The impact of comorbidity and clinical complexity on retention in HIV care

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Certificate of Original Authorship

I, Shiraze Bulsara, declare that this thesis is submitted in fulfillment of the requirements for the award of Doctor of Philosophy (Clinical Psychology), in the Graduate School of Health at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all the information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.

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My primary purpose in developing this research series was to further our understanding of factors which can impede the progress, well-being and QoL of people living with HIV (PLHIV). As a clinical psychologist who has worked with this population for over 12 years, I recognise how marginalised this cohort has been and continues to be. This has fuelled a passion to improve the way in which we support these, often vulnerable, clients with complex clinical presentations. I am also passionate about clinicians from varied disciplines working together in the best interests of the people we support. This body of work has highlighted just how important interdisciplinary, coordinated, and collaborative care is, especially within the public health system.

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Glossary

90-90-90 - Global targets relating to 90% of people living with HIV being aware of their status, 90% of those on treatment, and 90% of those virally suppressed

ABM – Andersen Behavioral Model of Health Service Use

ADLs – Activities of Daily Living

AIDS - Acquired immune Deficiency Syndrome

Albion - The Albion Centre; A tertiary Interdisciplinary HIV Clinic in Sydney (NSW), AUSTRALIA

AMO - Attending Medical Officer

aOR - Adjusted Odds Ratio

ART - Antiretroviral Therapy

ATSI - Aboriginal or Torres Strait Islander; Indigenous Australians

AUC - Area Under the Curve

BBV - Blood Borne Virus

BMI - Body Mass Index

CALD - Culturally and Linguistically Diverse

Cascade – The HIV Care and Treatment Cascade

CCRS - Clinical Complexity Rating Scale

CCRS-HIV - Clinical Complexity Rating Scale for HIV

CD4 - Cluster of Differentiation 4 cells; Cells involved in the immune response, and implicated in HIV-infection

CDC - Centers for Disease Control and Prevention

CI - Confidence Interval

CMA - Crystal Methamphetamine

CNS - Central Nervous System

CVD - Cardiovascular Disease

DSP - Disability Support Pension; Welfare payment in Australia for those with an assessed disability which prevents them from working

eMR – Electronic Medical Record

EACS – European AIDS Clinical Society

EU - European Union

GP - General Practitioner

HAART - Highly Active Antiretroviral Therapy

HAV - Hepatitis A Virus

HBV - Hepatitis B Virus

HCV - Hepatitis C Virus

HETI - Health Education and Training Institute

HIV - Human Immunodeficiency Virus

HIV-DNA - HIV Deoxyribonucleic Acid

HIV-RNA - HIV Ribonucleic Acid

HPV - Human Papilloma Virus

HREC - Human Research and Ethics Committee

HRSA - The U.S. Health Resources and Services Administration

IVDU - Intravenous Drug Use

LDCs – Least developed countries

LTFU - Lost to Follow Up

MSM - Men who have sex with men

MTCT - Mother to child transmission

NSP - Needle and Syringe Program

NSW – New South Wales; a State within Australia, whose capital city is Sydney

OI - Opportunistic Infection

OR - Odds Ratio

PBS - Pharmaceutical Benefit Scheme; an Australian government program which provides subsidised prescribed medications to Australian residents

PD - Personality Disorder

PH – Physical Health (complexity domain; CCRS-HIV)

Phlebotomy Test - Blood test

PLHIV/PLHIV - People living with HIV

PrEP – Pre-Exposure Prophylaxis

PSY – Psychosocial (complexity domain; CCRS-HIV)

PTSD - Posttraumatic Stress Disorder

QA/QI - Quality Assurance/Quality Improvement

QoL - Quality of Life

SESLHD - South East Sydney Local Health District; a local health district (LHD) within NSW Health

SMI - Severe Mental Illness

STI - Sexually Transmitted Infection

T Cells - Lymphocyte developed in the thymus gland, central to the immune response, and implicated in HIV-infection

TAFE - Technical and Further Education Institutes; Tertiary educational facilities in Australia

