HAND. Respondents in the 45 – 64 year age group expressed the greatest levels of concern, and reported varied levels of comfort discussing HAND with others. Hopcroft et al. (2013) suggest that as PLHIV age, with an increasing duration of HIV infection, they become increasingly concerned about cognitive impairment. However this study found no statistically significant differences in respondents’ duration of HIV infection and concern about HAND.

It was encouraging that many respondents who had discussed their concerns about HAND reported a positive response to those discussions. Many had already noticed changes in cognition among people in their social networks, but generally did not feel comfortable to talk to their friends directly about this. As almost one-third of respondents indicated that additional resources about HAND would be helpful to facilitate discussions with formal and informal supports, this could be one relatively simple and cost-effective solution to reducing fear and apprehension and promote early recognition of HAND. Resources could be used to provide ideas on how to communicate experiences to others, and could increase confidence to access medical review if signs and symptoms of HAND become apparent (Moore et al., 2015; Morgan et al., 2012).
Although many respondents stated they had experienced some signs and symptoms of cognitive decline (which could be indicative of HAND), the only statistically significant symptom related to HIV duration was the inability to organise things as they used to. This symptom has potential impacts on general health and quality of life through a decreased ability to organise medical reviews, self-care, medication supply and adherence, and activities of daily living (Cody and Vance 2016).

Moore et al. (2015) noted that cognitive performance was inversely related to time spent engaged in passive leisure activities. In this study, many PLHIV were not in paid employment, with over one-third receiving a government benefit. As respondents were not specifically asked about their social engagement, it cannot be assumed that they were not engaged in social activities, yet it was found that those not employed or studying did appear to experience forgetfulness more often than those who were currently employed.

**Limitations**

This was a small exploratory study aiming to understand current perspectives about HAND among PLHIV. Although the sample size was small, responses were received from across Australia. In the statistical analysis, small numbers within some sub-samples may have affected results, however, this was the rationale for also reporting effect sizes. It is entirely possible that survey respondents had a specific interest or concern about HAND and were therefore more willing to complete the survey. Survey questions did not request respondents to quantify the period of time related to their experience of signs and symptoms of HAND. For those who were not currently working, further questions about how they use their time, especially for those who live alone would be useful to explore. The respondent’s age was not significantly associated with self-reported symptoms, which may be due to the small number of responses of respondents over 65 years. Similarly, medium effect sizes for differences
between HIV duration and being slower in thinking or more forgetful are possibly due to those who have been HIV positive for longer having had more time to monitor their cognition and lack of statistical significance is likely attributable to small sample sizes in the ‘Don’t know’ categories for these variables.

Further research would be useful focusing on comparable HIV-negative age groups; assessment of functional symptoms in PLHIV, and assessment of health provider awareness and assessment skills. Additionally, exploring the opinion of PLHIV regarding the role of stigma and discrimination associated with HAND, and the potential impact these may have on accessing care and support and the early diagnosis of HAND are important future areas of study.

**Conclusion**

PLHIV are an ageing cohort and many have experienced stigma and discrimination in their past (Karamouzian et al., 2015; Skinner & Mfecane, 2004). If PLHIV are fearful or have concerns about HAND, they may be less likely to access medical care. Health care providers can make greater use of resources to encourage PLHIV to discuss their concerns, thereby facilitating earlier diagnosis and treatment of HAND (Chambers et al., 2015). Further, opportunities to increase social engagement and passive leisure activities among PLHIV should be encouraged, as these may positively affect cognition at the same time as potentially improving support to ageing PLHIV (Rueda et al., 2014).

This study has yielded some important and unexpected results indicating that PLHIV are concerned about HAND and are living with uncertainty and vulnerability, particularly as they age. The collaborative development of resources may assist health professional and
other caregivers with improving and facilitating discussion about HAND, which may lead to reducing anxiety and to enhanced opportunities for clinical review.

Acknowledgments

We kindly thank the staff of Positive Life NSW who assisted in Survey Monkey platform development and all those who completed the survey.

Disclosure statement

No potential conflict of interest was reported by the authors.
References


Table 1: Social-demographic information of survey participants (n=126)

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Geographic region of birth</strong></td>
<td>Australia</td>
<td>78 (62)</td>
</tr>
<tr>
<td></td>
<td>Asia</td>
<td>10 (8)</td>
</tr>
<tr>
<td></td>
<td>United Kingdom</td>
<td>10 (8)</td>
</tr>
<tr>
<td></td>
<td>New Zealand</td>
<td>9 (7)</td>
</tr>
<tr>
<td></td>
<td>North America</td>
<td>8 (6)</td>
</tr>
<tr>
<td></td>
<td>Africa</td>
<td>6 (5)</td>
</tr>
<tr>
<td></td>
<td>Europe</td>
<td>2 (1)</td>
</tr>
<tr>
<td></td>
<td>Middle East, South America, PNG (one each)</td>
<td>3 (3)</td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td>English</td>
<td>120 (95)</td>
</tr>
<tr>
<td></td>
<td>Non-English</td>
<td>6 (5)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Male</td>
<td>116 (92)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>8 (6)</td>
</tr>
<tr>
<td></td>
<td>Transgender</td>
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<tr>
<td><strong>Sexuality</strong></td>
<td>Homosexual</td>
<td>106 (84)</td>
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<tr>
<td></td>
<td>Heterosexual</td>
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</tr>
<tr>
<td></td>
<td>Queer</td>
<td>6 (6)</td>
</tr>
<tr>
<td></td>
<td>Bisexual</td>
<td>2 (1)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2 (1)</td>
</tr>
<tr>
<td><strong>Age range (years)</strong></td>
<td>18-44</td>
<td>36 (29)</td>
</tr>
<tr>
<td></td>
<td>45-64</td>
<td>82 (65)</td>
</tr>
<tr>
<td></td>
<td>&gt;65</td>
<td>8 (6)</td>
</tr>
<tr>
<td><strong>Employment</strong></td>
<td>Full time</td>
<td>55 (44)</td>
</tr>
<tr>
<td></td>
<td>Part time</td>
<td>19 (15)</td>
</tr>
<tr>
<td></td>
<td>Pension (aged/disability)</td>
<td>47 (37)</td>
</tr>
<tr>
<td></td>
<td>Other e.g. student</td>
<td>5 (4)</td>
</tr>
<tr>
<td><strong>HIV status</strong></td>
<td>HIV positive</td>
<td>120 (96)</td>
</tr>
<tr>
<td></td>
<td>HIV negative</td>
<td>6 (5)</td>
</tr>
<tr>
<td><strong>HIV duration</strong></td>
<td>Range (years)</td>
<td>&lt;1-35</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>15.4 (10.28)</td>
</tr>
</tbody>
</table>
Table 2: Experience of respondents who had heard of HAND (n = 94)

<table>
<thead>
<tr>
<th>Experience</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-reported</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Concern about HAND</td>
<td>52/94(^a) (55)</td>
<td>42/94 (45)</td>
</tr>
<tr>
<td>Anxiety at thought of discussing HAND</td>
<td>48/52(^b) (92)</td>
<td>4/52 (8)</td>
</tr>
<tr>
<td>Has spoken about concerns</td>
<td>30/52(^b) (58)</td>
<td>22/52 (42)</td>
</tr>
<tr>
<td>Had positive response when spoke to someone</td>
<td>23/30(^c) (77)</td>
<td>7/30 (23)</td>
</tr>
</tbody>
</table>

\(^a\) 94 = the total number who have heard of HAND; \(^b\) 52 = total number concerned about HAND; \(^c\) 30 = total number who had spoken to someone about HAND

Table 3: Cognitive symptoms and HIV duration (in years)

<table>
<thead>
<tr>
<th>Sign or symptom present</th>
<th>Yes</th>
<th>No</th>
<th>Don’t know</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>n</td>
<td>Mean (SD)</td>
<td>n</td>
</tr>
<tr>
<td>Slower in thinking</td>
<td>15.3 (9.68)</td>
<td>68</td>
<td>16.6 (10.58)</td>
<td>48</td>
</tr>
<tr>
<td>Harder to organise</td>
<td>17.3 (9.99)</td>
<td>74</td>
<td>11.9 (10.13)</td>
<td>32</td>
</tr>
<tr>
<td>More forgetful</td>
<td>14.7 (9.86)</td>
<td>65</td>
<td>17.4 (9.91)</td>
<td>47</td>
</tr>
<tr>
<td>Less pleasure</td>
<td>13.7 (9.60)</td>
<td>47</td>
<td>16.6 (10.17)</td>
<td>61</td>
</tr>
</tbody>
</table>

*Post Hoc test indicated statistically significant difference in mean HIV duration between No/Yes responses: p = 0.012, Cohen’s d = 0.054
CHAPTER SIX

Professional caregiver assessment

6.1 Overview and research question

Some PLHIV do not have the support of an informal caregiver, may live alone and/or may lack insight into their own health state. This leads to question, who fulfils the role of observing changes in daily functioning or cognition when a PLHIV does not have personal insight or the support of an informal caregiver? The Phase 2 study was designed to examine the role of community based HIV professional caregivers in the early identification of HAND. A cross-sectional study aimed to determine what type of patient information professional caregivers were collecting related to identifying risk of HAND as part of their initial and follow-up health assessments. The file audit method was used to examine the research question:

3. What information collected by HIV community based teams identifies patients at risk of HAND?

6.2 Major findings

Documentation was incomplete in every one of the 262 audited patient records. The specific clinical information related to identifying risk factors for HAND that was missing from patient records included: nadir CD4+ T cell count (missing in 91%), HIV viral load (missing 36%); support of current informal caregiver (missing in 19%) and; living circumstances (missing in 14%). Information recorded in files was largely from secondary sources, for example, self-reported by the PLHIV. Further, documented information was confirmed in
only 52 (30%) of the 262 records. Information classified as ‘confirmed’ was that provided directly by the person’s doctor, GP, HIV specialist or directly reported during attendance at medical appointments. The audit results revealed that clinical assessment records made by community based health professionals contained very minimal information that was relevant for identifying risk of HAND in PLHIV.

6.3 Conclusion

Access to integrated information is important for communication between service providers, the coordination of efficient and effective patient care, and for referral to further medical review or testing. Incomplete documentation in paper or electronic medical records does not only impact the integration of care for PLHIV and lead to poor health outcomes, but as shown in this study, may also be missing risk factors for the early identification of HAND. Professional caregivers are in a position to access, record and share knowledge of the psychosocial circumstances and health risk factors of PLHIV. Documentation of risk factors by community health professionals is important for the early identification of those who may be at risk of HAND, especially where informal care is absent.

6.4 Statement from co-authors confirming authorship contribution of the PhD candidate

Chapter Six is published as:


All authors made substantial contributions to editing and revising the manuscript.
As co-authors of the paper titled: “Potential impacts of poor communication on early diagnosis of HIV associated neurocognitive disorder”. We confirm that Denise Cummins made the following contributions:

i. Concept and design of the study;

ii. Collected, managed and analysed the data;

iii. Primarily responsible for the interpretation of results;

iv. Drafting, revising and writing up of the manuscript for submission to peer-reviewed journals.

All authors read and approved the final manuscript.

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<tr>
<td>Aggar, C</td>
<td></td>
<td>12/10/18</td>
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<td>O’Connor CC</td>
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</table>

In addition to the statement above as supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

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</thead>
<tbody>
<tr>
<td>Professor Donna Waters</td>
<td></td>
<td>06.08.2018</td>
</tr>
</tbody>
</table>
Title: Potential impacts of poor communication on early diagnosis of HIV-associated neurocognitive disorder

Abstract

Aim

To ascertain whether community-based health care providers were collecting appropriate information to identify patients at risk of HIV associated neurocognitive disorder and whether related documentation was complete.

Background

HIV associated neurocognitive disorder is a treatable neurological condition that can affect more than 20% of those infected with the HIV. Signs and symptoms of cognitive impairment may be subtle, therefore documentation of medical and social information could be beneficial in identifying those at risk.

Design

Cross sectional descriptive study.

Methods

An audit of patient records was completed by two community-based interdisciplinary teams with particular attention to the documentation of clinical and social indicators for those at risk of HIV associated neurocognitive disorder. Data were collected over a four-week period during 2015.

Results

Data were retrieved from both electronic medical record systems and hard copy patient records. Documentation was incomplete in every patient record (n=262), including the absence of important clinical data relating to nadir CD4+T cell count (91%), HIV viral load (36%), current caregiver (19%) and living circumstances (14%). Up to 40% of recorded
medications and results were unconfirmed by the person’s medical practitioner.

**Conclusion**

Poor documentation can lead to incomplete information, which can delay early intervention for those at risk of HIV associated neurocognitive disorder. Collection and recording of patient data needs to be consistent, as complete documentation is essential for integrating care, provision of clinical support and importantly, for identifying those at risk of developing HIV associated neurocognitive disorder.

**Key words**

Nurse, interdisciplinary teams, communication, information technology, electronic medical record, HIV/AIDS, community care, HIV associated neurocognitive disorder
SUMMARY STATEMENT

Why is the research needed?

- HIV associated neurocognitive disorder is a treatable neurological condition that can affect more than 20% of people living with HIV.
- Diagnosis is by exclusion, therefore access to complete patient information is essential to detect patients at risk of developing this condition.
- Poor documentation could impact the early identification of those at risk of developing HIV associated neurocognitive disorder, with missing information leading to delayed medical assessment, diagnosis and treatment.

What are key findings?

- There are issues relating to missing and incomplete data when both electronic medical records and hard copy patient records (hybrid systems) are used.
- Incomplete documentation was noted for every patient record in the audit, including clinical data necessary for the early identification of risk factors for HIV associated neurocognitive disorder.

How should findings be used?

- To develop strategies to improve the utility of hybrid systems to facilitate access and sharing of patient information across community-based teams.
- To promote regular auditing of electronic medical records.
- To develop case definitions for HIV associated neurocognitive disorder.
INTRODUCTION

People living with the Human Immunodeficiency Virus (HIV) may experience increasingly multifaceted health and treatment challenges as they age. HIV is now considered a chronic disease (Clifford & Ances, 2013; Lai, Tarwater & Hardy, 2006) and subsequently, people living with HIV (PLWH) are at increased risk of co-morbid medical conditions. HIV associated neurocognitive disorder (HAND) is one such condition this is known to cause disability in up to 20% of PLWH (Antinori et al., 2007; Clifford & Ances, 2013; Heaton et al., 2010). Similar to other patients with chronic conditions, PLWH are cared for by a team of health care providers who may not work in the same location. Specialist community-based HIV teams often have an intimate knowledge of their patients’ health and well-being and the utilisation of electronic medical records (eMRs) enables a sharing of this information with other services (Ingram et al., 2017). Improved communication offers greater opportunity to identify and assess those who may be at risk of developing HAND to achieve early diagnosis and integrate care (Odlum et al., 2012).

Australia is moving towards a national eMR, which will allow individuals to control healthcare provider access to their health information (NSW Health, 2013). Access to shared information through eMRs enables health care providers to develop strategies to manage complex chronic conditions, potentially reduce further risk and better integrate care, especially in vulnerable communities such as for PLWH (Kim et al, 2016).

Early recognition of HAND is important as treatment offers opportunity for improved clinical outcomes for PLWH (Robertson et al., 2007). HAND is often diagnosed by exclusion and requires several testing methods as there are currently no biological markers for a definitive diagnosis (Atluri, Kurapati, Samikkannu, & Nair, 2014). Known clinical risk factors for HAND include low nadir CD4 T cell count (McCombe, Vivithanaporn, Gill, & Power, 2012), past history of AIDS defining central nervous system disease (Fabiani, Pinto, & Bruschi,
2013) and Hepatitis C co-infection (Schouten et al., 2012). Furthermore, other medical co-
morbidities with signs and symptoms that may mimic cognitive change, such as vascular or
metabolic disorders, need to be ruled out (Kamminga, Cysique, Lu, Bachelor, & Brew, 2013;
Nightingale et al., 2014).

Recognition of HAND is also improved by enhanced knowledge of social circumstances,
medical history and current health risk factors of PLWH. The clinical indicators of HAND
should also be documented. Awareness of social circumstances is significant as PLWH may
be socially isolated due to age (Reuda, Law, & Rouke, 2014), gender or sexual orientation
(Grierson, Pitts, & Koelmeyer, 2013). PLWH who live alone and/or do not have the support
of an informal caregiver may not notice subtle cognitive changes indicative of HAND
(McDonald, Elliott, & Saugers, 2013). Community-based health professionals may be the
only regular contact able to observe signs and symptoms of cognitive change when providing
ongoing care and support.

Because optimal communication of patient information is essential to identify those who may
be at risk of developing HAND, and provides an opportunity for early assessment, health
professionals have the potential to facilitate the early diagnosis of HAND and impact on the
health outcomes of PLWH (Sittig & Singh, 2011) through complete and accurate
documentation.

THE STUDY

Aims:

This descriptive study aimed to ascertain whether two interdisciplinary community based
HIV specialist teams were collecting accurate and appropriate information to identify patients
at risk of HAND (HIV information, social and clinical indicators) and whether their
documentation was complete.

**Design:**

Data were derived from a file audit of patient data collected by members of the community-
based teams over a four-week period.

**Participants:**

The two unique interdisciplinary community-based HIV specialist teams participating in this study are located in the State of New South Wales (NSW), Australia. Employed by two separate health districts, the teams cover 18 local government geographical areas with a combined total population of approximately 1,430,000 people of which, approximately 52% speak a language other than English at home. Delivering health services to an estimated 9,970 people living with HIV in inner city Sydney and urban regions of NSW (NSW HIV Strategy, 2015), these two teams provide care to the highest, and second highest number of PLWH in the State (n=5432, 31% and n=2857, 16.5%, respectively) (Sydney Local Health District website; South Eastern Sydney Local Health District Website; NSW HIV Strategy, 2015). Both interdisciplinary community-based HIV specialist teams utilise patient health records as a means of compiling and communicating patient data. The teams have access to the electronic medical record system maintained by the health district in which they are employed; the Community Health Information Management Enterprise (CHIME) and the Cerner Corporation Supplier of Health Information Technology (CERNER).

Each team has a manager and ten members including social workers, occupational therapists, physiotherapists, dietitians, mental health nurses and primary health nurses. The teams provide clinical care and case management for patients with complex needs related to HIV
diagnosis. Each team works closely with local HIV inpatient and outpatient services, general hospitals and other health services, non-government organisations and family doctors within their respective locations to provide integrated care for PLWH across NSW. In one location, the HIV team (Team 1) uses a specifically built HIV electronic medical record (eMR) which allows local health district staff direct access to patient information, including the tracking of appointments and pathology results (CERNER). For those patients who access medical services external to the local health district, team members have to request information directly from the patient’s doctor. This system currently does not have capability to scan other documents into the eMR, therefore hard copies of clinical notes continue to be available within the paper-based medical record to file external reports. In the second location, the HIV team (Team 2) uses an eMR which currently does not link to any other clinical services within their local health district (CHIME); therefore, it is a standalone system relying on documents pertaining to the patient being scanned into the eMR. Antecedent paper based medical records are not readily available at this location as they are in secure storage at another site and there is a waiting time to access these records.

**Data collection**

The audit of the electronic and paper-based records of all patients seen by both teams was conducted over a four-week period in 2015 and was completed by individual team members (allowing each professional, as key worker, four-weeks to review their patient files and transcribe information). An electronic spreadsheet, pre-populated with labelled data fields relevant to HIV care was sent to a lead member of each team, who then distributed the spreadsheet to other team members. Individual team member had access to their local version of an eMR, and limited access to hard copy clinical notes from which they retrieved the requested information and transcribed this onto the electronic spreadsheet for each patient in
their care over the nominated period. The completed spreadsheet was returned to the lead member who collated all data onto one spreadsheet which was de-identified prior to returning to the researcher. Requested data fields included demographic, social and health information, including co-morbid medical conditions. Pathology results were requested, with particular interest in clinical indicators pertaining to HAND such as nadir CD4+ T cell count, current CD4+ T cell count, HIV viral load and information regarding prescribed HIV medications. Newly referred patients (within the four-week period) who had not been assessed were excluded from the audit.

For the purposes of this study, information was considered confirmed if it was documented directly by the patient’s medical practitioner (either the HIV specialist or family doctor), or was witnessed by the team member (such as being present during a medical appointment) and transcribed into the patients record or eMR. Information was considered unconfirmed if it was provided by any other means such as directly from the patient, from hospital discharge summaries (which may have been based on incidental care such as an emergency department admission), from non-government organisations, or from specific reports documenting only limited or second hand information. Collated data from both HIV specialist teams were exported to SPPS (V21 IBM Corporation Armonk, NY, USA) for statistical analysis.

**Ethical considerations**

The study was approved by the Human Research Ethics Committee of the Sydney Local Health District, NSW, Australia and Human Research Ethics Committee, South Eastern Sydney Local Health District, NSW Australia and endorsed by the Human Research Ethics Committee of the University of Sydney, NSW, Australia.
Data analysis
Data from the spreadsheet was transferred for analysis using IBM SPSS for Statistics (SPSS
Version 21, IBM Corporation Armonk, NY, USA). Data were checked for data entry errors.
Analysis included calculation of descriptive statistics. Demographic variables and variables
related to HIV and HAND are reported as number (n) and percentage, or mean and standard
deviation, as appropriate (Field, 2013).

Validity and reliability/rigour
The spreadsheet was pre-populated with column titles and descriptors for consistency of data
collection and to minimise errors. As data were collected by clinical experts in HIV care,
team members were invited to comment on the content validity of selected audit variables.
The researcher met with each team and provided training to ensure consistency with data
collection. Data were checked for missing values and outliers, with return to the team
member by the lead member for confirmation if required.

RESULTS
During the four week study period, each community team provided direct care to 131 HIV
infected patients (total 262). Initial examination of the data revealed no statistical differences
between data collected at each location, therefore, results are reported for the combined
dataset.

Of the 262 files audited, the mean age of clients was 49.6 years (SD 11.2). Ninety-one
percent (n=238) were male, 8% (n=21) female and 1% (n=3) transgender. Sixty nine percent
(n=181) were born in Australia and 31% overseas (n=81). The most common language
spoken was English 93% (n=243) and other languages 7% (n=19).
Community HIV team members receive information from several sources: HIV specialist doctor, family doctor, emergency and/or hospital discharge letters, test reports, non-government organisations and the patient themselves. Thirty percent (n=78) of documented medical and social information was provided directly by the patient, 7% (n=18) from other services, 5% (n=13) from discharge plans. It was not clear who had provided the information for 34% (n= 89) of recorded data. Thirty percent (n=52) of documented information was classified as confirmed in that it was provided directly by the person’s family doctor, HIV specialist or transcribed directly during attendance at medical appointments.

**Missing Information**

Recorded data were found to be either missing or incomplete for several of the key data fields including HIV related information and co existing medical co morbidities. Table 1 shows that a large proportion of the audited patient records (up to 91%) had no documented evidence of predictors of HAND, for example, the nadir CD4+ T cell (91%, n=238) and current CD4+ T cell count (33%, n=87). Further, the duration of HIV diagnosis was missing in 22% (n=59) of the audited records.

Key documentation about social support was also incomplete. Data about informal caregivers was missing in 19% (n=50) of the clinical records, and information about sexual orientation and whether PLWH were living alone was missing in 8% (n=21) and 14% (n= 37), respectively.

<Table 1 here>

Table 2 shows that 76% (n=199) of PLWH receiving care during the four-week study period had been prescribed antiretroviral (ART) medications with confirmation of prescription of
ART by medical practitioner evident in 16% (n=32) of clinical notes. The actual ART drug prescribed was documented in only 53% (n=139) of the clinical notes examined during the study period, and was not recorded at all within 47% (n=123) of files.

Some ART drugs are known to have higher central nervous system penetration (CNS CPE) to cross the blood brain barrier and this is relevant to treatment success (Letendre, Ellis, Ances, McCutchan, 2010). Yet, no documentation of the calculated score for CNS CPE could be found in any of the eMR or paper-based medical records. Knowledge of which medications are prescribed is the basis of HIV care and could influence how clinicians review the patient in relation to monitoring for side effects, drug interactions, developing strategies to prevent or treat co-morbid conditions and for deciding when to change treatment.

**DISCUSSION**

This descriptive study aimed to ascertain whether community-based HIV health care providers were collecting necessary and sufficient information to identify patients at risk of HIV associated neurocognitive disorder and whether that documentation was complete.

The results show that a considerable amount of clinical and social information was not documented in the patient’s clinical notes or eMR. This finding calls into question the accuracy of assessment and implies that the signs and symptoms of HAND may not be being optimally reviewed or formally investigated, thereby impacting on the early diagnosis of this condition.

Whilst both interdisciplinary teams had access to an electronic record system, there was variance in how each team could document information into the eMR depending on which system that they had access to, and how external information was uploaded or transcribed.
into this system. A large amount of clinical information that is central to HIV care was not
documented, and often not confirmed by a medical practitioner. Specifically, key information
relating to the care of PLWH and the early identification of symptoms of HAND was
frequently not documented. Similarly, ART medications prescribed to treat HIV may be
modified to have a higher penetration across the blood brain barrier (Letendre, at al., 2010).
Although the audit revealed that many patients were currently prescribed ART medications,
documentation of the drug name and dose was frequently missing. As a basic tenet of care,
health professionals should be aware of which ART drugs the person is currently prescribed
in order to ascertain whether the regimen can or should be switched to that which has
improved CNS penetration.

As PLWH have complex health modalities and treatments, confirmation of information from
their medical practitioner is essential. Each team received information about patients from
varied sources and some information was secondary, being provided by reports from other
health professionals or agencies. Patients also provided much of the information themselves,
which may or may not be accurate. Up to 40% of information documented in the patient
records was unconfirmed by the patient’s practitioner. In addition, as HAND is a diagnosis of
exclusion, knowledge of other existing medical conditions, or the signs and symptoms of
these, is important (Nabha, Duong & Timpone, 2013) as some co morbid medical conditions
may mimic the signs and symptoms of HAND (Kamminga et al., 2013; Nightingale et al.,
2014). Confirmation of co morbid medical conditions by a medical practitioner was found in
only 16% of the audited records. Additionally, awareness of co morbid conditions in the
patient could lead to strategies being developed to reduce risk factors such as cardiovascular
disease. It is clearly important to ascertain permission during the initial assessment to contact
the patient’s doctor for access to health records, including a list of current medications.
Development of a process to regularly update and routinely audit information in the eMR would also be beneficial.

Awareness of the patients’ social circumstances is significant as PLWH may be socially isolated, may live alone and/or not have the support of an informal caregiver (Reuda et al., 2014; McDonald, et al., 2013; Grierson, et al., 2013). Limited awareness of social information may impact patient care as many PLWH could be experiencing mild signs and symptoms of HAND which may be attributed to other conditions such as ageing. This study found that patient living circumstances were not documented in 14% of clinical records included in the audit, and it was unknown from 19% of patient records whether PLWH had the support of a caregiver. Community HIV specialist teams may be crucial as initial observers of signs and symptoms which could be indicative of HAND, especially if the patient does not have an informal caregiver. This information is important for planning care and support, and for identifying which patients are at increased risk of developing HAND.

To broaden the utility of eMR data, case definitions must be specified and expanded to identify and characterize chronic conditions (Souri et al, 2017) such as HAND. Case definitions can also develop disease surveillance and health knowledge (Souri et al., 2017) and encourage a more efficient use of the eMR for PLWH. Collaborative data recorded by health professionals involved in a patient’s care can provide rapid feedback to the patient’s health team and specific information for the future development of case definitions relating to HAND. Furthermore, use of the eMR has already proven beneficial for case management of PLWH (Schnall, et al., 2011) and may allow the health care provider to develop individualized education for the PLWH (Schnall, et al., 2011) such as medication adherence, which is an important symptom of HAND.
Meaningful use of an eMR should result in improved coordination of patient centred care (Kokkonen, Davis, Lin, Debade, Felman, & Fleischer, 2003). Access to clinical information was identified as a problem for both teams. Both had access to hardcopy paper documents and a variant of an eMR, but patient data was held in several locations, causing difficulties in accessing information (Bowman, 2013) and the potential to lead to errors, lost documents and delays in decisions. Good communication is essential for providing optimal clinical care. The quality of documentation in the patient record is contingent on the accuracy and completeness of the information entered into the system by all staff involved in the person’s care. Access to clinical records is also vital for integrated shared care and improved understanding of the patients’ circumstances (NSW Health, 2013). Good documentation promotes efficiency, patient wellbeing, safety and continuity of care through shared clinical decision-making, leading to improved access to care through enhanced referral processes (NSW Health, 2013). The integrity, reliability and accuracy of documented health information is vital for the delivery of quality healthcare across the continuum (Bowman, 2013; Odlum et al., 2012).

Limitations

The audit of records was over a short period of time. The limitations of this study included that the teams used varied eMR systems, which prevented comparison of how information is uploaded to each system and how it is accessed by team members.

CONCLUSION

Complete documentation of the patient’s medical history, social circumstances, medications and current health would lead to increased awareness of potential risk factors and clinical indicators for HAND in PLWH and importantly, help to identify which patients require enhanced monitoring for HAND. Health care providers need to provide complete and verified documentation following their assessment and delivery of clinical care to PLWH to enhance
the sharing of accurate information between all health care providers involved in the patients care. The development of standardized and integrated data collection templates within eMRs would support regular assessment and monitoring.

Acknowledgements

We appreciate the support of lead team members Angela Langton and Matthew O’Rouke and all HIV team members for their generous contribution to accessing and collating data for the study and to Judith Fethney for assistance with statistical analysis.

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Conflict of interest

No conflict of interest has been declared by the authors.
REFERENCES


Table 1: Documentation of HIV and co-existing medical conditions

<table>
<thead>
<tr>
<th>HIV information</th>
<th>Documented % (n)</th>
<th>Not documented % (n)</th>
<th>Documented information confirmed by medical doctor % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4+ T cell Nadir</td>
<td>9% (24)</td>
<td>91% (238)</td>
<td>3% (8)</td>
</tr>
<tr>
<td>HIV viral load</td>
<td>64% (167)</td>
<td>36% (95)</td>
<td>13% (35)</td>
</tr>
<tr>
<td>Current CD4+ T cell count</td>
<td>67% (175)</td>
<td>33% (87)</td>
<td>15% (38)</td>
</tr>
<tr>
<td>HIV Duration</td>
<td>88% (203)</td>
<td>22% (59)</td>
<td>15% (38)</td>
</tr>
<tr>
<td>Co-existing medical condition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis C virus infection</td>
<td>78% (204)</td>
<td>22% (58)</td>
<td>16% (43)</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>59% (155)</td>
<td>40% (107)</td>
<td>16% (43)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>58% (152)</td>
<td>42% (110)</td>
<td>16% (43)</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>56% (146)</td>
<td>44% (116)</td>
<td>16% (43)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>48% (127)</td>
<td>52% (135)</td>
<td>16% (42)</td>
</tr>
</tbody>
</table>
## Table 2: Prescribed HIV medications

<table>
<thead>
<tr>
<th>Medication Information</th>
<th>Yes % (n)</th>
<th>No % (n)</th>
<th>Not documented % (n)</th>
<th>Documented information confirmed by medical doctor % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribed ART medications</td>
<td>76% (199)</td>
<td>15% (39)</td>
<td>9% (24)</td>
<td>16% (32)</td>
</tr>
<tr>
<td>Documentation of which ART medication</td>
<td>53% (139)</td>
<td>0% (0)</td>
<td>47% (123)</td>
<td>40% (105)</td>
</tr>
<tr>
<td>CNS CPE*</td>
<td>0% (0)</td>
<td>0% (0)</td>
<td>100% (262)</td>
<td>0% (n=0)</td>
</tr>
</tbody>
</table>

* central nervous system penetration score
CHAPTER SEVEN

Improving risk assessment for HAND

7.1 Overview and research question

Use of a risk assessment tool can enhance the clinical practice of HIV community-based teams to identify which PLHIV may be at risk of developing HAND and provide additional evidence at medical review. Phase 3 of this thesis was a modified Delphi study, in which a panel of experts guided the development of items for inclusion in an assessment tool to identify those at risk of HAND in a community setting.

This chapter presents the findings from a modified Delphi study to examine the final research question:

4. What assessment criteria are essential to identify those at risk of HAND in the community?

7.2 Major findings

More than 80% consensus was reached at each Delphi round for agreement on clinical and social information to include in a risk assessment tool to guide community based clinicians to assess PLHIV who may be at risk of developing HAND. The modified Delphi method permitted panel members to engage in decisions about Delphi rounds and concluded in the panel recommending the development of both an initial assessment and annual monitoring tool (with flow chart) for direct translation to community practice.
7.3 Conclusion

Known risk factors identified from the literature and new content from the findings of the earlier study phases was considered by panel experts to determine content for an initial risk assessment and an annual monitoring tool to monitor PLHIV for future changes in cognition which could be HAND. While not yet validated for clinical use, the initial tool is intended to be used as a precursor to formal medical assessment, with the purpose of annual monitoring to facilitate regular assessment for early formal medical review for this condition.

The risk assessment tools are a major outcome of the thesis. With the absence of published literature relating to the complexity of identifying HAND in PLHIV, the role of informal and formal caregivers, or the contribution of assessment by community based HIV teams, the studies performed for this thesis have resulted in the development of a consensus-based monitoring tool that after validation, could be used for the future assessment and early diagnosis of the approximately 20% of PLHIV who may develop HAND.

7.4 Statement from co-authors confirming authorship contribution of the PhD candidate

Chapter Seven is published as:


All authors made substantial contributions to editing and revising the manuscript.
As co-authors of the paper titled: “Assessing risk of HIV associated neurocognitive disorder: a modified Delphi study” We confirm that Denise Cummins made the following contributions:

i. Concept and design of the study;
ii. Collected, managed and analysed the data;
iii. Primarily responsible for the interpretation of results;
iv. Drafting, revising and writing up of the manuscript for submission to peer-reviewed journals.

All authors read and approved the final manuscript.

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<td></td>
<td>6.9.18</td>
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<tr>
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<td>10.10.18</td>
</tr>
</tbody>
</table>

In addition to the statement above as supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

Name                     Signature     Date       
Professor Donna Waters    06.08.2018
Title: Assessing risk of HIV associated neurocognitive disorder: a modified Delphi study

Abstract

Background:
People with HIV (PLHIV) are ageing and 20% are at risk of developing a neurological complication known as HIV associated neurocognitive disorder (HAND). Signs and symptoms of HAND may be subtle; however treatment can improve clinical outcomes.

Objective:
To identify and agree on a risk assessment and monitoring process for the regular review of patients at risk of HIV associated neurocognitive disorder.

Methods:
Between March and September 2017, twenty five experts from four community health care services participated in three rounds of a modified Delphi study to reach consensus on the items, monitoring period and format of assessment tools to identify risk of HAND in people living with HIV in the community.

Results:
More than eighty per cent consensus was reached at all three Delphi rounds. A flow chart, initial assessment and annual monitoring tool were developed for ongoing assessment of risk of developing HAND.

Conclusion:
Twenty per cent of PLHIV may develop HAND, a treatable condition. The use of a modified Delphi method led to the successful development of two risk assessment tools to identify those at risk of HAND. The initial assessment tool may be used as a precursor to formal assessment by medical and nursing staff, while the annual monitoring tool may assist community-based health professionals in their ongoing assessment of risk of HAND in PLHIV, facilitating early formal medical review for this condition.
Key words: Modified Delphi method, consensus, human Immunodeficiency virus, cognitive impairment, interdisciplinary teams
HIV is a chronic disease and as people living with HIV (PLHIV) age, they become susceptible to developing co-morbid conditions. Twenty per-cent of PLHIV globally are at risk of developing a subcortical neurodegenerative disease caused by HIV-1, known as HIV associated neurocognitive disorder (HAND) (Clifford & Ances, 2013). HAND is associated with morbidity and mortality in younger PLHIV and can cause various levels of disability (Skinner, Adewale, DeBlock, Gill, & Power, 2009). Cognitive changes attributable to HAND can be subtle and may become normalized by PLHIV (Gisslen, Price, & Nilsson, 2011; Cummins, 2014). These can include changes in language, memory, problem solving and slowing of psychomotor skills (Barber et al., 2014; Ghate, 2012). Early recognition is important as treatment of HAND offers opportunity for improved clinical outcomes for PLHIV (Robertson et al., 2007).

Risk factors for HAND include CD4+ T cell nadir count (lowest T cell count) (Ellis et al., 2011; Heaton et al., 2011); low CD4+ cell count (Schouten, et al., 2012; Heaton et al., 2011); current or past drug and alcohol use (Letendre, 2011; Elbert, et al., 2015), and hepatitis C co-infection (Schouten, et al., 2012). Additionally, knowledge of other co-morbid conditions impacting cognition (Nix & Tien, 2014) can add to poor neuropsychological performance, confounding the diagnosis of HAND (Nightingale et al., 2015; Kamminga, Cysique, Lu, Batchelor, & Brew, 2013). These include diabetes (Pinhero et al., 2016), cerebrovascular disease (Heaton et al., 2011; Tedaldi, Minniti, Fischer, 2015) and hypertension (Rodriguez-Penny et al., 2013; Tedaldi et al., 2015).

Lack of knowledge of risk factors, poor documentation of discussion during patient consultations (Cummins, Trotter & Murray, 2014) and difficulty locating patient information in electronic health records (Cummins, Waters, Aggar & O’Connor, 2015) all contribute to possible delays in the early recognition of risk of HAND in PLHIV. Although there are
several validated screening tools for HAND, none are universally applicable across all settings (Kamminga et al., 2013) and none are specific to community-based care, where the signs and symptoms of cognitive change may be observed by professional caregivers providing care to PLHIV in the home setting. Subsequently, a method for monitoring and collecting patient information over time could assist community-based health care professionals to identify PLHIV at risk of developing HAND or who are experiencing signs and symptoms of HAND which they may attribute to another cause.