TasP - Treatment as prevention

TB - Tuberculosis

U.K. - United Kingdom

U.S. - United States of America

U=U - Undetectable = Untransmissable

UDVL - Undetectable Viral Load

UNAIDS - Joint United Nations Program on HIV/AIDS

UTS - University of Technology Sydney

Viraemia - The presence of virus in the blood

VL - Viral Load

WHO - World Health Organization

Abstract

Significant advances in the medical management of HIV have heralded a new era of treatment which acknowledges psychosocial, as well as medical, comorbidity factors. However, policy guidelines, reporting requirements and directives are yet to be revised accordingly, with metrics for successful treatment continuing to be considered in medical terms alone. The importance of medical and/or psychosocial comorbidity in impacting well-being, quality of life, and optimal holistic HIV management has arguably been under-represented in reporting outcomes.

At present, biomedical markers such as viral load are used to measure treatment 'success'. Optimal holistic care should transcend viral load alone and include other measures such as overall functioning and health-related quality of life. Retention in care is a current metric within the HIV Care and Treatment Cascade, and the only one which allows for holistic monitoring or medical review by HIV specialists; however, at present, its full potential is not realised. Consistent definitions and means to measure retention are elusive, with differences within and between regions making comparisons difficult. However, retention remains an important component of the Cascade, as it affords the opportunity for optimal monitoring and timely intervention for biopsychosocial comorbidities which may ultimately impact disease progression and quality of life.

In the context of three key theoretical models (the Biopsychosocial Model, the Syndemic Model, and the Andersen Behavioral Model of Health Service Use), the present study series aims to review current definitions of retention in HIV care and understand its specific antecedents through a series of four empirical studies. A systematic literature review considers the global literature on the subject, while a local qualitative analysis of both clinician and client perspectives provides context within the Australian public health landscape. A third study describing the development of an HIV client complexity rating scale, to assess for comorbidity, is outlined. These results are then used to assess the impact on retention in an Australian cohort of people living with HIV, in the fourth and final study.

Results suggest a complex interplay of individual and contextual biological, psychological and social factors which impact retention in HIV care. Further, they suggest that particular interactions, or syndemics, beyond biomedical markers alone are implicated in poor retention in HIV care.

The results are discussed in the context of appropriate theoretical models to understand the factors and the nature of the relationships between them. Implications for future research, as well as policy and reporting guidelines, are discussed.

Chapter 1: Introduction

1.1 The early years

In 1981, the Centers for Disease Control and Prevention (CDC) received reports of rare cancers among gay men in New York and California, in the United States (U.S). By the end of that year, there were 337 reported cases within the U.S, with 130 of those already deceased. Within 12-months, this pattern of symptoms was defined as Acquired Immune Deficiency Syndrome (AIDS), and it became understood that the virus which caused this was known as Human Immunodeficiency Virus (HIV) (Centres for Disease Control and Prevention, 2017).

In Australia the first AIDS diagnosis was in 1982, with antibody testing becoming publicly available in 1985 (The Albion Centre, 2012). At this point, the legal and public health realms merged, and it became a criminal offence in the state of New South Wales (NSW), Australia for people living with HIV (PLHIV) and aware of their status to have condomless sex with a partner, without disclosing (see section 1.8 for more information). From the early days of the epidemic, HIV was considered to only impact the gay community, because of the high proportion of men who have sex with men (MSM) infected, a perception which has contributed to ongoing stigma and discrimination. This also contributed to the latency and paucity in the response from policy makers, the scientific community and the pharmaceutical industry in addressing what soon would become a global epidemic. The high fatality rate, coupled with a stigmatised view of homosexuality, meant an already marginalised community were

further marginalised and ostracised – a price the community continues to pay 35 years on, albeit lessened over time. In spite of both the structural discrimination and the silent response by those charged with treatment developments, a perishing yet galvanised gay community successfully advocated for the fast-tracked development of the medication which would eventually help make HIV a chronic illness.

During the early years of the HIV epidemic, global health agencies struggled to understand the nature of the virus, its causes, modes of transmission and management. The fatality rate was high, and by 1992 AIDS was the leading cause of death for U.S. men aged 25-44 (Centers for Disease Control and Prevention, 1993). It wasn't until the mid-1990's, approximately 15 years after the first reported case, that pharmacotherapy became available. The introduction of Highly Active Antiretroviral Therapy (HAART) was an important step in what would become a global public health initiative.

1.2 The biology of HIV

As its name suggests, HIV impacts the immune system which can make it difficult for the body to fight even simple infections (VIC Health, 2016). Transmission occurs through blood, semen/vaginal fluids, and breast milk. When left untreated, replication within the body can run rampant and allow a person's viral load (VL), or the number of copies of the virus per millilitre of blood, to increase. The body's natural defence to any infection is to develop cells to fight that infection; the cells which HIV attacks, thereby

leaving the body vulnerable to infection, are known as CD4 cells, or T-cells (U.S. Department of Health and Human Services, 2019b). In a person with well managed HIV, a typical profile would be a low VL (ideally undetectable; UDVL), and a high CD4 count. Conversely, a person with untreated HIV may have a high VL and low CD4 count, leaving them susceptible to opportunistic infections (OIs). The presence of one or more OIs, and/or a low CD4 count can result in an AIDS diagnosis (U.S. Department of Health and Human Services, 2019b); if untreated, OIs can lead to AIDS-related death. AIDS-related deaths have reduced globally by over 55% since their peak in 2004 (770,000 in 2018 compared to 1.7 million in 2004) (UNAIDS, 2019).

The biological underpinnings of HIV make it an incredibly 'intelligent' virus, and one which has taken some time to successfully manage medically. When HIV enters the body, it attaches itself to molecules on the CD4 cells (a type of lymphocyte involved in the body's immune response) and fuses with the cell membrane, allowing HIV to enter the cell. As a retrovirus, HIV uses an enzyme known as *reverse transcriptase* to convert its genetic material, HIV-Ribonucleic Acid (HIV-RNA), into HIV Deoxyribonucleic Acid (HIV-DNA). This allows the virus to enter the cell nucleus and combine with its genetic material. When HIV infects cells, its viral DNA integrates into the DNA of the host cell, and begins the process of replication (U.S. Department of Health and Human Services, 2019a).

1.3 HIV Today

Advances in the efficacy and tolerability of present-day antiretroviral therapy (ART) regimens to treat HIV have heralded substantial changes in the perception and management of the virus. Early treatment regimens of HAART, available in Australia in 1997 (The Albion Centre, 2012), were both lauded and problematic. High pill burdens and often debilitating side effects made HAART adherence difficult to attain, leading to an increase in OIs and ultimately death for many. Present day regimens, on the other hand, are relatively simple (often one pill per day), tolerable and highly effective when taken as prescribed (Ford et al., 2018). Newer ART medications are classified according to their function; resistance to medications in one class has the potential to preclude use of others within the same class. With poor adherence, the virus has the capacity to 'learn', mutate and develop resistance. Thus, medication adherence has always been imperative for the ongoing successful management of HIV-infection.

As our capacity to effectively treat and manage the biomedical aspects of HIV infection, replication and transmission has developed, so too has our recognition of the role of other non-medical factors in impacting overall well-being, functioning, capacity to manage HIV, and quality of life (QoL). While once an acute and often fatal disease, HIV is now considered a chronic and manageable illness, and though life expectancy for PLHIV remains lower than that for the general population, they are approaching parity (Mayer, 2011). Eradication of the virus remains elusive, and sustained viral suppression remains the goal of treatment and metric for 'success'. Successful biomedical management of HIV requires consistent (and presently, lifelong)

adherence to ART, with regular monitoring to ensure ongoing optimal impact of the medication on the virus. However, viral suppression does not account for other factors which commonly impact PLHIV, and therefore (arguably) should not be the only metric by which success is measured (Chan et al., 2018).

1.3.1 The global epidemic

While the medical understanding and management of HIV has improved to a point which heralds its trajectory from an acute to a chronic illness in countries with advanced economies, this profile has not been achieved in least developed countries (LDCs) at the same rate. Lack of access to newer medications and condoms, as well as the other basic necessities of food and clean water, means that globally HIV remains one of the deadliest viruses, with an estimated 36.9 million people infected worldwide (World Health Organization, 2019). The prevalence of HIV remains highest in the World Health Organization (WHO) African region, accounting for nearly two thirds of PLHIV worldwide (World Health Organization, 2019). In resource-limited countries, mother-to-child transmission (MTCT) was a significant contributor to new infection rates. This risk can be mitigated if expectant mothers living with HIV take newer medications to achieve viral suppression, deliver via caesarean section, and bottle feed their babies; present estimates suggest that 80% of expectant mothers are able to access ART (World Health Organization, 2018a). While accessibility to newer ART medications is often easier in countries with advanced economies, obstacles remain for LDCs to be afforded access to the same quality of medication; however, this is improving, with 2018 data suggesting new infections in the WHO African region reduced by 24%, and

HIV-related deaths reduced by 40%, compared to 2010 (World Health Organization, 2018c).