The identification of HAND is multifactorial and complex. Therefore, a modified Delphi method was chosen to elicit the expert knowledge, varied viewpoints and rich experience of stakeholders to gain consensus on the development of risk assessment tools for use by community-based health professionals as a precursor to formal medical review (Hong et al., 2010). The Delphi method follows an iterative multi-stage process to combine opinion from a group of experts (termed ‘panel members’) into group consensus. Requirements for the expertise of Delphi panel members include knowledge and experience of the issues under investigation, willingness and time to participate and good communication skills (Adler & Ziglio, 1996). Individuals who are primary stakeholders with first-hand experience are targeted to elicit and enhance knowledge about the subject (Anderson & Schneider, 1993; Jones, 1974).

The selection of content or target issue presented to the Delphi panel is also important as it will translate directly to the quality of the results (Judd, 1972). There are no universally agreed guidelines for the Delphi method (Evans, 1997), and as such, flexibility exists in the design and applicability to the objectives of the study. In the traditional Delphi method, content for the first round is usually obtained from a literature review and further rounds
enable a number of individuals to provide their opinion anonymously, thus avoiding dominance of one person’s opinion (Boulkedid, Abdoul, Loustau, Sibony, & Alberti, 2011; Linestone & Turoff, 1978). Modifications to the traditional Delphi process occur when a hybrid of techniques are used, such as face to face meetings, using secondary data, or incorporating the qualitative views of participants (Keeney, Haason, & McKenna, 2006; Diamond et al., 2014; van Vliet et al., 2016; Eubank et al., 2016). In this study, use of a modified Delphi method facilitated experts in the field of HIV and HAND to contribute their knowledge and experience to the development of assessment and monitoring tools through both face-to-face and email communication rounds.

AIM
To achieve group consensus on the appropriate content of assessment tools to assist community based health professional to detect and monitor PLHIV at risk of developing HAND.

METHOD
The traditional Delphi method follows a series of structured “rounds” in which panel members examine the evidence to reach a consensus about the target issue (Keeney et al., 2006). Typically, panel members rate indicators of the target issue, and then ratings are compiled, summarized and distributed for review before the next round (Davies et al., 2011). Each panel member makes a judgement (often using a Likert or categorical scale) to agree or disagree with the issue under consideration and so determine consensus (Jones & Hunter, 1995). As part of the method, the responses from each round are fed back in summarized form to the participants who are then given an opportunity to respond again to the emerging data (Boulkedid et al., 2011). Commitment to participate in a multi-round Delphi method can be inferred by the round-by-round response rate (Keil, Tiwana, & Bush, 2002).
The modified Delphi method chosen for this study aimed to capture opinions from panel members utilising varied approaches to develop clinically relevant topic areas and questions for two risk assessment tools (initial and monitoring) for community-based teams caring for PLHIV. A literature review generated topic areas for consideration and was confirmed by the expert panel through three small group meetings; one large face-to-face meeting with all panel members present; and through the use of email communication. Each round of results led to the development of content for the next round.

**Expert panel members**

Criteria for selection of expert panel members was 1) health professionals who worked in a community setting, 2) who provided clinical care and support to PLHIV and 3) provided care for someone who had a diagnosis of HAND. It was anticipated that expert panel members would have the opportunity to provide opinion both as individuals, and as a group, following open and robust discussion of the issues at the face-to-face meeting at which all members were present.

Between March and September 2017, twenty five experts from four community health care teams based in the state of New South Wales, Australia, participated in three rounds of a modified Delphi study to reach consensus on the items, monitoring period and format of assessment tools to identify risk of HAND in PLHIV in the community. Staff from each service represent a diversity of clinical backgrounds and a range of experience in providing holistic patient centered care for PLHIV with complex care needs in the community. Panel members also work across a range of geographical areas (inner city, suburban and rural settings). One team offers a primary statewide service caring exclusively for PLHIV who
have a diagnosis of HAND and their informal caregivers. Two are interdisciplinary teams consisting of nurses, dietitians, physiotherapists, social workers and occupational therapists who provided care and support to PLHIV at home. The fourth service offers specialist HIV nursing support for PLHIV providing clinical care, assessment and referral of PLHIV with complex care needs related to HAND, mental health and substance abuse.

Literature review and consensus statement development

Medline, Cinahl and Embase databases were searched for full text English language publications offering high quality evidence for the selection of items for both the initial assessment and monitoring tools. Information was reviewed regarding risk factors for HAND, other co-morbid conditions which could mimic cognitive signs and symptoms not attributable to HAND but which may confound diagnosis of HAND, validated screening tools for HAND and relevant social factors that may increase complexity of diagnosis such as living alone. Topic selection was also discussed with medical and psychiatry experts, with selected topics presented to the panel for initial discussion around the development of consensus statements.

The definition of consensus for the Delphi method is varied and depends on the relative importance of an issue (Keeney et al., 2006). Lynn (1986) suggests that there should be at least ten participants when a target of 80% consensus is required to achieve content validity. For the purpose of this study, participants were made aware that a minimum of 80% consensus and interquartile range less than 2.5 (Kittell-Limerick, 2005) would be required to assess and determine agreement in any round. The study was approved by the local Human Research Ethics Committee. XXXXXXXXXXXX
**Round 1: Small group meetings**

The researcher met each of the four community-based health teams separately to discuss the background of the research study and the expectations of the Delphi method. Written information was provided with the participant consent form and there was an opportunity for participants to ask questions for further explanation or clarity. All team members (available pending annual and maternity leave) at each location agreed to participate as panel members for this study. A demographic survey was distributed at the small group meetings to collect information about the participant’s background and experience. Participants were made aware of the possibility of several Delphi rounds pending 80% consensus to reach agreement by panel members in order to accept the item; that the results of one round would inform the next round in a sequential process; and that feedback would be provided from the previous rounds.

Panel members were invited to consider several topics identified from the literature review to be included as subject areas for the development of questions for the assessment tools. Nine topic areas had been identified for consideration within the initial assessment tool, with five areas identified for the annual monitoring assessment tool. Experts could also provide comments and suggest additional topics to be considered for both tools. Presented in the form of a survey to the groups, members responded using a five-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = undecided, 4 = agree, 5 = strongly agree) to indicate their level of support for the topic areas. Panel members had up to two weeks to respond, with individually completed surveys returned anonymously to the researcher.
**Round 2: Large group meeting**

At Round 1, each service stated they would prefer a large group meeting for the next round to enable a more robust discussion from varied points of view and to minimise time constraints. Consensus data from Round 1 was summarized into two draft questionnaires: the initial and the annual risk assessments. Both drafts were reviewed by a medical expert for appropriateness, relevance and accuracy prior to the meeting. A draft flow chart was presented for panel members to consider the process needed to guide community-based professionals and/or variably experienced clinicians through the risk assessment process. The draft of the initial assessment tool had 41 questions/statements for consideration, and the annual monitoring tool had 12 questions/statements. Each panel member was given a paper copy of the assessment tools and questions were also presented on video screen. Following robust discussion, panel members were invited to consider each of the 53 individual statements/questions for both tools and indicate their agreement or disagreement of the item’s inclusion by a show of hands. Where there was disagreement or lack of consensus for a statement/question, open discussion was facilitated until consensus was reached of at least 80% of the group, or the statement/question was excluded.

**Round 3: Consensus statements**

Both tools were further revised and formatted to reflect Round 2 consensus agreement and sent via email to each panel member for individual review. As Round 2 was clearly not anonymous, Round 3 gave panel members an opportunity to independently and anonymously review the final draft documents and provide any further comments. It had been agreed in the large group meeting that if changes to the draft assessment tools were minimal, and if response exhaustion was reached at Round 3 with over 80% consensus, a further round (Round 4) would not be necessary. It was also agreed in Round 2 that five volunteers from
the group (each from a different clinical discipline) would pilot the initial assessment tool on one patient each (total of five people) to assess content and face validity, and record the length of time required to complete as the next stage of the study.

RESULTS
Twenty-five panel members from four community-based health services participated in a modified Delphi process to identify topics and agree on the final content of two assessment tools for patients at risk of HAND. The panel also elected to retain the summary flow chart presented during Round 2 as an aide to completion of the assessment tools, and agreed that the monitoring risk assessment should be conducted on an annual basis for PLHIV in the community. All 25 members participated in all three rounds. The response rate to surveys and questionnaires presented to the panel was 100% for each round. Response exhaustion was reached within three rounds.

Members of the expert panel had a mean age of 45 years and all had completed some type of higher education. Some participants had been working within their specific health disciplines for up to 33 years (mean 16 years) and had been employed in their current position providing care to PLHIV for up to 16 years (Table 1).

Results of the first Delphi round revealed more than 80% agreement from panel members for eight of the nine topic areas identified from the literature to be included in the initial risk assessment tool (Table 2). As questions about legal issues attained only 60% agreement from the panel, this topic area was excluded from the initial assessment tool content for consideration in Round 2. The five subject areas considered by the expert panel for inclusion in the annual monitoring risk assessment tool reached 100% consensus as shown (Table 2).
The face-to-face meeting for Round 2 lasted two hours and included further discussion about omitting questions related to legal issues. Panel members collectively agreed that incorporating legal issues relating to last will and testament, living will and guardianship would be confronting for patients at the time of an initial risk assessment and unlikely to make a significant contribution to the overall risk identification of HAND. All agreed (100% consensus) that a flow chart would be a beneficial adjunct to guide risk assessment, especially for new or inexperienced staff. Panel members were concerned about the length of time to complete the initial risk assessment containing 41 items and requested mapping to avoid repetition of routinely collected patient information such as date of birth, gender and past health conditions. There was debate regarding the necessity of asking the PLHIV about their living circumstances, finances and quality of life. Group consensus was that knowledge of whether a person lived alone and/or had limited informal supports could impact on the observation of signs and symptoms indicative of cognitive change. While two panellists indicated they felt uncomfortable asking, these questions were retained.

Round 2 also offered opportunity for the panel to agree on a preferred format for the risk assessment tools. While some panel members suggested the shorter annual monitoring tool could be used for both initial and annual reviews, the majority of panel members agreed that the collection of baseline clinical and other information from the initial assessment would be useful for ongoing comparison at patient follow-up. At the end of Round 2, more than 80% consensus had been reached on the content and format of a flow chart, an initial assessment and annual risk monitoring tool for the detection of risk of HAND in PLHIV. The email distribution of the three draft documents to each panel member following Round 2 prompted
only one response to change wording from ‘Do you have housing issues’ to ‘Do you have stable housing’?

As 100% consensus had been achieved after three rounds of the Delphi process, the content and face-validity of the initial risk assessment tool is currently being trialed. While some group members were concerned about how long it would take to complete the initial risk assessment with a patient, early results from the pilot study suggest this can be achieved in 18 – 20 minutes.

DISUSSION

Early identification of HAND in PLHIV is important as clinical intervention may have a positive impact on changes to cognition. With minimal evidence pertaining to the role of community-based health professionals identifying PLHIV at risk of HAND, the researchers believe this to be the first application of a modified Delphi process to develop HAND risk assessment and monitoring tools for providing community-based care to PLHIV.

More than 80% consensus was reached for all but one topic area included in the final version of both the initial and annual assessment tools. Panel members thought that asking patients about legal issues such as their last will and testament could be confronting for the patient, and this line of question was not considered appropriate for an initial assessment. Some thought this question was appropriate at a later date, whilst others did not feel they had sufficient skills to discuss this with their patients. As this was the only item initially identified by the literature review that was excluded, it raises a question about when and how such conversations are currently occurring. Further training in legal issues around end of life may
be beneficial for professional caregivers, especially those who are inexperienced or feel uncomfortable discussing end of life with a patient. The home environment is often a more comfortable, supportive environment for patients to ask questions and reflect on what is important to them. Additionally, this environment may provide greater opportunity to discuss cognitive rehabilitation with the patient and their caregiver.

The professional caregiver is in a unique position to observe for signs and symptoms of HAND while providing care in the home or community. Early results from piloting the initial risk assessment tool with patients has staff noting the value of collecting relevant information pertaining to HAND in a single document that gives an overall picture of the person. Information documented in an initial risk assessment is thereafter available as a comparison for annual monitoring of cognitive changes as the PLHIV ages, and raises awareness of co-existing medical conditions and risk factors such as smoking. As PLHIV are an ageing population, knowledge of their personal social circumstances is also significant for their community-based care. Some PLHIV may have minimal informal support from caregivers who would usually be best placed to notice subtle changes in their cognition (Murray et al., 2016). A regularly visiting professional caregiver, with detailed knowledge of the personal circumstances of the PLHIV, may therefore be the only alternative observer of changes in cognition whilst providing care in the home.

It has been shown that panel involvement in developing guidelines is a predictor of successful implementation in a clinical setting (Hong et al, 2010). The modified Delphi method chosen for this study (Keeney et al., 2006; Diamond et al., 2014; van Vliet et al., 2016; Eubank et al., 2016) permitted panel members to have ownership of the outcome of each round. The full retention of all panel members during each round may be an indicator of their commitment to
PLHIV, their interest in the subject area and/or the need for resources to support their work. Their working relationship with the researcher may also have influenced the retention of panel members. The face-to-face meetings provided a forum to openly debate issues, while any actual or perceived bias from dominant group members was able to be addressed by providing individuals with further opportunities to forward individual comments via email. Consensus methods such as the Delphi method have high face validity. As both the initial assessment and annual monitoring tool record medical and social information, each could be modified for implementation in local environments.

**Limitations**

The selection of experts from four HIV services in only one state of Australia could be considered a limitation of this study, however, it is equally important in a Delphi method to include participants with experience of the specific health condition and key population.

Lack of anonymity in face-to-face meetings may have limited contribution, obliged members to conform to discussion or allowed some participants to dominate the group. Validity may also have been compromised when panel members changed their view due to discussion and strong opinions expressed in the face-to-face meeting. This was managed by asking other panel members to explicitly consider the question from another point of view to illicit further discussion. Additionally the researcher attempted to minimise any bias following the large group meeting by sending final drafts via individual email to give each panel member as an opportunity to provide further (anonymous) comment.

**Conclusion**
A modified Delphi process was used to develop an evidence and consensus-based initial risk assessment and annual monitoring tool for PLHIV at risk of developing HAND. The risk assessment aims to facilitate early referral to formal medical review if risk factors are present, and to document relevant social and health information for PLHIV. The Delphi method was successful in identifying and achieving consensus from experts about what information is required to improve clinical care and risk assessment for PLHIV in the community. A flow chart or guideline to accompany the tools was also retained for ease of use.

The initial risk assessment and annual monitoring tool developed in this study may also have utility for health professionals with limited knowledge of the risk factors or signs and symptoms of HAND. The tools can be used in different clinical or geographical settings, as patient information collected at baseline (the initial risk assessment) remains useful alone or as a comparison at annual follow up. Once face and content validity of the tools has been established through the current pilot study, the next step is to implement the use of both tools as a routine standard of care in personalised electronic health records. This will provide an opportunity for the affected PLHIV to undergo regular monitoring and early referral for medical review, with the potential for early diagnosis and treatment if cognitive changes indicative of HAND are found.

Acknowledgments

Thanks to the panel members who participated in this study. Thank you to Mr. Michael Smith for his ongoing support to this study. Thanks to medical and psychiatric doctors for reviewing the draft documents.

REFERENCES


Ghate, M. (2012). Neurocognitive studies in HIV infected individuals in India. *Nari Bulletin*

National AIDS Research Institute (ICMR), 3 (2), 5-7


This flow chart is a guide for multidisciplinary clinicians to use when initiating assessment of the PLHIV who may be at risk of developing HAND.

- **Screening by multidisciplinary staff**
  - (initial or annual monitoring risk assessment tool)

- **Outcome of screening**
  - (nothing/monitor/refer to nurse/Occupational therapist (OT) for further assessment)

- **Assessment by nurse/OT**
  - (additional assessments e.g. mental health screen/activities of daily living)

- **Outcome of nurse/OT review**
  - (nothing/monitor/referral to medical doctor for review)

- **Outcome of medical review**
  - (nothing/monitor/radiological test/neuropsychological test/change medications); documentation in patient file
Table 1: Demographic profile of Delphi participants

<table>
<thead>
<tr>
<th>Participants in Delphi study</th>
<th>N=25</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (range)</td>
<td>45 years (34 - 59 years)</td>
<td>21 (84)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing 4 (16)</td>
</tr>
<tr>
<td>Educational qualification</td>
<td>Masters Degree</td>
<td>17 (68)</td>
</tr>
<tr>
<td></td>
<td>Bachelor of Arts</td>
<td>5 (20)</td>
</tr>
<tr>
<td></td>
<td>Bachelor of Science</td>
<td>2 (8)</td>
</tr>
<tr>
<td></td>
<td>Graduate Diploma</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Health Discipline</td>
<td>Nurse</td>
<td>9 (36)</td>
</tr>
<tr>
<td></td>
<td>Social worker</td>
<td>6 (24)</td>
</tr>
<tr>
<td></td>
<td>Dietician</td>
<td>4 (16)</td>
</tr>
<tr>
<td></td>
<td>Occupational therapist</td>
<td>3 (12)</td>
</tr>
<tr>
<td></td>
<td>Psychologist</td>
<td>2 (8)</td>
</tr>
<tr>
<td></td>
<td>Counselor</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Mean years working in discipline (range)</td>
<td>16 years (6 - 33 years)</td>
<td></td>
</tr>
<tr>
<td>Mean years in current position (range)</td>
<td>6 years (1 month- 16 years)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Initial and annual assessment topics from Round 1

<table>
<thead>
<tr>
<th>Topics selected for Initial assessment tool</th>
<th>n=25</th>
<th>&gt;80% agreement</th>
<th>Average rating (Scale 1 – 5)</th>
<th>Median (Scale 1 – 5)</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for referral</td>
<td>24/25</td>
<td>96%</td>
<td>4.56</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Social information</td>
<td>24/25</td>
<td>96%</td>
<td>4.48</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>HIV information</td>
<td>24/25</td>
<td>96%</td>
<td>4.72</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>General health information</td>
<td>24/25</td>
<td>96%</td>
<td>4.64</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Mental health</td>
<td>25/25</td>
<td>100%</td>
<td>4.60</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Medication issues</td>
<td>24/25</td>
<td>96%</td>
<td>4.72</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Legal issues</td>
<td>14/25</td>
<td>60%</td>
<td>3.30</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Questions for the patient</td>
<td>24/25</td>
<td>96%</td>
<td>4.64</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Documentation of the outcome of the assessment</td>
<td>24/25</td>
<td>96%</td>
<td>4.64</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Topics selected for Annual monitoring tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes in health in last 12 months</td>
</tr>
<tr>
<td>Changes in social circumstances in last 12 months</td>
</tr>
<tr>
<td>Cognitive changes in last 12 months (noted by patient)</td>
</tr>
<tr>
<td>Cognitive changes in last 12 months (noted by informal caregiver/partner if present)</td>
</tr>
<tr>
<td>Documentation of changes and outcome assessment</td>
</tr>
</tbody>
</table>
Chapter 8

Conclusions, recommendations and dissemination of knowledge

Background

This final chapter discusses the overall findings of this thesis. The discussion is sequenced in accordance with the phased methodology chosen to answer the research questions and discusses of the overall strengths and limitations of the study phases, the significance of findings to practice, and conclusions for future recommendations. The chapter concludes with a proposal for additional contributions to the evidence-base for the improved community care of PLHIV who may be at risk of HAND.