1.3.2 HIV in countries with advanced economies

In resource-rich countries, access to new ART regimes and HIV medical specialists means the epidemic is largely under control medically. However, even in countries with advanced economies there is variability with regards to these aspects. In the U.S. for example, there are financial costs to access medical care and medications, which is in contrast to countries like Australia, Canada, Brazil, the United Kingdom (U.K.), and many European countries where universal healthcare is available. This discrepancy in cost and subsequent access to treatment can explain the differences in the rates of new infections and HIV-related engagement within these regions.

In resource-rich countries, HIV is most prevalent in MSM; in 2017 in the U.S, MSM transmission accounted for 66% of all new HIV diagnoses, and 82% of diagnoses among males (Centers for Disease Control and Prevention, 2017). Across European countries, the rates are similar with MSM contact accounting for 60% of new diagnoses across 10 European Union (EU) countries (European Centre for Disease Prevention and Control, 2018). Specifically in the U.K, diagnoses among MSM accounted for 45% of new infections which remained the highest when compared to other transmission groups (Public Health England, 2018). In Australia, MSM transmission accounted for 63% of new infections in 2017 (Kirby Institute, 2018). However, recent Australian epidemiological data indicate that the rates of transmission via heterosexual sexual contact increased by 10% between 2013 and 2017, with 46% of late diagnoses

(i.e. with a CD4 count less than 350 cells/μL) attributable to heterosexual sexual contact (Kirby Institute, 2018). These rates point to a need for public health strategies to broaden to include populations other than MSM.

One key difference between countries with advanced economies and LDCs is the focus of care has altered in the former to sustain the gains made, with increased acknowledgement and understanding on the role of other, non-medical, factors in effectively and holistically managing HIV.

1.4 Priority populations

Global public health responses to HIV management require thoughtful consideration of resource allocation. For this reason, annual surveillance data within regions is released to identify key target areas, or 'priority populations', which require most attention. The WHO has identified a number of such priority populations, where the risk of HIV infection is higher irrespective of population type or local context. These are: MSM; people who inject drugs; people in prisons and other closed settings; sex workers and their clients; and transgender people (World Health Organization, 2018a). People with severe mental illness are a less studied population, yet also disproportionately affected by HIV (Ayano et al., 2018; Firth et al., 2019). Region-specific priority populations also exist; for example, Aboriginal and Torres Strait Islander (ATSI) people, and culturally and linguistically diverse (CALD) communities within NSW, Australia (NSW Health, 2015).

1.5 The public health response to managing HIV

A key explanation for the improvements in HIV management in countries with advanced economies rests on the response of governments and relevant agencies to develop public health responses to stem the tide of new infections. Examples from the Australian public health response include the introduction of needle syringe programs (NSPs), a harm minimisation approach to allow people who inject drugs to access unused injecting equipment, thus reducing the risk of sharing and transmission (Brown, O'Donnell, Crooks, & Lake, 2014). A second effective strategy has been the decriminalisation of sex work and support of licenced brothels in some states in Australia, with regulations implemented regarding regular sexually transmitted infections (STI) tests, and provision of condoms (Fawkes, 2014). A third public health strategy was the introduction of antenatal screening for HIV (Giles, Hellard, Lewin, & Mijch, 2006), and a commitment to supporting expectant mothers to access ART, such that MTCT is now extremely rare in Australia. Most recently, pre-exposure prophylaxis (PrEP) has become readily available for those at risk of infection, including MSM and others in serodiscordant relationships.

1.6 Treatment as Prevention (TasP)

Adherence to ART is important not only for an individual's health, but also from a public health perspective (Drew et al., 2017). It is currently well understood, through evidence-based research and within the community, that an undetectable viral load means HIV is untransmissible [U=U] (Bavinton et al., 2014; Rodger et al., 2019; Rodger et

al., 2016; The Lancet, 2017). It is also widely accepted that commencing ART as soon as possible after diagnosis heralds optimal health outcomes for PLHIV (Babiker et al., 2013; Lundgren et al., 2015). Treatment as Prevention (TasP) is now considered best practice, as we increasingly recognise the role of effective HIV medical treatment not only in treating HIV, but also in preventing transmission. Therefore, for the individual and the broader community, early ART initiation and adherence, regular monitoring, and effective management of HIV-infection remain imperative for optimal individual and public health outcomes.

1.7 The biomedicalisation of the HIV response

The focus of research, treatment and policy throughout the course of the HIV epidemic has largely been biomedical (e.g. TasP), with some authors suggesting this biomedicalised response has been at the expense of an integrated social narrative (Kippax & Stephenson, 2012). While these authors focussed their discussion on testing and prevention strategies, this can also be extended to HIV treatment approaches.

Narrowly focussed biological approaches at the height of the epidemic were appropriate, as reducing mortality was the priority. These approaches remain highly relevant in the present day, however the move from acute to chronic illness heralds a shift to consider other psychosocial factors in conjunction (Havelka, Despot Lučanin, & Lučanin, 2009). A key underpinning, which is often missed, is that even biomedical strategies have to be considered in a psychosocial context, as they have social and

behavioural change at their core (Aggleton & Parker, 2015; Kippax & Stephenson, 2012). Indeed, none of the recent successful biomedical advances in HIV could have been implemented without consideration of the role of psychosocial factors, despite these factors not being explicit in public health guidelines. For example, TasP is only successful in the context of medication adherence, which is fundamentally built upon behavioural and psychosocial principles (Amico, Mugavero, Krousel-Wood, Bosworth, & Merlin, 2018). In addition, a 'progressive narrowing' of international HIV conferences, which deemphasises the psychosocial domains and increases the focus on the purely medical aspects of HV management, has also been noted (Aggleton & Parker, 2015). Thus, as an international sector, the response to HIV has retained its biomedical focus, to the exclusion of other relevant factors. While not a deliberate omission, it highlights a prioritisation of biomedical factors while neglecting others.

Effective public health messaging must be simple and specific to target its audience, and this has been demonstrated to be effective in the 'U=U' campaign, where the message is simply "remain undetectable and the virus is untransmissable" (The Lancet, 2017). This campaign does not address the psychosocial context around medication adherence which is necessary to remain undetectable, despite its relevance, because doing so would complicate and potentially attenuate the message. Yet this is somewhat problematic as it 'misses' an essential component. As a sector, in translating the research evidence into policy documents, we may have forgone the context. In an effort to simplify the message, we may have lost the nuance. Despite a recognition of

the broader context of HIV in the earlier days of the epidemic, we appear to be continuing to narrow the focus.

This response has, intentionally or not, shifted the narrative and the practicalities of HIV management. Perhaps the largest practical result is the funnelling of funding and resources to medicalised prevention strategies (e.g. PrEP, Test and Treat) – arguably at the expense of others. At present, current reporting guidelines and metrics for 'success' are focussed on the reporting of VL alone; despite the recognition of the importance of psychosocial factors, these are not reflected in our measurements. This argument does not negate the importance of an UDVL, or monitoring to achieve the same. However, it does suggest that solely focussing on this aspect might be too narrow and ultimately self-defeating. While biomedical advances certainly herald a new era for HIV management and there is no denying the significant impact these have had on our response to the epidemic, the excitement surrounding their success has neglected to account for the context in which they thrive. While the context is favourable to adherence (e.g. for high functioning clients), this is not an issue. However, for those with more complex care needs, the management of HIV can deteriorate.