8.1 INTRODUCTION

The absence of an evidence base informing the experience of PLHIV, the role of their informal and formal caregivers, and the contribution of community health care teams to identifying those at risk of HAND was a significant impetus for this thesis. This lack of published literature also determined the pragmatic approach and explanatory sequential design that was selected.

The significance of this thesis is evidenced by the publication of four peer-reviewed research papers already contributing evidence to address this gap in the literature. The acceptance of a range of oral and poster presentations describing the approach and outcomes of the thesis at national and international research conferences outlined at the end of this chapter is further
evidence of the contribution this research has already made in closing some of the existing gaps in knowledge for the broader HIV communities and caregivers.

8.2 SUMMARY OF FINDINGS

Despite searching back to literature published at the beginning of the AIDS epidemic in the 1980s, few studies had explored the personal experiences of PLHIV and their caregivers with regard to HAND. Even fewer studies exist to inform whether or how PLHIV and their caregivers might actually identify the signs and symptoms of HAND, and if so, what they could or would do with this information to facilitate early diagnosis, intervention and treatment to reduce the prevalence and severity of this condition.

Anecdotal conversations with PLHIV in clinical practice had prompted the candidate to collaborate in the development of a self-assessment booklet titled *HIV associated MND: How to recognise signs and symptoms* (Totter & Cummins, 2008) more than 10 years ago. The booklet outlined various statements and questions relating to cognitive change for PLHIV to reflect upon and to consider in their therapeutic encounters with health professional caregivers. This led the candidate to conduct the preliminary pilot study, in which PLHIV were asked to retrospectively reflect on their experience of signs and symptoms that may be indicative of HAND within the context of a prospective observational multi-site study. Informal caregivers were also invited to participate in this study, as it was identified that they may they have unique insights into the experiences of PLHIV and are well placed to provide a more complete picture as observers of the daily functioning and experiences of PLHIV who they live with or care for.
A pragmatic methodological approach using an explanatory sequential design with mixed method studies was chosen in an attempt to unravel the complex insights and experiences of PLHIV, and their informal and professional caregivers regarding their experiences of HIV associated Neurocognitive Disorder (HAND). The explanatory sequential design aimed for representation of the multiple realities and viewpoints of PLHIV and their caregivers by building on the emerging results of each study phase to generate research questions from the specific experiences of the participants to enrich understanding and provide a more complete picture of the complex phenomenon that is HAND.

8.2.1 PLHIV and their informal caregivers can identify HAND

PLHIV are an ageing population. The mean age of the 121 participants contributing to the preliminary pilot study was 49 years, and similar to anyone who is ageing, were at a same or greater risk of developing a range of other age-related health conditions, including HAND. Forty per cent of participants in the preliminary study lived alone and only 36% nominated a caregiver for the study. Of the small purposive sample, 61% percent of participants and 57% of caregivers identified more than four signs and symptoms of cognitive change. As a result of this study, 16 of the 121 participants were referred for neuropsychological examinations and four were subsequently diagnosed with HAND. Significantly, all four showed an improvement in cognition after changes to their medication regimes.

This study not only showed that PLHIV were indeed able to identify signs and symptoms of cognitive impairment, but also enabled some PLHIV who otherwise may not have been identified to be referred for early neuropsychological assessment and treatment. Results from the preliminary pilot study indicated that both caregivers and PLHIV could identify HAND and in fact, the self-reflection of PLHIV and the observations of their informal caregivers was
instrumental to some participants being referred for further investigation and the eventual diagnosis of HAND. Others were identified for ongoing monitoring, which similarly, may have not happened otherwise. As HAND remains largely a diagnosis of exclusion, it is clear that PLHIV and their informal caregivers can play an important part in the identification of signs and symptoms. In the absence of informal caregivers, this role may fall to community or other health professionals who are in regular contact, but only if these formal caregivers are aware of and apply the essential assessment criteria required to identify those at risk of HAND in the community.

8.2.2 PLHIV and their caregivers have experience of HAND

The preliminary pilot study was conducted with a small cohort of purposively selected participants from one city (Sydney) in Australia. However, determining that this group of PLHIV and their caregivers could identify the signs and symptoms of HAND led to consideration of whether awareness and experience of HAND was also present among a broader population of PLHIV? A workshop with PLHIV and caregivers attending an international HIV conference facilitated by the candidate in 2014 had also indicated that there was concern about HAND, but workshop participants were unclear who to approach about their concerns and what to do about them. Following the conference, a ‘think tank’ was held with local experts and community HIV organizations (Cummins, Waters, Aggar, Crawford, & O’Connor, 2017). This led to the development of an online survey in partnership with Positive Life NSW, a peak peer organization in Australia, to explore whether PLHIV are aware of and/or concerned about HAND, or whether PLHIV were experiencing signs and symptoms of cognitive changes and/or observing them in others.
While the number of participants in the Phase 1 study was similar to the pilot, the sample included a broader and more diverse group of respondents living across Australia and showed that overall, these participants were also aware of HAND, and more than half expressed concern about it. As in the preliminary pilot study, PLHIV were experiencing signs and symptoms which may be related to HAND and as previously reported by Cohen et al., (2015), some PLHIV in this study had begun to experience signs and symptoms of HAND in their mid-40’s. A perhaps unsurprising finding was that those who had been living with HIV for a longer period were more likely to have knowledge or experience of HAND in themselves or others.

A common sign of non-HIV dementia is the decreased ability to organize (Clifford & Ances, 2013). Results from the online survey revealed a statistically significant association between the duration of HIV infection and self-reporting of a decreased ability to organize things. This symptom has potential to impact on many self-care activities for PLHIV such as regular attendance at medical reviews, personal care and hygiene, medication supply and adherence, and activities of daily living (Cody & Vance, 2016). In addition to affecting general health, losing the ability to organize may also increase HIV infectivity if, for example, the person is not regularly taking cART medication, consequently has a higher HIV viral load, and is possibly engaging in high risk sexual behaviour.

8.2.3 Resources for communication

An unexpected finding of the Phase 1 study was that many of the PLHIV who were concerned about HAND also expressed anxiety about discussing this subject with others. They expressed fear for the future and loss of mental capacity and independence – despite many receiving a positive response when they had raised the subject of HAND. Many
respondents had also noticed changes in cognition among peers in their social networks, but generally did not feel comfortable to talk to their friends directly about this.

As almost one-third of the 126 respondents in Phase 1 indicated that additional resources about HAND would be helpful to facilitate discussions with formal and informal supports, this could be one relatively simple and cost-effective solution for reducing fear and apprehension and to promote education for the early identification of HAND. Resources that offer information about HAND and provide suggestions for how to discuss the condition with both formal and informal supports may help alleviate the concerns of PLHIV, as fear about a diagnosis of HAND has been associated with a delay in seeking help (Chambers et al., 2015; Gagnon, 2015). Additionally, some PLHIV have experienced stigma and discrimination in their past and are fearful of stigma in their future (Karamouzian, Akbar, Haghdooost, Setayesh, & Zolala, 2014; Skinner & Mfecane, 2004). If PLHIV have concerns about HAND, and are fearful of possible stigma and discrimination, they may be less likely to access medical care (WHO, 2008). As an additional outcome of this study, two resources were developed, and focus tested with PLHIV who have a diagnosis of HAND, and these are available online and in print (Appendix Two). Following focus testing of both resources and further discussions with PLHIV, a specific support group for PLHIV with HAND was established. The current group is facilitated by social workers.

8.2.4 Contribution of professional caregivers

Findings from the preliminary pilot and Phase 1 studies have already contributed to increasing knowledge and awareness of HAND. In addition to offering further resources for communication within and between PLHIV and their caregivers, HIV community teams in NSW have also started implementing individual care plans for PLHIV who have noticed that
declining organizational skill is affecting their ability to maintain activities of daily living. These findings also prompted the candidate to consider the situation of PLHIV who do not have the support of an informal caregiver, or those whose informal support is at distance, for example, living in another city or state and/or those who live alone. These considerations highlight the advantage of using pragmatism as a paradigm for this thesis, as emerging data allowed for further exploration of the phenomenon and influenced the direction of the next phase of the study which was to ask whether professional caregivers could act as an alternate to an (absent) informal caregiver in identifying cognitive change in PLHIV at risk of HAND?

The proposition, therefore, was that HIV community teams are also uniquely placed to identify those PLHIV who are at risk of HAND based on their access to current and past medical history, awareness of the persons’ social circumstances and daily functioning, and observation of the home environment over time. As PLHIV had indicated in the online survey that they were concerned about HAND, the next phase aimed to determine what measures HIV community teams were using to identify which PLHIV in their care were at risk of developing HAND. HIV community teams record their clinical care and assessments in various electronic medical record (eMR) systems and hard copy patient records. Evidence for the proposition that professional caregivers could make a contribution to observing for cognitive change in PLHIV, and identify other risk factors for HAND, might therefore be recorded in these patient records.

However, the results of the Phase 2 study clearly showed that a considerable amount of clinical and social information was not documented in the patient’s clinical notes or eMR. Information about risk factors for HAND was incomplete in every single patient record.
audited for the study, and further, was predominantly from a secondary source (often the patient) or unconfirmed (by copies of test results or by the patient’s doctor).

This finding calls into question the accuracy of documentation and comprehensive assessment by professional caregivers and implies that the signs and symptoms of HAND may not be being optimally reviewed or formally investigated, thereby impacting referral for early medical review and possible diagnosis. Complete and accurate documentation is essential, as PLHIV who have stable HIV health may only be monitored every four to six months by their HIV prescriber and a HIV community team member. This is possibly the only regular opportunity for professional caregivers to observe for cognitive changes and to record evidence of health maintenance or decline. Further, integrated models of care rely on the sharing of patient assessment information, which does not currently appear complete.

8.2.5 Improving risk assessment for HAND

As the Phase 2 study had shown that HIV community teams were collecting limited and incomplete information on PLHIV in their care, the question of how to improve assessment to identify those at risk of HAND in the community was a logical next step. Using knowledge gained from the previous study phases, it was proposed that improving the awareness of risk factors for HAND among both informal and formal caregivers could be achieved through better communication and screening for specific clinical and social factors indicative of risk.

The expert Delphi panel assembled for the Phase 3 study were easily able to reach consensus on essential assessment criteria to identify those at risk of HAND in the community. The panel also recommended that assessment criteria be presented as an initial risk assessment screening tool to collect baseline medical and social information, with further identification of items to include for annual monitoring. The initial assessment tool was proposed as a
precursor to formal assessment by medical and nursing staff, while the annual monitoring tool was proposed to assist community-based health professionals in their ongoing assessment of risk of HAND in PLHIV, facilitating early formal medical review for this condition.

Therefore, an initial risk assessment screening tool and an annual monitoring tool were also major outcomes from this thesis. These tools were developed using essential assessment criteria recommended by the expert panel who collectively contributed their significant experience of working in a community setting with PLHIV, and with those who have a diagnosis of HAND. The risk assessment tools developed from this study are designed to have utility for health professionals with limited knowledge of the risk factors or signs and symptoms of HAND and as requested by the expert panel, are accompanied by a flow chart to guide clinicians through the assessment process (Appendix Four).

8.3 STRENGTHS AND LIMITATIONS

This work has highlighted the importance of supporting PLHIV and their caregivers to identify HAND and each of the study phases has contributed to improving understanding and knowledge about the experience of PLHIV and the complexity of diagnosing HAND. A background of only 12 identifiable studies published over the past 28 years describing the experiences of HAND among PLHIV and their informal and professional caregivers determined the need for a pragmatic approach to this thesis. The choice of an explanatory sequential design using mixed methods allowed for emerging findings to drive the research direction across three study phases but had both strengths and limitations. The first two studies required participants to be able to read and speak English. This was a limitation of
these studies which failed to represent the views of PLHIV who may not read and write in English, or those who are unable to access online resources. Future research would need to include translation of written material to other languages (such as for developing resources for communication about HAND and online surveys) and access to interpreters.

Fundamental to the development of this thesis was first establishing whether PLHIV and their informal caregivers could actually identify some of the signs and symptoms of HAND. In the absence of a background literature, it could not be assumed that in asking research questions about HAND, people living with HIV and/or their caregivers knew what they were being asked about. The preliminary pilot study was completed at three clinical sites, offering the initial viewpoints of PLHIV and their informal caregivers from locations across the city of Sydney. The clinics were a stand-alone inner-city HIV clinic, an inner-city sexual health clinic and a suburban hospital immunology clinic. The preliminary pilot study was designed to follow the HIV positive patient through their usual standard of care at the clinic they attended. Designed as an observational study, there was no HIV-negative matched comparison group. The self-assessment questionnaire (booklet) had been developed specifically for the observational study and had not been validated. The researchers relied on their own professional judgement and incidental anecdotal evidence from caring for PLHIV to nominate which of the four or more signs and symptoms of cognitive decline identified from the booklet were to be made aware to medical staff – in other words, the team collectively determined their own criteria for referral. Following the usual standard of clinical care, a small number of PLHIV were referred for formal neuropsychological testing, with four subsequently being diagnosed with HAND. Further analysis was unable to be completed due to the purposive sampling method and small participant numbers. However, the intention of this preliminary pilot study was to gain a snapshot of data and foundational knowledge
where none previously existed. This pilot study was instrumental in influencing the subsequent direction of the thesis to explore the complexity of HAND.

The Phase 1 online survey was able to utilize the broader profile of Positive Life NSW to target a wider population of PLHIV to give voice their experiences and concerns about HAND. Limitations of this study were the equity of access to an online survey offered through a social media account and the three week timeframe during which the survey was open. While this undoubtedly influenced the survey response rate, the candidate was required to comply with the schedule of the host of the online platform. The researchers made a decision to only recruit via this method as other methods of recruitment would have required many ethics submissions to a broad range of organizations possibly yielding only small numbers of participant’s through each. Although this sample size was also small, responses were received from across Australia. Small numbers within some sub-samples may have affected statistical results, however, this was the rationale for also reporting effect sizes. It is entirely possible that survey respondents who had a specific interest or concern about HAND were over-represented in the sample. Survey questions did not request respondents to quantify the period of time related to their experience of signs and symptoms of HAND and did not ask about stigma. Additionally, those without access to a computer or computer skills were presumably excluded from completing the survey online.

The file audit of records from Phase 2 was completed over a short period of time (one month). Other limitations of this study included that each service used different eMR systems, which prevented a comparison of how information is uploaded to each system and how health professionals access it. However, the formal caregivers (health professionals) from the two HIV community teams in Sydney whose file documentation was audited have
extensive clinical experience providing clinical care and support to PLHIV and were very open to improving their service. Additionally, participation by both teams in the file audit allowed for comparison and combination of data. All data were de-identified prior to being analysed by the candidate and none were shared with any third party.

The selection of experts who participated in the modified Delphi study were from four HIV services and included formal caregivers from Phase 2 who were committed to providing further insights and improvements in service delivery to PLHIV. As Delphi participants were all from one state of Australia (New South Wales), this could be considered a limitation of this study, however, it is equally important to the Delphi method that selected participants have relevant experience of the specific health condition and key population. As the State with the largest population of PLHIV, and as members of the original services developed more than 30 years ago to care for people with HIV in Australia, panel members were drawn from the unique statewide (NSW) service (AIDS Dementia and Psychiatric HIV Service). This service has more than 20 years of experience in providing care, support and case management to PLHIV with cognitive impairment and therefore, panel members were likely representative of Australian HIV experts.

Lack of anonymity in the face-to-face Delphi meetings may have limited participant contribution, obliged members to conform to the discussion, or allowed some participants to dominate the group. Validity may also have been compromised when panel members changed their view due to discussion or strong opinions expressed in the face-to-face meeting. This was managed by asking other panel members to explicitly consider the question from another point of view to illicit further discussion. Additionally, the candidate attempted to minimise bias following the second large group meeting by sending the final
drafts of agreed items for the screening and monitoring tools via individual email addresses to give each panel member an opportunity to provide further (anonymous) comment.

8.4 SIGNIFICANCE OF FINDINGS

HIV-Associated Neurocognitive Disorder is associated with significant morbidity and mortality for people living with HIV and can cause various levels of disability. Because HAND is a potentially treatable condition, the early identification of signs and symptoms is important for prompt diagnosis and the opportunity to reduce prevalence and severity (Skinner et al., 2009). However, the identification and diagnosis of cognitive impairment is complex and multifactorial, and as identified in Chapter 2, the diagnosis of HAND is often achieved by excluding other conditions (Nabha et al., 2013). Further, as PLHIV age, they are similarly at increased risk of developing comorbid conditions. Regular engagement with HIV community teams could provide greater opportunity to develop strategies to detect and manage co-morbid conditions such as diabetes and cardiovascular disease which may further impact their cognitive health. For those diagnosed with HAND, HIV community teams can provide case management services. These teams are also beneficial for PLHIV who have complex health needs in addition to HAND and can develop individual cognitive rehabilitation strategies for the assimilation of health and social support services.

The findings of this thesis strongly support the important role of informal and professional caregivers in providing valuable insights into the physical, social and emotional wellbeing of PLHIV. As such, these findings support the work of others (McDonald, Elliott, & Saugeres, 2013), who concluded that informal and professional caregivers can notice changes in behaviour or within the home environment of PLHIV which may have otherwise gone unnoticed. Informal caregivers have been shown to have a positive impact on the health of
PLHIV (Uchino, 2004). In addition to supporting the management of symptoms of cognitive change, informal caregivers assist by arranging and/or escorting the PLHIV to medical and clinic appointments and facilitating medication management and adherence, thereby contributing to the potential for early review for the diagnosis and treatment of HAND. Further, some PLHIV may lack insight into cognitive changes they are experiencing as these changes may be subtle or assumed to be due to morbidity associated with ageing. For others, informal caregivers may live some distance from the person and so the level of support may be limited (Schnall et.al, 2018).

If the PLHIV does not have the regular support of an informal caregiver, professional caregivers based in the community setting can act as an alternative in their absence. Professional caregivers can observe cognitive risk factors for HAND, however, the results of the Phase 2 study clearly show that these health professionals may need further support to conduct regular assessment of significant and essential risk criteria. Furthermore, for those PLHIV in a relationship, where both are HIV positive and both at risk of developing HAND, the support of a professional caregiver could act as a sentinel to any changes. There are approximately 26,444 PLHIV in Australia (Kirby, 2017), of whom an estimated 20% are at risk of developing HAND. This equates to approximately 5,288 PLHIV in Australia developing HAND. Early intervention, diagnosis and treatment are important and can have a profound impact on the health and wellbeing of PLHIV and the coordinated delivery of their health services. Raising awareness of HAND among PLHIV, and their informal and formal caregivers, may improve identification of those PLHIV at risk of developing HAND.

The findings of studies within this thesis have also noted that communication about HAND may be an issue; both between PLHIV and their informal and professional caregivers, and
between health service professionals. The development of two specific resources about HAND was an additional outcome of the thesis. The resources are now in circulation (including online) and aim to provide information to the community and open a dialogue about cognitive decline in PLHIV. The file audit noted poor documentation in the clinical notes of PLHIV which is likely to be impacting integrated care and the possible health outcomes of PLHIV. Strategies have been developed locally to improve documentation by the HIV community teams involved and communicated more broadly via the publication in Chapter Six and in conference presentations as below.

Finally, an initial risk assessment tool and annual monitoring tool have been developed for HIV community teams and others to use in community or other settings to identify which PLHIV may be at risk of HAND and require referral for early assessment. It is anticipated that with development of this form for electronic medical record formats, annual monitoring of changes in social circumstances, clinical indicators and cognition can be readily reviewed by health professionals to detect early signs and symptoms of cognitive decline. This is especially relevant to PLHIV who live alone and do not have the support of an informal caregiver who might normally observe daily changes in cognition, or in the situation where two PLHIV live together and may both be at risk of developing HAND.

8.5 CONCLUSION

This study has provided new knowledge pertaining to PLHIV and their informal and professional caregivers’ experiences of identifying and communicating about HAND. The practical significance of this study is that as PLHIV age they may experience mild signs and symptoms of cognitive impairment that could be HAND. Early identification and diagnosis is essential, as HAND is a potentially treatable condition (Skinner et al., 2009).
The personal experiences of PLHIV and their informal caregivers should be considered by professional caregivers when assessing the person. This is not only a central tenet of person-centred care, but informal caregivers of PLHIV may have their own experience to share and can provide unique insights into the daily social and physical functioning of those they care for. Improvements in communication and documentation would provide a more complete picture of the circumstances of PLHIV and facilitate better integration (and likely efficiency) of care. If the PLHIV does not have the support of an informal caregiver and/or lives alone, professional caregivers are also well placed to observe for cognitive changes. A HAND risk assessment and annual monitoring tool has been developed by clinical experts to identify PLHIV at risk of HAND and enable early referral and diagnosis.

8.6 RECOMMENDATIONS

The following initiatives and strategies arising from the findings of this thesis are recommended for future implementation in HIV community services within New South Wales:

1. To acknowledge and include the personal experiences of PLHIV and their informal caregivers’ in clinical assessment as both can contribute valuable insights to aid in the early diagnosis of HAND;

2. To assess all patients with HIV with an initial risk assessment tool and complete an annual follow up using a monitoring tool;
3. To make the risk assessment tools developed as part of this thesis freely available on the electronic medical record systems of public health services so these become a best-practice standard of care for HIV community-based teams;

4. To increase awareness of cognitive decline in PLHIV by providing a copy of the HAND resource from Positive Life NSW to all PLHIV and their informal caregivers before or at their initial risk assessment;

5. To use the risk screening process as an opportunity to support PLHIV with personal health strategies to reduce the detrimental effects of co-morbid conditions and provide case management to those with HAND if needed;

6. To provide focused monitoring for PLHIV who do not have support of an informal caregiver &/or live alone.

8.7 RECOMMENDATIONS FOR FURTHER RESEARCH

Future research should consider the inclusion of PLHIV and informal caregivers from non-English speaking backgrounds and invite PLHIV to contribute to the prioritization, design and development of future projects as co-researchers. Other recommendations for future research include:

- A longitudinal study to document the prevalence and incidence of HAND as PLHIV age in the local population, including common risk factors and signs and symptoms;

- A longitudinal study of outcomes from using the initial risk assessment tool and annual monitoring tool with all patients engaging community-based HIV services to develop a streamlined pathway for referral for formal review of cognitive changes which may be HAND;
• Exploration of stigma and discrimination related to the development and diagnosis of HAND and whether this affects future access to health and social care;
• Exploration of advanced care planning among PLHIV diagnosed with HAND;
• Design and evaluation of a cognitive rehabilitation program for PLHIV with HAND;
• Assessment of informal and professional caregiver’s knowledge relating to HAND to design specific education for these groups.

8.8 DISSEMINATION OF KNOWLEDGE

In addition to publications, findings from the preliminary pilot study and subsequent three study phases reported in this thesis have been peer-reviewed and accepted for presentation at the following national and international conferences during the period of candidature:

1. Australian Primary Health Care Nurses Association 10th Annual Conference
10-12 May 2018, Brisbane, Australia (Poster presentation)

_How can nurses identify the experience of cognitive impairment for people living with HIV, leading to early diagnosis? Cummins D, Waters D, Aggar C, O’Connor C, C._

2. 17th Alzheimer’s Biennial National Dementia Conference
18-20 October 2017, Melbourne, Australia (Oral poster presentation)

_Development of assessment tools for HIV community based health care professionals to detect people living with HIV who may be at risk of HIV associated neurocognitive disorder (HAND). Cummins D, Waters D, Aggar C, O’Connor C, C._

3. 39th Australasian Society for the Study of Brain Impairment (ASSBI) Conference
Where to next? Developing resources to assist people living with HIV associated Neurocognitive Disorder (HAND). Crawford D, Cummins D, Waters D, Aggar C, O’Connor C, C.

4. 4th Asia Pacific Global Summit & Expo on Healthcare
18-20 July 2016, Brisbane, Australia (Oral presentation)
Are current assessment protocols capable of identifying people at risk of HIV associated cognitive impairment? Cummins D, Waters D, Aggar C, O’Connor C, C.

5. 14th Social Research Conference on HIV, Viral Hepatitis and Related Diseases
31 March-1 April 2016, Sydney, Australia (Oral presentation)
“Losing Part of me”. Cummins D, Waters D, Aggar C, O’Connor C, C.

Report from survey data for NSW Ministry of Health available at:
At the Research Reports/ Submission page

7. 6th International HIV and Ageing Conference
6-7 October 2015, Washington DC, USA (Poster presentation)
Recognition of cognitive impairment by community health professionals to identify at risk patients for referral and assessment. Cummins D, Waters D, Aggar C, O’Connor C, C.

8. 26th Annual Conference of the Australasian Society for HIV Medicine
16-18 September 2015, Brisbane, Australia (Two oral poster presentations; one poster presentation)

**HIV associated neurocognitive impairment: A developing concern?** Cummins D, Waters D, Aggar C, O’Connor C, C.

*A patient self-assessment tool to recognise signs and symptoms of HIV cognitive impairment.*

Cummins, D, Murray, K, Trotter, G, Batterham, M, O’Connor, C, C.

**Is it important what information we collect? The mystery of the missing data.** Cummins, D, Waters D, Aggar C, O’Connor C, C.

9. **23rd Annual Conference of the Australasian Society for HIV Medicine**

26-28 September 2013, Canberra, Australia (Poster presentations)

“It’s not in the notes”. Cummins D, Murray K, Trotter G,

*Does the caregiver notice mild cognitive impairment?* Cummins D, Murray K, Trotter G, Batterham, M, O’Connor, C, C.
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APPENDICES

Appendix One:
Preliminary study: Ethics approval including participant information, participant consent; one year follow up participant information. All related documents: participant questionnaire, demographic survey, medication chart and Booklet “HIV associated mild neurocognitive disorder”

Appendix Two:

Appendix Three:
Phase 2 ethics approval, participant information, participant consent form; copy of file audit items.

Appendix Four:
Phase 3 ethics approval, Delphi information sheet; participant information; participant consent (health professional and client); Health professional demographic survey; Likert scale (for initial and monitoring tools); Initial risk assessment tool, annual monitoring tool, and flow chart for HAND assessment; Pilot survey for health professional
Appendix One
24 February 2011

Mr G Trotter
Department of Clinical Immunology
Level 10 West 1, Building 75
Royal Prince Alfred Hospital

Dear Mr Trotter,

Re: Protocol No X10-0354 & HREC/10/RPAH/618 - “A Prospective observational multi-site study, to validate the usefulness of a client self assessment tool (HIV-Associated MND-Mild Neurocognitive Disorder) leading to possible early medical intervention and support for HIV positive clients with mild signs of cognitive impairment in an outpatients setting”

The Executive of the Ethics Review Committee, at its meeting of 3 February 2011, considered your correspondence of 24 January 2011. In accordance with the decision made by the Ethics Review Committee, at its meeting of 8 December 2010, ethical approval is granted.

The proposal meets the requirements of the National Statement on Ethical Conduct in Human Research.

This approval includes the following:

- Information for Participants (Master Version 2, 5 January 2011)
- Participant Consent Form (Master Version 2, 6 January 2011)
- Participant Demographic Questionnaire (Master Version 3, 6 January 2011)
- Time Guide (Master Version 2, 5 January 2011)
You are asked to note the following:

- This letter constitutes ethical approval only. You must NOT commence this research project at ANY site until you have submitted a Site Specific Assessment Form to the Research Governance Officer and received separate authorisation from the Chief Executive or delegate of that site.

- This approval is valid for four years, and the Committee requires that you furnish it with annual reports on the study’s progress beginning in February 2012.

- This human research ethics committee (HREC) has been accredited by the NSW Department of Health as a lead HREC under the model for single ethical and scientific review and is constituted and operates in accordance with the National Health and Medical Research Council’s National Statement on Ethical Conduct in Human Research and the CPMP/ICH Note for Guidance on Good Clinical Practice.

- You must immediately report anything which might warrant review of ethical approval of the project in the specified format, including unforeseen events that might affect continued ethical acceptability of the project.

- You must notify the HREC of proposed changes to the research protocol or conduct of the research in the specified format.

- You must notify the HREC and other participating sites, giving reasons, if the project is discontinued at a site before the expected date of completion.

- Where appropriate, the Committee recommends that you consult with your Medical Defence Union to ensure that you are adequately covered for the purposes of conducting this study.

Should you have any queries about the Committee’s consideration of your project, please contact me. The Committee’s Terms of Reference, Standard Operating Procedures, membership and standard forms are available from the Sydney South West Area Health Service website.

A copy of this letter must be forwarded to all site investigators for submission to the relevant Research Governance Officer.

The Ethics Review Committee wishes you every success in your research.

Yours sincerely,

Lesley Townsend
Executive Officer
Ethics Review Committee (RPAH Zone)
Mr Garry Trotter  
10 West 1 Ambulatory Care  
Level 10 Royal Prince Alfred Hospital  
Missenden Rd  
CAMPERDOWN NSW 2050

Dear Mr Trotter,

Lead HREC Reference: HREC/10/RPAH/618  
SSA Reference: SSA/11/LPOOL/203  
Local Reference: 11/131

Title: A prospective observational multi-site study, to validate the usefulness of a client self assessment tool (HIV-Associated MND-Mild Neurocognitive Disorder) leading to possible early medical Intervention and support for HIV positive clients with mild signs of cognitive impairment in an outpatients setting.

Thank you for submitting an application for authorisation of this project.

I am pleased to inform you that the Chief Executive has granted authorisation for this study to take place at the following site(s):

- Liverpool Hospital

The participant documents approved for use at this site are:

- Participant Information Sheet: Site specific for Liverpool Hospital, Version 1.1, 19th October 2011  
  BASED on MASTER Information for Participants, Version 2.0, 5th January 2011

- Consent Form: Site specific for Liverpool Hospital Version 1.1, 5th July 2011  
  BASED on MASTER Consent Form, Version 2.0, January 2011

The following conditions apply to this research project. These are additional to those conditions imposed by the Human Research Ethics Committee that granted ethical approval:

1. All reference made to SSWANS or SWILH should be replaced to South Western Sydney Local Health District throughout the documents.
2. Change complaints email address from john.caro@swlahs.nsw.gov.au to research.support@swlahs.nsw.gov.au.
3. Proposed amendments to the research protocol or conduct of the research which may affect the ethical acceptability of the project, and which are submitted to the lead HREC for review, are to be submitted to this office.
4. Amendments to the research protocol or conduct of the research which may affect the ongoing ethical acceptability of the project, are to be submitted to this office.
5. Please note that you are responsible for making the necessary arrangements (e.g. identity pass; signed confidentiality agreement and vaccine compliance as per NSW Health Policy Directive PD2011_005) for any researcher who is not employed by the South Western Sydney Local Health District and is conducting the research on-site.

Yours sincerely,

Merofa Ghazal  
Acting Coordinator Ethics & Research Governance
Ethics & Research Governance Office  
South Western Sydney Local Health District (SWSLHD)  
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A prospective observational multi-site study, to validate the usefulness of a client self
assessment tool (HIV-Associated MND-Mild Neurocognitive Disorder) leading to possible
early medical intervention and support for HIV positive clients with mild signs of cognitive
impairment in an outpatients setting

INFORMATION FOR PARTICIPANTS

Introduction:

You are invited to take part in a research study to validate the effectiveness of a self
assessment resource for HIV positive clients to enable identification of early signs of
cognitive impairment. If found useful, such a resource would enable people to discuss these
issues with their HIV clinician, who may then suggest further investigation. The study will
also help identify the incidence of early signs of cognitive impairment amongst people who
are HIV positive.

The study is being conducted within this institution by:

1. Mr Garry Trotter - Clinical Nurse Consultant HIV/AIDS, RPAH.
3. Dr O’Connor RPAH Sexual Health Service.
4. Ms L Healey Social Worker RPAH Sexual Health Service.
5. Mr Ken Murray-Clinical Nurse Consultant HIV/AIDS, Liverpool Hospital.

Study Procedures:

If you agree to participate in this study, you will be asked to sign the Participant Consent
Form.

The study involves completing a short demographic questionnaire at the clinic and then
taking a short booklet home to read about issues concerning memory and the ability to
function on a day to day basis. As well, you can elect to ask someone close to you, such as a
family member or close friend, for their objective opinion on your mental functioning, but
this is entirely up to you and is not compulsory.

You will be contacted at home by a nurse from the clinic about 2 weeks after this booklet is
given to you for your answers and/or you may elect to have a face to face discussion with
your nurse. If you elect to have help from a friend or relative you will need to give the
investigator permission to contact them and/or you may elect for the person to accompany
you to the interview.

MASTER Information for Participants, Version 2, JANUARY/05/2011
RPAH Information for Participants, Version 1, 10/03/2011
In addition, the researchers would like to have access to your medical record to obtain information relevant to this study.

Risks:

There are no risks to completing this study.

Benefits:

We intend that this research study furthers medical knowledge and may improve treatment of mild neurocognitive impairment in the future, and we believe that it will be of direct benefit to you.

Costs:

Participation in this study will not cost you anything, nor will you be paid.

Voluntary Participation

Participation in this study is entirely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason. Whatever your decision, please be assured that it will not affect your medical treatment or your relationship with the staff who are caring for you. Of the people treating you, only those named above and your treating Doctor will be aware of your participation or non-participation.

Confidentiality

All the information collected from you for the study will be treated confidentially, and only the researchers named above and your treating doctor will have access to it. The study results may be presented at a conference or in a scientific publication, but individual participants will not be identifiable in such a presentation.

Further Information

When you have read this information, Mr Garry Trotter will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact him on: (02)95158814 or Phone RPAH on: 95156111 and ask for Page: 88388.
This information sheet is for you to keep.

Ethics Approval and Complaints

This study has been approved by the Ethics Review Committee (RPAH Zone) of the Sydney Local Health Network. Any person with concerns or complaints about the conduct of this study should contact the Executive Officer on (02) 9515 6766 and quote protocol number X10-0354.

MASTER Information for Participants, Version 2, JANUARY/05/2011
RPAH Information for Participants, Version 1, 10/03/2011
A prospective observational multi-site study to evaluate the usefulness of a client self
assessment tool (HIV-Associated MND-Mild Neurocognitive Disorder) leading to possible early
medical intervention and support for HIV positive clients with mild signs of cognitive impairment
in an outpatient setting.

PARTICIPANT CONSENT FORM

I, .................................................................................................................... (Full Name)

Of .................................................................................................................. (Address)

Have read and understand the Information for Participants on the above named research study and
have discussed the study with ..........................................................................

I have been made aware of the procedures involved in the study, including any known or expected
inconvenience, risk, discomfort, or potential side effect and of their implications as far as they are
currently known by the researchers.

I understand that my participation in this study will allow the researchers and others, as described
in the Information for Participants, to have access to my medical record, and I agree to this.

I freely choose to participate in this study and understand that I can withdraw at any time.
I also understand that the research study is strictly confidential.
I hereby agree to participate in this research study.

NAME: ..............................................................................................................

SIGNATURE: ....................................................................................................

DATE: ..............................................................................................................

NAME OF WITNESS: ......................................................................................

SIGNATURE OF WITNESS: .............................................................................

Please photocopy signed form
STAGE TWO

This is the next stage of the study you enrolled in: “A prospective observational multi-site study to evaluate the usefulness of a client self assessment tool (HIV-Associated MND-Mild Neurocognitive Disorder) leading to possible early medical intervention and support for HIV positive clients with mild signs of cognitive impairment in an outpatient setting.”

Instructions:

Once again you need to read the statements and just tick the box next to the statement you agree with. Remember when you are doing this to think about any changes in the last 12 months.

I freely choose to participate in this study and understand that I can withdraw at any time.
I also understand that the research study is strictly confidential.
Neurocognitive Impairment Study - Check list for staff

If clients are ineligible for the study, please record the number corresponding to relevant exclusion criteria as listed below.