1.8 HIV as a chronic disease

As a result of the developments in HIV management, HIV is now considered a chronic illness, rather than the acute and often fatal disease it once was (Deeks, Lewin, & Havlir,

2013). This shift has led to universal changes, not only in the medical management of HIV, but also with respect to legal implications regarding HIV transmission. One example of this in the context of TasP is disclosure laws. Until recently (October 2017) in NSW, Australia, the Public Health Act considered non-disclosure of an STI (including HIV) prior to sexual contact to be a criminal offence. Recent changes to this Act advise that PLHIV are now legally required to *take reasonable precautions* to avoid HIV transmission, in order to avoid legal consequences (AIDS Council of NSW & HIV/AIDS Legal Centre, 2017).

Now as a chronic and manageable illness, the public health response to HIV must also evolve, and requires innovative thinking to effectively continue along the path towards 'Ending HIV'. While the medical management of HIV-infection is largely under control in countries with advanced economies, the best outcome is viral suppression rather than eradication at this point, as the sector works towards a cure. Broadening our perspective and attending to other non-medical aspects (in the context of policy and reporting guidelines as well as clinical practice), which can ultimately impact the efficacy of medical interventions, is imperative until eradication is achieved; the role of psychosocial as well as biological factors must be considered.

1.8.1 An ageing cohort of PLHIV

An unprecedented consequence of the introduction of ART and its capacity to effectively treat HIV-infection is that, for the first time, there is an ageing cohort of PLHIV. This naturally begets an increase in the frequency and range of non-AIDS

comorbidity which can impact the individual, such as memory impairment, physical frailty, and other age-related conditions. It is widely understood that HIV is associated with a number of non-AIDS comorbidities and that adherence to ART reduces the impact of these factors on the person and increases life expectancy, although this remains slightly lower than the general population (Deeks & Phillips, 2009).

There is evidence to suggest the prevalence of comorbid presentations, including a combination of medical and psychosocial factors such as substance use and heart disease, is higher among PLHIV than the general population (Petoumenos et al., 2017b). In addition, there is a mixture of evidence to suggest that HIV might accentuate and/or accelerate the presence and clinical trajectory of comorbidities (Woods, 2019). Multiple large international cohort studies have examined the factors associated with ageing in PLHIV, including comorbidity, such as the APPLES study in Australia (Petoumenos et al., 2017b), the ACRIA study in the U.S. (Erenrich, Seidel, Brennan-Ing, & Karpiak, 2018), the ASTRA study in the U.K (McGowan et al., 2017), the HALL study from the U.K (Rosenfeld & Anderson, 2018), and data from the HIV Health and Rehabilitation survey in Canada (O'Brien et al., 2018). Results from these studies suggest a higher degree of comorbid factors in older than younger counterparts (O'Brien et al., 2018; Petoumenos et al., 2017b), concern about perceived control (O'Brien et al., 2018), and uncertainty regarding the potential impact of HIV and associated medications on 'normal' ageing (Rosenfeld & Anderson, 2018). In addition, the ASTRA study found that age since diagnosis (versus chronological age) was associated with a higher prevalence of comorbidities including depression, anxiety and challenges with activities of daily living (ADLs) (McGowan et al.,

2017). Furthermore, the ACRIA study noted that over 50% of respondents were dealing with symptoms of mental illness and/or difficulties with ADLs, as well as indicating a high degree of loneliness and financial strain in their cohort (Erenrich et al., 2018). Such results indicate the important role of psychosocial, in addition to medical, comorbidity factors in impacting ageing among PLHIV. Given this high prevalence for comorbidity with HIV, managing an ageing cohort will likely become increasingly complex and require an interdisciplinary approach.

1.9 Comorbidity and complex clinical presentations

Given the changing nature of HIV, and advances in biomedical management, there is increased attention on other comorbidities which can have an additive or interactive effect on the medical management of HIV, particularly in the context of an ageing population of PLHIV. Psychosocial comorbidity (such as mental illness or social/welfare concerns), in particular, is increasingly the focus of clinicians working within an interdisciplinary framework who recognise the biological, psychological, and social antecedents to complex clinical presentations in PLHIV. Moreover, such complex clinical presentations are often complicated by funding systems within publicly funded healthcare settings in Australia; although universal healthcare is available, there is some suggestion that existing *"funding systems do not accommodate or incentivise proactive care, instead facilitating a narrow set of responses"* (Kuipers et al., 2011, p. 22). This clinical complexity must be effectively identified, monitored, and treated in order to support medical interventions and improve a range of health outcomes; not just