Exclusion Criteria:
1. Newly diagnosed
2. Pre existing cognitive impairment
3. Those in social chaos
4. Those with poor English language skills
5. Those affected by drugs or alcohol
6. Those with current untreated depression (may become eligible once depression is treated)

Clients agreeing to participate in the cognitive impairment study need to be given:

1. Form 1: Ethics. □

2. They need to sign Form 2: Consent. □

3. They need to complete Form 3: Demographic information. □

4. They need to complete as much as possible of Form 4 & Form 5: □
   clinical/medications information.

5. Then clinicians’ place completed paperwork into Nicky’s drop down. □

NB: **Clients need to leave with a booklet for themselves and one for a carer (if applicable). Client will be contacted by a staff member in 2 weeks to go through booklet. Carer will be contacted in 1 week to confirm participation in the study.
FORM 4:

Clinical/Demographic Information

Age
How long HIV positive
Current Viral load
Current T cell count
Nadir

HIV Medications:
Current drugs (see form 5)
Last change in medication regimen (Year)
How long on HIV medications
Date of last change in medications (Month/Year)

Current:
HCV □ Yes □ No
Hypertension □ Yes □ No
Antihypertensive medications □ Yes □ No
Hypercholesterolaemia □ Yes □ No
Hyperlipidemia □ Yes □ No
Sleep apnoea □ Yes □ No
Diabetes □ Yes □ No
CPL score

Past:
History of CNS Disease □ Yes □ No

Updated 03/02/2012
## FORM 5: CURRENT ANTIRETROVIRAL MEDICATIONS

**Date:**  
[ ]___/___/___  

**Tick box of current medications:**  

### NNRTI  

<table>
<thead>
<tr>
<th>Nevirapine</th>
<th>Efavirenz</th>
<th>Entravirine</th>
</tr>
</thead>
</table>

### NRTI/NtRTI  

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<thead>
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<th>AZT</th>
<th>Combivir</th>
<th>DDI</th>
</tr>
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<tbody>
<tr>
<td>Emtricitabine</td>
<td>Kivexa</td>
<td>Lamivudine</td>
<td>Stavudine</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Trizivir</td>
<td>Truvada</td>
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### Protease Inhibitors  

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<tbody>
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<td>Kaletra</td>
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<td>Tipranavir</td>
</tr>
</tbody>
</table>

### Entry Inhibitors  

| Fuzeon | Maraviroc |

### Integrase Inhibitors  

| Raltegravir |

### Combined Classes  

| Atripla |

**CHANGE IN MEDICATIONS**

**Date:**  
[ ]___/___/___  

**Which drugs:**  
1.  
2.  
3.  
4.  

**NB:** **Medications to be entered onto sheet 3 of Excel.**  

*Updated 03/02/2012*
HIV-Associated MND
(Mild Neurocognitive Disorder)

How to recognise the signs and symptoms
Now that effective treatments for HIV are available, there has been a steady decline in the number of people with HIV-related dementia. However, between 30% to 60% of people with HIV may get much milder mental symptoms, known as mild neurocognitive disorder (MND), from the virus.¹

Regardless of your HIV blood results (viral load and CD4 count) you may be at risk of MND. This is because the virus can have a toxic effect on the brain, and unfortunately not all of the drugs used to treat HIV penetrate the brain equally.

MND is NOT dementia, and is potentially very treatable.

Many people are worried that mild mental problems will develop into dementia. However, for the majority of people this will not happen. But it is still important that you identify the symptoms of MND in its early stages rather than ignore them and hope they’ll go away.

These symptoms develop gradually. You may think you are well, but as the changes are not sudden they can be difficult for you to immediately identify.

Also, some of the signs of MND can be misread as depression, getting older or being more stressed. In some cases, it is only when you and your partner, family or friends look back that these subtle changes are obvious.
Don’t Panic!

Simply be aware of any changes in your mental state so that you can get effective treatment early.

If you notice any changes in your mental abilities, even if you don’t think they are really important, you should talk to your healthcare professional.

In a short routine appointment you may not be asked about your mental health, so bring this subject up if you have any concerns at all.

Following are some questions you can ask yourself

You may need to think carefully about your answers and look back over time to see if you have noticed any changes.

Sometimes these changes are very slow and subtle, so it may help to ask people who know you well if they have also noticed any changes.
• Do you have to concentrate more to get the same things done?
• Are you slower at doing usual tasks?
• Are you feeling more mentally under pressure that usual?
• Do you find you are less accurate with tasks than in the past?
• If you get distracted in the middle of doing a task, do you find it difficult to return to it?
• Do you get more distracted than in the past and then forget what you were going to say next?
• Have you or others noticed that sometimes you go off at a tangent in conversations?
• Do you find that you sometimes need to re-read information to understand it?
• Is it more difficult to do several things at once, such as watching TV and having a conversation at the same time?
- Have you noticed you don't go out socially as much as you used to?
- Do you have a reduced interest in social things?
- Are you less socially motivated that you used to be?
- Are you less talkative in conversations?
- Are you now more irritable with others?
- Does it take more effort to concentrate on conversations, with your mind sometimes wandering?
- Do people find you are less expressive than you used to be?
• Do you find it more and more difficult to remember things, such as appointments or taking your medications?
• Do you find you can’t quite remember something, although it is on the tip of your tongue?
• Have you noticed an increase in losing track of what you were going to do, such as walking into a room but forgetting why you went there?
• Have you found you are losing track in conversations?
• Do you more frequently lose things such as your mobile phone, keys or forget where you parked the car?
• Do you need to use a diary or electronic reminders more often than in the past to remind you of appointments?
• Are you now more likely to forget special days, like birthdays?
• Are you making more mistakes at work, such as forgetting to return phone calls or getting the times of meetings mixed up?
• Do you use reminder notes more than you used to?
• Do you find that sometimes you have difficulty doing up buttons or buckles?
• Are your keyboard skills not as good as they used to be?
• Are you more clumsy than normal?
• Has your driving got worse?
• Have you noticed that your writing has become messier? Has there been a change in your signature?
• Do you trip more often?

• Are you now putting off important tasks?
• Do you find that you are more tired, both mentally and physically, by the end of the day?

If you have answered Yes to a number of these questions, then you should speak to your regular healthcare professional about your concerns. Further inquiries or tests may need to be made, as there are other possible reasons for these symptoms aside from HIV.
Handy Hints if you’re diagnosed with HIV-Associated MND

✓ Allow more time to do tasks to avoid time pressures
✓ Do tasks in shorter bursts of time
✓ If you are getting tired or losing concentration, stop what you are doing, have a break and come back to it
✓ Focus on one task at a time
✓ Break problems down into smaller parts before you think about them
✓ Make lists to remind you of things to be done
✓ Use memory aids, such as a diary or electronic reminders for things you need to do or a medication box for your tablets
✓ Take notes in meetings, of conversations and important information you need to remember
✓ Pre-prepare notes for discussion in meetings or appointments
✓ If possible, try to establish routines
✓ Try to plan activities ahead of time
✓ Take time and more care with physical tasks, such as driving
✓ Discuss these issues openly with your healthcare professional
Checking responses to booklet.

After reading the booklet are there some changes you have noticed when you look back over time? Sometimes these changes are very slow and subtle. Let's go through the booklet...

Concentration
- Do you have to concentrate more to get the same things done?
- Are you slower with usual tasks?
- Are you feeling more mentally under pressure?
- Do you find you are less accurate with tasks than in the past?
- If you get distracted in the middle of doing a task do you find it difficult to return to it?
- Do you get more distracted and then forget what you were going to say next?
- Have you or others noticed that sometimes you go off at a tangent in conversations?
- Do you find that you sometimes need to reread information to understand it?
- Is it more difficult to do several things at once? (such as watching TV and having a conversation at the same time)

Social
- Have you noticed you don't go out socially as much as you used to?
- Do you have a reduced interest in social things?
- Are you less socially motivated than you used to be?
- Are you less talkative in conversations?
- Are you now more irritable with others?
- Does it take more effort to concentrate on conversations, with your mind sometimes wandering?
- Do people find you are less expressive than you used to be?

Coordination
- Do you find that sometimes you have difficulty doing up buttons or buckles?
- Are you more clumsy than normal?
- Has your driving got worse?
- Have you noticed that your writing has become messier? Has there been a change in your signature?
- Are your keyboard skills not as good as they used to be?
- Do you trip more often?
Memory

- Do you find it more and more difficult to remember things such as appointments or taking your medications?
- Do you find you can’t quite remember something although it is on the tip of your tongue?
- Have you noticed an increase in losing track of what you were going to do? (walking into a room but forgetting why you went there)
- Have you found you are losing track in conversations?
- Do you more frequently lose things such as mobile phone, keys or forget where you parked the car.
- Are you needing to use a diary more than in the past to remind you of appointments?
- Are you now more likely to forget special days like birthdays?
- Are you making more mistakes at work such as forgetting to return phone calls and getting the times of meetings mixed up?
- Do you use reminder notes more than you used to?

Coping

- Are you now putting off important tasks?
- Do you find that by the end of a day you are more tired both mentally and physically?

Thank you
Appendix 2
6 February 2014

Ms D Cummins
Redfern Health Centre
103-105 Redfern Street
REDFERN NSW 2016

Dear Ms Cummins,

Re: Protocol No X13-0314 & HREC/13/RPAH/426 - “HIV associated cognitive impairment: client characteristics and professional caregiver experiences”

The Executive of the Ethics Review Committee, at its meeting of 30 January 2014, considered your correspondence of 10 January 2014. In accordance with the decision made by the Ethics Review Committee, at its meeting of 11 December 2013, ethical approval is granted.

The proposal meets the requirements of the National Statement on Ethical Conduct in Human Research.

This approval includes the following:

- NEAF (AU/1/9224110)
- Information for Participants (Clients) (Master Version 4, 10 January 2014)
- Participant Consent Form (Clients) (Master Version 2, 10 January 2014)
- Information for Participants (Professional Caregivers) (Master Version 4, 10 January 2014)
- Participant Consent Form (Professional Caregivers) (Master Version 2, 10 January 2014)
6 February 2014

Ms D Cummins
Redfern Health Centre
103-105 Redfern Street
REDFERN NSW 2016

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- Information for Participants (Professional Caregivers) (Master Version 4, 10 January 2014)
- Participant Consent Form (Professional Caregivers) (Master Version 2, 10 January 2014)
• Stage 1: File Audit (Master Version 4, 10 January 2014)

• Stage 2: Professional Caregiver Interview (Master Version 3, 10 January 2014)

• Stage 3: Client Interview (Master Version 3, 10 January 2014)

You are asked to note the following:

• This letter constitutes ethical approval only. You must NOT commence this research project at ANY site until you have submitted a Site Specific Assessment Form to the Research Governance Officer and received separate authorisation from the Chief Executive or delegate of that site.

On the basis of this ethics approval, authorisation may be sought to conduct this study within any NSW public health organisation and/or within any private organisation which has entered into an appropriate memorandum of understanding with the Sydney Local Health District, Sydney Local Health Network or the Sydney South West Area Health Service.

The Committee noted that authorisation will be sought to conduct the study at the following sites:

• Redfern Health Centre, SLDH
• Darlinghurst Community Health Centre, SESLHD

• This approval is valid for four years, and the Committee requires that you furnish it with annual reports on the study’s progress beginning in February 2015. If recruitment is ongoing at the conclusion of the four year approval period, a full re-submission will be required. Ethics approval will continue during the re-approval process.

• This human research ethics committee (HREC) has been accredited by the NSW Department of Health as a lead HREC under the model for single ethical and scientific review and is constituted and operates in accordance with the National Health and Medical Research Council’s National Statement on Ethical Conduct in Human Research and the CPMP/ICH Note for Guidance on Good Clinical Practice.

• You must immediately report anything which might warrant review of ethical approval of the project in the specified format, including unforeseen events that might affect continued ethical acceptability of the project.

• You must notify the HREC of proposed changes to the research protocol or conduct of the research in the specified format.

• You must notify the HREC and other participating sites, giving reasons, if the project is discontinued at a site before the expected date of completion.
• If you or any of your co-investigators are University of Sydney employees or have a conjoint appointment, you are responsible for informing the University’s Risk Management Office of this approval, so that you can be appropriately indemnified.

• Where appropriate, the Committee recommends that you consult with your Medical Defence Union to ensure that you are adequately covered for the purposes of conducting this study.

Should you have any queries about the Committee’s consideration of your project, please contact me. The Committee’s Terms of Reference, Standard Operating Procedures, membership and standard forms are available from the Sydney Local Health District website.

A copy of this letter must be forwarded to all site investigators for submission to the relevant Research Governance Officer.

The Ethics Review Committee wishes you every success in your research.

Yours sincerely,

[Signature]

Lesley Townsend
Executive Officer
Ethics Review Committee (RPAH Zone)

HERC\EXCOR\14-02
REDfern Health Centre
Denise Cummins
Clinical Nurse Consultant
Sydney District Nursing Service

May 12th 2015

To whom it may concern

Re: Protocol No X13-0314 & HREC/13/RPAH/426- "HIV associated cognitive impairment: client characteristics and professional caregiver experiences"

I would like to request an amendment to the above study. I would like to distribute a survey via a HIV Non Government Organisation, Positive Life (PosLife). The aim of the survey is to ascertain People Living with HIV thoughts on HAND.

This would provide additional background information for the above study. Pos Life is a key HIV agency in NSW and staff will distribute the survey via Monkey Survey to their clients.

Please find attached a copy of the survey questions for your consideration. Please do not hesitate to contact me if you have any questions. Thank you.

Regards

Denise Cummins

Redfern Health Centre
103 – 105 Redfern Street, Redfern NSW 2016
Tel 012 5390 0444 Fax 012 9930 1678

Sydney Local Health District
ABN 17 520 269 052
Level 11 North, King George V Building
83 Missenden Rd
CAMPERDOWN, NSW, 2050
Tel 012 9515 9930 Fax 012 9515 9910
Email: sldn.ssw@elwealth.nsw.gov.au
Website: www.health.nsw.gov.au/sydhndh/
1 May 2014

Mr Matthew O'Rourke
SES LHD HIV Outreach Team
301 Forbes Street
Darlinghurst NSW 2011
ATTENTION: Denise Cummins

Dear Mr O'Rourke

RE: SSA Ref: 14/G/122
HREC / AURED Ref: HREC/13/RPAH/426
Project Title: HIV associated cognitive impairment: client characteristics and professional caregiver experiences

I refer to your Site Specific Assessment application for the above titled project. I am pleased to advise that on 30 April 2014, the Director of Operations – Planning and Population Health granted authorisation for the above project to commence at the HIV Outreach Team – Darlinghurst Health Centre.

The following conditions apply to this research project. These are additional to any conditions imposed by the Human Research Ethics Committee that granted ethical approval:

1. Proposed amendments to the research protocol or conduct of the research which may affect the ethical acceptability of the project, and are submitted to the lead HREC for review, are copied to the Research Governance Officer.

2. Proposed amendments to the research protocol or conduct of the research which may affect the ongoing site acceptability of the project are to be submitted to the Research Governance Officer.

If you have any queries relating to the above please contact the Research Support Office on (02) 9382 3587.

Yours sincerely

[Redacted]

Robert Smallcombe
Research Governance Officer

Prince of Wales Hospital
Community Health Services
Randwick NSW 2031

5/777 25/0711
5 May 2014

Ms D Cummins
Redfern Health Centre
103-105 Redfern Street
REDFERN NSW 2016

Dear Ms Cummins,

Re: Protocol No X13-0314 - “HIV associated cognitive impairment: client characteristics and professional caregiver experiences”

HREC/13/RPAH/426 SSA/14/RPAH/70

Thank you for submitting a Site Specific Assessment Form for this study. I am pleased to inform you that authorisation has been granted for it to be undertaken at the Redfern Health Centre.

The approved information and consent documents for use at this site are:

- Information for Participants - Clients (Redfern Health Centre Version 1, 12 February 2014) based on Master Version 4, 10 January 2014
- Participant Consent Form - Clients (Redfern Health Centre Version 1, 12 February 2014) based on Master Version 4, 10 January 2014
- Information for Participants - Professional Caregivers (Redfern Health Centre Version 1, 12 February 2014) based on Master Version 4, 10 January 2014
- Participant Consent Form - Professional Caregivers (Redfern Health Centre Version 1, 12 February 2014) based on Master Version 4, 10 January 2014

The following conditions apply to this research study. These are additional to those conditions imposed by the human research ethics committee (HREC) that granted ethical approval:

1. Proposed amendments to the research protocol or conduct of the research, which may affect the ethical acceptability of the study and which are submitted to the lead HREC for review, must be copied to me.
2. Proposed amendments to the research protocol or conduct of the research, which may affect the ongoing site acceptability of the study, must be submitted to me.

I wish you every success in your research.

Yours sincerely,

[Redacted]

Lesley Townsend
Research Governance Officer
SLHD (RPAH Zone)

RGO - Lesley/CORRES/X13-0314
REDFERN HEALTH CENTRE
Denise Cummins
Clinical Nurse Consultant
Sydney District Nursing Service

May 12th 2015

To whom it may concern

Re: Protocol No X13-0314 & HREC/13/RPAH/426- “HIV associated cognitive impairment: client characteristics and professional caregiver experiences”

I would like to request an amendment to the above study. I would like to distribute a survey via a HIV Non Government Organisation, Positive Life (PosLife). The aim of the survey is to ascertain People Living with HIV thoughts on HAND.

This would provide additional background information for the above study. Pos Life is a key HIV agency in NSW and staff will distribute the survey via Monkey Survey to their clients.

Please find attached a copy of the survey questions for your consideration. Please do not hesitate to contact me if you have any questions. Thank you.

Regards

Denise Cummins

103 – 105 Redfern Street, Redfern NSW 2016
Tel 012 9390 0444 Fax 012 9890 1678

Sydney Local Health District
ABN 17 520 269 052
Level 11 North, King George V Building
83 Missenden Rd
CAMPERDOWN, NSW, 2050
Tel 012 9315 9630 Fax 012 9315 9610
Email: shn:ssw@swhhs.nsw.gov.au
Website: www.health.nsw.gov.au/sydhnhr
3 July 2015

Ms D Cummins
Redfern Health Centre
103-105 Redfern Street
REDFERN NSW 2016

Dear Ms Cummins,

Re: Protocol No X13-0314 & HREC/13/RPAH/426 - “HIV associated cognitive impairment: client characteristics and professional caregiver experiences”

The Executive of the Ethics Review Committee, at its meeting of 23 June 2015 considered your correspondence of 12 May 2015 and gave its approval of the following:

- Survey for Positive Life (Master Version 1, 12 May 2015)

Yours sincerely,

Sharon Falleiro
Executive Officer
Ethics Review Committee (RPAH Zone)

HERC/EXECOR/15-06
HIV associated cognitive impairment: client characteristics and professional caregiver experiences.

INFORMATION FOR PARTICIPANTS- HIV Service Sector Providers

Introduction

You are invited to take part in a research study into HIV associated cognitive impairment: client characteristics and professional caregiver experiences.

The objective is to investigate whether the relationship with a professional caregiver and/or the experience of case management has a positive effect on the person with HIV associated cognitive impairment. There are some people living with HIV (PLHIV) who do not have a personal caregiver who is able to notice changes in a person’s behaviour which may be signs and symptoms of Minor Neurocognitive Impairment. The relationship with a professional caregiver may be an alternate, as this person is well placed to provide support for investigation of any behaviour change.

The study is being conducted within this institution by:

1. Ms Denise Cummins Clinical Nurse Consultant, Community Health, SLHD.
2. Ms Angela Langton, Acting Manager Positive Central, SLHD.
3. Mr Matthew O’Rourke, Clinical Nurse Consultant HIV Outreach Team, SESLHD.

This study is a component of the requirements for a higher degree at the University of Sydney under the supervision of Associate Professor Donna Waters, Dr Christina Aggar, University of Sydney and Associate Professor Catherine O’Connor, Director of RPA Sexual Health, SLHD.

Study Procedures

If you agree to participate in this study, you will be asked to sign the Participant Consent Form.

You will then be asked to take part in an interview with Denise Cummins. During the interview you will be asked about your opinions, knowledge and experiences of HAND and your relationship with your client. The interview will be audio-recorded and is expected to last between 30 and 60 minutes.

Benefits

While we intend that this research study furthers medical knowledge and may improve the care of PLHIV in the future, it may not be of direct benefit to you.

Costs

MASTER Information for Participants, Version 1, 18/08/2014
Participation in this study will not cost you anything, nor will you be paid.

Voluntary Participation

Participation in this study is entirely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason.

Confidentiality

All the information collected from you for the study will be treated confidentially, and only the researchers named above will have access to it. The study results may be presented at a conference or in a scientific publication, but individual participants will not be identifiable in such a presentation.

Further Information

When you have read this information, Denise Cummins will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact her on 93950444.

This information sheet is for you to keep.

Ethics Approval and Complaints

“This study has been approved by the Ethics Review Committee (RPAH Zone) of the Sydney Local Health District. Any person with concerns or complaints about the conduct of this study should contact the Executive Officer on 02 95156766 and quote protocol number X13-0314.”

“The conduct of this study at the Redfern Health Centre has been authorised by the Sydney Local Health District. Any person with concerns or complaints about the conduct of this study may also contact the Research Governance Officer on 95156766 and quote protocol number X13-0314.”
HIV associated cognitive impairment: client characteristics and professional
care giver experiences

PARTICIPANT CONSENT FORM – HIV Sector Service Provider

I, [name],

of [address],

have read and understood the Information for Participants on the above named
research study and have discussed the study with Denise Cummins.

I have been made aware of the procedures involved in the study, including any
known or expected inconvenience, risk, discomfort or potential side effect and of
their implications as far as they are currently known by the researchers.

I understand that the interview discussion will be audio-taped, and I agree to this.

I freely choose to participate in this study and understand that I can withdraw at any
time.

I also understand that the research study is strictly confidential.

I hereby agree to participate in this research study.

NAME:

SIGNATURE:

DATE:

MASTER Participant Consent Form, Version1, 18/08/2014
HIV Service Sector Provider Consent Form, Version # 1, 18/08/2014
NAME OF WITNESS:
........................................................................................................

SIGNATURE OF WITNESS:
.........................................................................................................
Questions for PosLife (HIV NGO). These will be distributed by Poslife as a survey.

1. Age_____
2. How long have you been HIV positive?_____
3. What is the postcode where you live?_____
4. Have you heard about HIV-related cognitive impairment (also known as HAND, HIV Dementia)?
   - Yes
   - No
   - Don't know
   If so, are you concerned or anxious about it?
   - Yes
   - No
   - Don't know
5. If so, what are your concerns?_____
6. Have you tried to talk to someone about this?  
   - Yes
   - No
   If not, is that because you are anxious/frightened to discuss this issue?  
   - Yes
   - No
7. If yes, who have you talked to? (You can tick more than one)
   - Partner
   - Family
   - Friends
   - GP
   - HIV specialist
   - Nurse
   - Social Worker
   - Treatment advisor
   - Other:_____
8. If so, how was their response?
   - You felt they listened to you
   - You felt they did not listen to you
   - You felt they did not listen and so you may not talk to them about it again
   - You felt they did not listen and so you would like to talk to someone else
9. Has someone who knows you well commented that they have noticed any recent changes in you, such as you are more forgetful, more tired at the end of the day or a little more irritable?  
   - Yes
   - No
   - Don't know
10. Do you know what services you can contact if you have concerns about HIV-related cognitive impairment?  
    - Yes
    - No
    - Don’t know
11. Have you noticed that you are slower in your thinking than you used to be? (e.g., it takes you longer than usual to do something like cooking a meal?)
    - Yes
    - No
    - Don't know
12. Have you noticed you are more forgetful than you used to be? (E.g., forget medications, where you put things like the keys)
    - Yes
    - No
    - Don’t know
13. Have you found it is harder to organise things than in the past? (E.g., need to use more reminders than in the past, lists)
    - Yes
    - No
    - Don't know

Master: Survey for Positive Life, Version 1, 12/05/2015

Page 1 of 2
14. Are you able to find pleasure in the things you used to enjoy?  
☐ Yes ☐ No ☐ Don't know

If you have friends who you know are HIV positive could you please answer the following ....

15. Have you noticed any unusual changes in your friends?  ☐ Yes ☐ No

16. If so, have you or would you feel comfortable in discussing this with them?  
☐ Yes ☐ No ☐ Don't know
   If not would you like some tips on how to do this?  ☐ Yes ☐ No ☐ Don't know

17. Are your friends commenting they are experiencing problems with their thinking?  
☐ Yes ☐ No ☐ Don't know

18. Offer an open free type field to raise any other issues or concerns.
Responses to If you are concerned about HAND what are these?

18 to 24 No Responses

25 to 34
• That my memory will fail, I will have to retire early, I will have no income protection and be in financial crisis
• Who can get it?
• I have been undetectable for couple of years now. I have been eating healthy and regular physical exercises as well. I noticed for a while that I am getting more and more absent minded, which is a big concern for me.
• Losing grip
• Getting it

35 to 44
• I had a partner who experienced it. In the absence of a traditional family structure I wonder what my future would hold should I go through the like.
• Fear of losing my memory and intellectual functioning
• That I won’t be aware of any decline
• A vague concern about what might happen in the future
• How and if it will affect my close friends and me
• How it would effect my being as well as brain function in the long term.

45 to 54
• Little, if no knowledge
• I'm experiencing HAND and am concerned about its progression
• Living alone, unpartnered and not being out with my HIV, I'm concerned about the possible impact
• Memory issues, concentration, multiple tasking issues, short attention span. All of these affect my day to day living issues as well as ability to work well in employment.
• Concern is related to an onset of Hand before I am able to experience more of life without a visible side to HIV and will I be treated well.
• I have had HIV related cognitive impairment, I am on specific meds that remedied this, and I often get checked by my psyche to make sure they're still working
• End of life decisions in case dementia sets in, ability to work and earn money in current career
• I don't want to be demented, I feel my brain is my only asset
• aware of current symptoms and the worsening of it in the future
• I do not wish to be a burden to my family and friends and lovers.
• like to no more about it
• poor memory which has been noticed by friends
• That I'll be diagnosed with it
56 to 54

- Have hard time with short term memory
- Do I have it
- That it will affect me
- That I will get HIV related dementia
- At moment I am very healthy but I am concerned what might happen as I get older because on my diagnostic I had Aids dimension not annoy more though.
- how in my later years this will compound on my general health and independence
- I have been diagnosed with it.
- no concerns.
- mental health!

55 to 64

- I suffer from hand
- What is it? will it affect me?
- Have had a couple of friends suffer from HAND. Concerned it might happen to others or me. Will there be a treatment?
- That it may effect me
- my mother had Parkinson's Disease & my father has Alzheimer's & vascular dementia
- The gradual onset of it may mean you don't know its happening until it has progressed significantly. Also I have CNS disease with HIV in my spinal fluid which affects my brain/nerve function
- To know the difference between age related or HIV
- Future effects
- Hopefully it's not for me
- If I will get it.
- That I might be experiencing symptoms.
- Am I affected by it.
- Becoming fully demented Losing my independence Unable to function within my environment Fear of starting to do inappropriate things, due to lack of awareness It seems to be a slow process - for me - so how aware will I be that I am losing awareness? Is there a point where I simply don't even know I've slipped over the edge?
- I may suffer from it

65 to 74

- how far it might progress
- If it effects me or not
Please list and other Comments

18 to 24

No responses

25 to 34

- I wish it all end
- I have been feeling completely exhausted lately. Fatigue is the word. All I want to do is sleep and can’t get enough of it.

35 to 44

- Do not think most people in the HIV community take HAND seriously enough and do not get tested for it when they need to. I have HAND and was one of those people who tried to avoid the signs and symptoms, even when I did do something about it I tried to avoid doing something about it. It took a further 2 years and a extremely serious life threatening neurological event to get totally tested and diagnosed properly with the condition, at that point, it was found the ARVs that I was taking was not treating the virus properly in the brain and treatment changes had to be made. HIV people in general on ARV’s need to take this condition more seriously as have met alot that just want to put it under the carpet. More info needs to put out their in regards to it...
- feeling clumsy such as dropping things more often when handling things
- Foggy brain Holpse cognitive processing at times  Input overload
- General health and well being in the long term. Things which can be done to minimize the risks of brain function.

45 to 54

- speed at resones IE answering phone, texting, using computer, focusing.
- I dont want to end up in a human waste facility, “rest home” Ignored and by some staff treated badly and by other staff, spoken about as if I am not there, most commentary would be negative and ridiculing me. I would like if I get that far, to have a BGF or Acon advocate who visits me no less than once per fortnight, but preferably once a week. I dont want to die lying in my own body waste, I dont want to be some brain dead vegetable that people are scared of or laugh at. I would rather an escape option, be it legal or not., before I would totally lose my mind I would organise my affairs and my animals and I would set a message to arrive at my doctors via smartphone... date / time / to whom... that I would most likely be past away by this date and to organise an ambulance or other, to pick up my body. Because there is no way I am willingly living the end of what was a hard enough life, I then sign off to an even harder and more degrading ending. I would rather go before any long term, visibly embarrassing traits develop... I just dont want my family seeing me like that.
- Although I have discussed this with friends who are HIV positive, it is obviously a sensitive subject. Many of my friends come from an era where there were many people who were cognitively impacted by HIV, and it brings up fear. There is also the issue of stigma, the idea
HIV associated cognitive impairment: client characteristics and professional caregiver experiences.

INFORMATION FOR PARTICIPANTS- Professional caregivers

Introduction
You are invited to take part in a research study into HIV associated cognitive impairment: client characteristics and professional caregiver experiences.

The objective is to investigate whether the relationship with a professional caregiver and/or the experience of case management has a positive effect on the person with HIV associated cognitive impairment. There are some people living with HIV (PLHIV) who do not have a personal caregiver who is able to notice changes in a person’s behaviour which may be signs and symptoms of Minor Neurocognitive Impairment. The relationship with a professional caregiver may be an alternate, as this person may be well placed to provide support for investigation of any behaviour change.

The study is being conducted within this institution by:

1. Mr Matthew O’Rourke, Clinical Nurse Consultant HIV Outreach Team, South Eastern Sydney Local Health District.

This study is a component of the requirements for a higher degree for Denise Cummins at the University of Sydney under the supervision of Dr Susan Ronaldson and Dr Christina Aggar, University of Sydney and A/Professor Catherine O’Connor, Director of RPA Sexual Health, SLHD.

Study Procedures
If you agree to participate in this study, you will be asked to sign the Participant Consent Form.

You will then be asked to take part in an interview with Denise Cummins. During the interview you will be asked about your experiences of providing case management and your relationship with your client. The interview will be audiorecorded and is expected to last between 30 and 60 minutes.

Benefits
While we intend that this research study furthers medical knowledge and may improve the care of PLHIV in the future, it may not be of direct benefit to you.

Page 1 of 2

MASTER Information for Participants, Version 4, 10/01/2014
Darlinghurst Health Centre Information for Participants, Version #1, 12/2/2014
Costs

Participation in this study will not cost you anything, nor will you be paid.

Voluntary Participation

Participation in this study is entirely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason.

Confidentiality

All the information collected from you for the study will be treated confidentially, and only the researchers named above will have access to it. The study results may be presented at a conference or in a scientific publication, but individual participants will not be identifiable in such a presentation.

Further Information

When you have read this information, Denise Cummins will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact her on 93950444. Matthew O'Rourke can be contacted on 93828666.

This information sheet is for you to keep.

Ethics Approval and Complaints

This study has been approved by the Ethics Review Committee (RPAH Zone) of the Sydney Local Health District. Any person with concerns or complaints about the conduct of this study should contact the Executive Officer on 02 98191999 and quote protocol number X13-0314.

It has been authorised by South Eastern Sydney Local Health district. For any further questions or complaints contact Research Governance Office on 02 93823587.
Appendix 3
**STAGE 1: FILE AUDIT**

1. Age
2. Gender
3. Sexuality
4. Living arrangements
5. Country of birth
6. Is English their first language? □ Yes □ No, if not which language _____________
7. Reason for referral (which discipline)/ or case management?
8. Do they have an identified caregiver they can rely upon? □ Yes □ No □ DK □
9. Current HAND diagnosis
10. Do they have… (Please tick)

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>HVC</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Sleep apnoea</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Diabetes</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>CPE score</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

**HIV Clinical information:**

11. How long HIV positive
12. Current T cell count
13. Viral load
14. T cell nadir
15. Current cART (combined antiretroviral drugs) □ Yes □ No
16. cART

Regimen ________________________________________________

_____________________________________________________

_____________________________________________________

_____________________________________________________

MASTER Stage 1: File Audit, Version 4, 12/02/2014
REDFERN HEALTH CENTRE
Denise Cummins
Clinical Nurse Consultant
Sydney District Nursing Service

June 13th 2017

Re: Protocol No X13-0314- “HIV associated cognitive impairment- client characteristics and professional caregivers experiences”
HREC/13/RPAH/426 SSA/14/RPAH/70

To whom it may concern

I would like to apply for an amendment for the above study. I have developed an assessment tool to be administered as a pilot study with patients by staff of Positive Central HIV Team SLHD and the HIV Outreach Team, SELHD.

Many people living with HIV may be experiencing mild signs and symptoms of cognitive decline which they may attribute to other conditions such as ageing. Early interventions can improve health and well being. It is anticipated that the use of this tool will help identify those HIV positive patients who may be experiencing cognitive signs and symptoms and provide support to have a medical review, with the aim to diagnose HIV associated neurocognitive disorder which can be treated.

Attached are the following documents: information for participants (clients and health care workers) consent forms, the tool and a copy of an evaluation for staff to complete.

Thank you for consideration of this amendment.

Regards

Denise Cummins

Redfern Health Centre
103 – 105 Redfern Street, Redfern NSW 2016
Tel 61 2 9395 0444 Fax 61 2 9690 1978

Sydney Local Health District
ABN 17 520 269 052
Level 11 North, King George V Building
83 Missenden Rd
CAMPERDOWN, NSW, 2050
Tel 612 9515 9600 Fax 612 9515 9610
Email: slhn.esu@sswhhs.nsw.gov.au

306
31 July 2017

Ms D Cummins
Redfern Health Centre
103-105 Redfern Street
REDFERN NSW 2016

Dear Ms Cummins,

Re: Protocol No X13-0314 & HREC/13/RPAH/426 - “HIV associated cognitive impairment: client characteristics and professional caregiver experiences”

The Executive of the Ethics Review Committee, at its meeting of 6 July 2017 considered your correspondence of 13 June 2017 and subsequently considered your correspondence of 31 July 2017 and gave its approval of the following:

- Information for Participants – Healthcare workers (Master Version 1, 13 June 2017)
- Participant Consent Form – Healthcare workers (Master Version 1, 13 June 2017)
- Information for Participants – Clients (Master Version 1, 13 June 2017)
- Participant Consent Form – Clients (Master Version 1, 13 June 2017)
- Questionnaire / Risk Assessment Tool (Master Version 2, 31 July 2017)
- Evaluation Survey (Master Version 1, 13 June 2017)

Yours sincerely,

[Redacted]

Merela Ghazal
Acting Executive Officer
Ethics Review Committee (RPAH Zone)

HERO/EXECOR/17-08

Sydney Local Health District
ABN 17 520 269 052
www.slhd.nsw.gov.au
HIV associated neurocognitive disorder (HAND) Study

DELPHI STUDY INFORMATION SHEET

I would like to invite you to take part in a Delphi consensus study. Before you decide whether or not you would like to take part, it is important for you to consider why the research is being done and what it will involve. Please read this information sheet carefully.

What is a Delphi study?
The Delphi technique seeks to obtain consensus on the opinions of experts, termed panel members, through a series of structured questionnaires. As part of the process, the responses from each “round” are fed back in summarised form to the participants who are then given an opportunity to respond again to the emerging data. The Delphi is therefore an iterative multi-stage process designed to combine opinion into group consensus.

What is the purpose of the study?
Up to 30% of PLHIV may be at risk of developing HAND regardless of viral suppression. As they are an ageing population they are also at risk of developing co morbidity medical conditions, some of which may mimic S&S of cognitive impairment. Many PLHIV may experience mild S&S of HAND which they may attribute to other issues such as ageing or stress or they may downplay them. Signs and symptoms of HAND may negatively affect quality of life and the person’s health as it may influence medication adherence therefore early recognition could promote health and well being.

There is no biological marker or definitive screening tool which can be used across all settings. Observation of the person and knowledge of their medical and social history (including HAND risk factors) may be key in flagging those at risk. Community based health care providers may as alternate caregivers are well placed to notice cognitive changes in the person whilst providing care.

Why have I been invited to take part?
You are a member of a unique community based HIV service. As an established expert in this field I am keen to gain your views about how to what information you think should be collected to assess PLHIV who may be at risk of HAND. Whilst providing care you are in a unique position to notice any cognitive changes in the person especially those who do not have support of an informal caregiver and those who may be experiencing mild signs and symptoms.

Two cognitive assessment tools have been developed; an initial assessment tool, to be completed once and a shorter monitoring tool to be completed annually. Both of these are for your consideration as expert experienced health care providers to PLHIV in a community setting.

What will I be asked to do if I take part?
I am inviting you to participate as a Delphi panel member. This would involve answering a brief questionnaire related to the two cognitive tools.
It is envisaged that this should take approximately 10-15 minutes to complete. In future rounds you would subsequently receive a summary of the group’s responses. Until consensus is achieved further rounds may be needed. In order to allow timely conclusion of the study we would respectfully request a response time of 2 weeks for completion of each round.

Participation is voluntary.

Who is organizing and funding the research?
This research project is a component of doctorate studies of Denise Cummins focusing on professional caregivers in a community setting. The Delphi study will be conducted by Denise Cummins, clinical nurse Consultant SLHD and supervised by Professor Donna Waters, Dean, School of Nursing University of Sydney, Dr Christina Aggar, Senior Lecturer, Southern Cross University and A/Prof Catherine O’Connor director of Sexual Health Services, SLHD.

Confidentiality
No personal information will be collected and survey responses will be collated anonymously. All responses received in the study will be strictly confidential, and your identity will not be divulged. Completion of questionnaires will be assumed informed consent as there is no identifying features on questionnaires. Direct quotes to free-text answers may be used as part of the study report or later Delphi iterations, but these will be not be traceable back to you.

Data protection
Data collected will be stored as per recommendations of Ethics.

Research ethics
The study was approved by the Human Research Ethics Committee of the Sydney Local Health District, NSW, Australia and Human Research Ethics Committee, South Eastern Sydney Local Health District, NSW Australia and endorsed by the HREC of the University of Sydney.

What do I do now?
Thank you for reading this information sheet and for considering taking part in this research. If you are happy to proceed please indicate you have given consent and complete the following survey. If you have any questions or concerns please do not hesitate to contact me.
Contact details 93850444,
denise.cummins@sswhs.nsw.gov.au

Thank you

Denise Cummins
HIV associated cognitive impairment: client characteristics and professional care giver experiences
PARTICIPANT CONSENT FORM – Health care worker

I, .......................................................... [name]
of .......................................................... [address]

have read and understood the Information for Participants on the above named research study
and have discussed the study with Denise Cummins.

I have been made aware of the procedures involved in the study, including any known or
expected inconvenience, risk, discomfort or potential side effect and of their implications as far
as they are currently known by the researchers.

I understand that the questionnaire will be completed by myself with the client, and I agree to
this.

I freely choose to participate in this study and understand that I can withdraw at any time.

I also understand that the research study is strictly confidential.

I hereby agree to participate in this research study.

NAME: ........................................................................................................................................

SIGNATURE: ....................................................................................................................................

DATE: ............................................................................................................................................

NAME OF WITNESS: ......................................................................................................................

SIGNATURE OF WITNESS: .............................................................................................................
COGNITIVE SCREENING TOOL- DELPHI METHOD

Please tick or fill in where applicable for the following questions

1. Which Service do you work for (please tick)
   - □ ADAPHS
   - □ HOT
   - □ Positive Central
   - □ SDN

2. Age ________

3. Your Highest Qualification
   - □ HSC
   - □ Diploma
   - □ BA
   - □ Masters
   - □ PhD
   - □ Other ________

4. Discipline
   - □ Dietician
   - □ Nurse
   - □ Mental Health Nurse
   - □ OT
   - □ Physiotherapist
   - □ Social worker
   - □ Other ____________

5. Employment
   Years working in your discipline ________

   Years in your current position ________

Thank you
Community HAND screening tools.

Background

There are 2 tools: initial cognitive assessment to be completed once and then a shorter annual monitoring tool.

- During the provision of clinical care and support, professional caregivers may observe mild changes in the patient which could indicate early signs of HAND.

- The screening tools should flag community clients for signs and symptoms (S&S) of HAND, especially those who are ageing may live alone, with little supports of an informal caregiver (who would usually observe any S&S which could be HAND).

- Having an initial and monitoring tool may assist community based health care workers to assess clients for early investigation by their doctor; and additionally providing the doctor with enhanced information.

- Each screening tool has several key sections with questions relating to each item.

- As you are experts providing care to PLHIV in community you may noticed slight changes in the person &/or their environment. It is important to know their past and current health background as there are several risk factors for the HAND the person may have such as CD4 nadir, current CD4 count and viral load, HCV, previous head injury.

- Other conditions such as depression and cardiovascular risk factors such as high cholesterol, high triglycerides and smoking may mimic some S&S of HAND, so it is important to know if the PLHIV have these to develop strategies to reduce them.

- Being aware of home circumstances is important as community health care professionals are well placed as an alternate caregiver to notice any changes which may indicate HAND especially in its milder form.
**Community cognitive RISK screening tool - to be completed once**

On the Likert scale please consider the following items to be included in an initial assessment tool.

<table>
<thead>
<tr>
<th>Instructions: please CIRCLE ONE response on Likert Scale for each item</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>undecided</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>REFERRAL REASON</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Case management, specific clinician, housing, medications, etc some S&amp;S patient referred for may indicate HAND</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>SOCIAL INFORMATION</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Current housing, informal supports, what type of supports provided; income source - difficulty paying bills</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>HIV INFORMATION</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Date of diagnosis + BBV, Nadir, Current CD4 and VL, prescriber, GP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>MEDICATION INFORMATION</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>ARVs? Current list, adherence issues</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OTHER HEALTH CONDITION</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>---</td>
<td>------------------------</td>
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</tr>
<tr>
<td>5</td>
<td>Co morbid conditions can mimic S&amp;S of HAND: CV disease, Cholesterol, smoking.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>MENTAL HEALTH</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Depression can mimic S&amp;S of HAND, memory issues, other mental health conditions, neuropsychological test complete</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>LEGAL ISSUES</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Thought about future (Last will and testament, POA, guardianship etc)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>QUESTIONS FOR THE PATIENT</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>OUTCOME OF SCREENING</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Referral to Nurse/Ot for enhanced assessment of HAND (e.g. ADLs and MOCA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### ANNUAL MONITORING TOOL - completed annually

<table>
<thead>
<tr>
<th>Instructions: please CIRCLE ONE response on Likert Scale for each item</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>undecided</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANY CHANGES IN PAST 12 MONTHS</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Discussion of any changes in last 12 months (housing, carer, medical events, ADLs)

ASK THE PATIENT

Questions to patient (memory problems, slower in thinking etc)

ASK THE CARER (If they have one)

If they have a carer - have they noticed any changes

DOCUMENT CHANGES AND REFER TO NURSE/OT

Table to document what the changes are

OUTCOME OF ASSESSMENT
HIV associated cognitive impairment: client characteristics and professional caregiver experiences.

INFORMATION FOR PARTICIPANTS- Health care workers

Introduction

You are invited to take part in a research study into HIV associated cognitive impairment: client characteristics and professional caregiver experiences.

The objective is to develop an assessment tool to identify people who may be at risk of HIV associated neurocognitive disorder (HAND). It is anticipated that the use of this tool would help identify and assist clients to have a medical review for any signs and symptoms they may be experiencing which could be HAND.

The study is being conducted within this institution by:
1. Ms Denise Cummins Clinical Nurse Consultant, Community Health, SLHD.
2. Ms Angela Langton, Acting Manager Positive Central, SLHD.
3. Mr Matthew O’Rourke, Clinical Nurse Consultant HIV Outreach Team, SESLHD.

This study is a component of the requirements for a higher degree at the University of Sydney under the supervision of A/Prof Donna Waters, Dr Christina Aggar, Southern Cross University and Dr Catherine O’Connor, Director of RPA Sexual Health, SLHD.

Study Procedures

If you agree to participate in this study, you will be asked to sign the Participant Consent Form.

The study involves completing an assessment tool with the patient. It is anticipated it could takes about 20 minutes to complete with the patient and then a small post evaluation which will take approximately 5 minutes.

Risks

All medical procedures - whether for diagnosis or treatment, routine or experimental - involve some risk of injury. In addition, there may be risks associated with this study that are presently unknown and unforeseeable. In spite of all precautions, you might develop medical complications from participating in this study.

The risks of participating in this study are:
During the interview process various issues may arise which participants may want to discuss further with a counsellor. A counsellor will be available if required.

Benefits

MASTER Information for Participants, Version 1, 13/06/2017
SITE SPECIFIC Information for Participants, Version 1, 13/06/2017
To review the assessment tool which will be used as a standard of care for all clients of the service - to flag those who may be experiencing any cognitive symptoms that may be HAND; and to arrange medical follow up for early investigation and possible treatment.

**Costs**

Participation in this study will not cost you anything, nor will you be paid

**Voluntary Participation**

Participation in this study is entirely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason. Whatever your decision, please be assured that it will not affect your medical treatment or your relationship with the staff who are caring for you.

**Confidentiality**

All the information collected from you for the study will be treated confidentially, and only the researchers named above will have access to it. The study results may be presented at a conference or in a scientific publication, but individual participants will not be identifiable in such a presentation.

**Further Information**

When you have read this information, Denise Cummins will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact her on 93950444.

This information sheet is for you to keep.

**Ethics Approval and Complaints**

This study has been approved by the Ethics Review Committee (RPAH Zone) of the Sydney Local Health District. Any person with concerns or complaints about the conduct of this study should contact the Executive Officer on 02 9515 6766 and quote protocol number No X13-0314.
HIV associated cognitive impairment: client characteristics and professional care giver experiences

PARTICIPANT CONSENT FORM – Health care worker

I, .................................................................................................................. [name]
of
..........................................................................................[address]

have read and understood the Information for Participants on the above named research study
and have discussed the study with Denise Cummins.

I have been made aware of the procedures involved in the study, including any known or
expected inconvenience, risk, discomfort or potential side effect and of their implications as far
as they are currently known by the researchers.

I understand that the questionnaire will be completed by myself with the client, and I agree to
this.

I freely choose to participate in this study and understand that I can withdraw at any time.
I also understand that the research study is strictly confidential.
I hereby agree to participate in this research study.

NAME: ...........................................................................................

SIGNATURE: ....................................................................................

DATE: ..............................................................................................

NAME OF WITNESS: ...........................................................................

SIGNATURE OF WITNESS: .................................................................
HIV associated cognitive impairment: client characteristics and professional caregiver experiences.

INFORMATION FOR PARTICIPANTS- Clients

Introduction

You are invited to take part in a research study into HIV associated cognitive impairment: client characteristics and professional caregiver experiences.

The objective is to develop an assessment tool to identify people who may be at risk of HIV associated neurocognitive disorder (HAND). It is anticipated that the use of this tool would help identify and assist clients to have a medical review for any signs and symptoms they may be experiencing which could be HAND.

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3. Mr Matthew O’Rourke, Clinical Nurse Consultant HIV Outreach Team, SESLHD.

This study is a component of the requirements for a higher degree at the University of Sydney under the supervision of A/Prof Donna Waters, Dr Christina Aggar, Southern Cross University and Dr Catherine O’Connor, Director of RPA Sexual Health, SLHD.

Study Procedures

If you agree to participate in this study, you will be asked to sign the Participant Consent Form.

The study involves completing an assessment tool. The assessment tool will be done with a staff member from Positive Central or the HOT team. They will ask you the questions on the tool and write down your responses and will document the time it took to complete the questions. It is anticipated it could take about 20 minutes.

Risks

All medical procedures - whether for diagnosis or treatment, routine or experimental – involve some risk of injury. In addition, there may be risks associated with this study that are presently unknown and unforeseeable. In spite of all precautions, you might develop medical complications from participating in this study.

The risks of participating in this study are:
During the interview process various issues may arise which participants may want to discuss further will a counsellor. A counsellor will be available if required.

Benefits

MASTER Information for Participants, Version 1, 13/06/2017
SITE SPECIFIC Information for Participants, Version 1, 13/06/2017
To review the assessment tool which will be used as a standard of care for all clients of the service - to flag those who may be experiencing any cognitive symptoms that may be HAND; and to arrange medical follow up for early investigation and possible treatment.

Costs

Participation in this study will not cost you anything, nor will you be paid

Voluntary Participation

Participation in this study is entirely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason. Whatever your decision, please be assured that it will not affect your medical treatment or your relationship with the staff who are caring for you.

Confidentiality

All the information collected from you for the study will be treated confidentially, and only the researchers named above will have access to it. The study results may be presented at a conference or in a scientific publication, but individual participants will not be identifiable in such a presentation.

Further Information

When you have read this information, Denise Cummins will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact her on 93950444.

This information sheet is for you to keep.

Ethics Approval and Complaints

This study has been approved by the Ethics Review Committee (RPAH Zone) of the Sydney Local Health District. Any person with concerns or complaints about the conduct of this study should contact the Executive Officer on 02 9515 6766 and quote protocol number No X13-0314.
HIV associated cognitive impairment: client characteristics and professional care giver experiences

PARTICIPANT CONSENT FORM - Clients

I, .................................................................[name] of .................................................................[address] have read and understood the Information for Participants on the above named research study and have discussed the study with Denise Cummins.

I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort or potential side effect and of their implications as far as they are currently known by the researchers.

I understand that the questionnaire will be completed and reviewed, and I agree to this.

I freely choose to participate in this study and understand that I can withdraw at any time.

I also understand that the research study is strictly confidential.

I hereby agree to participate in this research study.

NAME: ........................................................................................................................................

SIGNATURE: ...........................................................................................................................

DATE: .........................................................................................................................................

NAME OF WITNESS: ...................................................................................................................

SIGNATURE OF WITNESS: ........................................................................................................
Risk Assessment for HIV associated neurocognitive disorder

Some people are experiencing changes in their behaviour such as memory, which could be due to many things. This assessment will help gather information for us to help you and to arrange further assessment if needed. Other conditions such as heart disease, substance use and depression can have similar signs and symptoms as changes in cognition such as memory, so we need to ask questions concerning your medical history.

A staff member will ask you the questions and write down your responses. If you answer positively to some of the questions the staff member will ask you if you would like to discuss the issues more with a nurse or occupational therapist.

Please tick or write response to each question.
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Please tick or write response to each question.

Date of Assessment:

REASON FOR REFERRAL

☐ Case management ☐ Health information ☐ Health assessment and referral

☐ Symptom management ☐ Support for co-morbid conditions ☐ Medication issues

☐ Other: __________________________________________________

SOCIAL INFORMATION

1. Do you have stable/unstable housing? ☐ Yes ☐ No

2. Do you have the support of an informal caregiver you can rely on (partner, family, friends)?

☐ Yes ☐ No If Yes, who (name and contact number)_____________________

3. What type of support do they currently provide?

☐ practical (transport, shopping etc)

☐ emotional

☐ financial

☐ Other____________________

4. How often do they provide this support?___________

5. Do you have any difficulty with:

☐ Paying bills ☐ Buying food ☐ Paying for medications ☐ Paying the rent

Master Questionnaire for participants Version 2, 31/07/2017
2. Have you been diagnosed with any other medical conditions or have an risk factors:
   □ hypertension  □ high cholesterol  □ high triglycerides
   □ family history of health issues such as heart disease, Alzheimer’s disease
   □ central nervous system (eg: brain injury, Alzheimer’s, stroke, Parkinson’s disease)
   Please specify________________________
   □ other__________________________

SUBSTANCE AND/OR ALCOHOL USE

1. Do you currently use alcohol and/or recreational drugs? □ Yes □ No
2. How long have you used recreational drugs or drank alcohol for?__________
3. What substance?________________________
4. How often do you use it?________________
5. Have you used alcohol or other drugs in the past and stopped? □ Yes □ No
6. Have you ever experienced an overdose of drugs? □ Yes □ No
7. Do you smoke cigarettes? □ Yes □ No

MENTAL HEALTH

1. Do you have any of the following:
   □ Diagnosed depression  □ Diagnosed anxiety  □ Diagnosed cognitive impairment
   □ Schizophrenia  □ Bipolar  □ Other mental health diagnosis
   ____________________________

The following questions are related to any changes you may have noticed over the last 12 months. Have you:

1. Noticed any changes in your mood (more irritable, becoming less socially engaged)?
   □ Yes □ No
2. Forgotten appointments, forgotten to pick up medications etc?
   □ Yes □ No  If so what?__________________________

Master Questionnaire for participants Version 2, 31/07/2017
3. Do you feel you are slower when reasoning, planning activities or solving problems than you used to be?

   □ Yes □ No If so, what?______________________________________

4. Have you noticed any changes in physical skills in last year such as stumbling, tripping, handwriting having problems texting, tying?

   □ Yes □ No If so, what______________________________________

5. Do you have more difficulty paying attention than you used to?

   □ Yes □ No If so what______________________________________

6. Are you needing to use more reminders for appointments, special dates etc? □ Yes □ No

7. Have you noticed any changes in social interaction (eg not going out as much, not been involved when people visiting)?

   □ Yes □ No If so, what______________________________________

8. Have people around you said anything to you about noticing the above in you within last year?

   □ Yes □ No

9. Have you talked to anyone about this? □ Yes □ No

10. Have you had medical review for any of these symptoms? □ Yes □ No

11. Have you had any of the following tests:

    □ Neuropsychological exam, is so (where, date)_______________

    □ MRI, □ cat scan □ lumbar puncture

12. Have you noticed any changes in things you do at home (eg taking longer or less interest)

    □ housework □ watching TV □ sleeping □ other activities______________

13. Do you engage in physical activity? □ Yes □ No If Yes how often and what activity____

14. How is your sleeping?_________

**OUTCOME OF SCREENING**

Identified changes? □ Yes □ No

Refer to Nurse/OT for review? □ Yes □ No

Master Questionnaire for participants Version 2, 31/07/2017
HIV INFORMATION
1. When was your HIV diagnosis? _____
2. Current CD4+ T cell Count _____
3. Current Viral load _____
4. Nadir (lowest ever) CD4+ T cell count _____

Medication Information
1. Are you currently taking antiretroviral medications? □ Yes □ No
2. What is the current medication list? ________________________________

3. Do you have any problems getting your supply of medication? □ Yes □ No
4. Does anyone help you with your medications? □ Yes □ No
   If yes, What support do they provide? (Eg collect drugs, help you take them)
5. Have you ever had trouble taking medications? □ Yes □ No
   What kind of trouble (forgetting, cost etc) __________________________
6. Have you stopped and started taking medications in the past? □ Yes □ No
   If yes, why ________________________________
7. How many doses have you missed in the last 7 days ______ last 28 days

OTHER MEDICAL CONDITIONS
1. Have you been diagnosed with any other blood borne virus?
   □ Hepatitis B
   □ Hepatitis C
   □ HIV
   □ Other ________________

Master Questionnaire for participants Version 2, 31/07/2017
ANNUAL MONITORING TOOL

Ask the following questions:

ANY CHANGES IN PAST 12 MONTHS...

Have you noticed any changes in last 12 months? □ Yes □ No

Has anyone else mentioned any changes? □ Yes □ No

Have you had any medical events in last 12 months? □ Yes □ No

Have there been any changes in housing or supports since last assessment? □ Yes □ No

ADL function (any changes): □ Yes □ No if yes, what ______________________

ASK THE PATIENT...

Are you slower in your thinking than you used to be? □ Yes □ No

Are you more forgetful than you used to be? □ Yes □ No

Is it harder to organise things? □ Yes □ No

Are you able to find pleasure in the things you used to enjoy? □ Yes □ No

Tell me any changes you have noticed________________________

ASK THE CAREGIVER (if they have one)... 

Have you noticed any changes? □ Yes □ No

If so, what________________________

DOCUMENT CHANGES AND REFER TO Nurse/Occupational therapist

<table>
<thead>
<tr>
<th>Social situation</th>
<th>Yes /No</th>
<th>Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employment</td>
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<tr>
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<td>Medical issues</td>
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<tr>
<td>Cognitive changes (behavioural/motor)</td>
<td></td>
<td></td>
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</tbody>
</table>

OUTCOME OF ASSESSMENT

Identified changes? □ Yes □ No

Refer to Nurse/Occupational therapist for review? □ Yes □ No
RISK Assessment for HIV associated neurocognitive disorder
Evaluation survey (Delphi Study)

Date

Please complete the following questions after to have completed the risk assessment tool with the patient. Please provide comment on how you felt completing the assessment form with the patient.

1. How long did it take to completed assessment tool with the patient? 

2. Were the instructions clear? □ Yes □ No

   Comment

3. Was the language easy to understand by the patient? □ Yes □ No

   Comment

4. Was the medical terminology understandable? □ Yes □ No

   Comment

5. Did you think the questions elicited useful information from the patient? □ Yes □ No

   Comment

6. Other comments

   

   

   

   

Thank you

MASTER Evaluation Survey for participants, health care workers, Version 1, 13/06/2017
COGNITIVE SCREENING FLOW CHART

Screening by multidisciplinary staff

Outcome of screening
(none, monitor, refer to nurse/OT for further assessment)

Referral to nurse/OT
(Assessment: MoCA etc, ADLs, )

Outcome of nurse/OT review
(none, monitor/referral to GP for further investigation)

Outcome of medical review
(none/monitor/neuropsych/ neurology/change medications)