viral suppression, but also overall well-being and QoL. However, in the context of current global HIV targets and guidelines for care delivery, there is little opportunity to report on the broad range of outcomes associated with chronic illness. Some studies have investigated the relationship between comorbidity, functioning and QoL in PLHIV, suggesting that lower QoL is associated with a range of medical and psychosocial comorbidities (Zeluf-Andersson et al., 2019a). Likewise, Lazarus and colleagues noted the important role of comorbidity in QoL, particularly in the context of an ageing cohort of PLHIV (Lazarus et al., 2016). Understanding comorbidity and the complex clinical presentations which can ensue, as well as their impact on key outcomes, is a focus of the present study series.

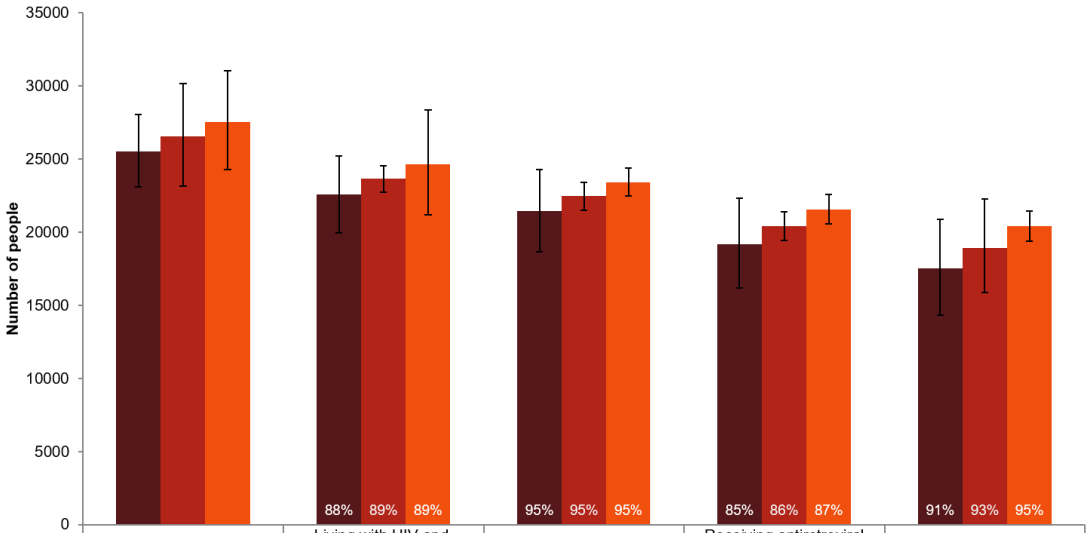
Historically, VL alone has been used to measure 'success' although this has recently been challenged, with many suggesting optimal holistic care should move beyond viral suppression alone (Kall, Marcellin, Harding, Lazarus, & Carrieri, 2019; Safreed-Harmon et al., 2019). The HIV Outcomes Coalition, a group of European clinicians and researchers, have developed guidelines for holistic long-term care of PLHIV, the recommendations of which were presented to the European Parliament in 2017. A central theme is that prevention, treatment and management of comorbid issues known to impact PLHIV should remain at the centre of their care. This document also recognises the importance of individualised targets and care plans developed by an interdisciplinary team, and the need to expand reporting guidelines to include long-term HIV care and holistic outcomes (HIV Outcomes Coalition, 2017). Furthermore, these recommendations explicitly identify the need to expand clinical outcomes (and by extension, reporting

guidelines and metrics of 'success') to include an assessment of 'health-related QoL' in the context of long-term HIV care, in addition to VL (HIV Outcomes Coalition, 2017). This expansion, if adopted, directly relates to The HIV Care and Treatment Cascade (Cascade) reporting guidelines and global 90-90-90 targets.

1.10 The HIV Care and Treatment Cascade and 90-90-90 targets

The Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets (UNAIDS, 2014) aim for 90% of PLHIV to know their diagnosis, 90% of those to be regularly taking ART, and 90% of those to be virologically suppressed. These ambitious global targets for 2020 have shaped HIV management in recent years. By contrast, the Cascade has five stages, which detail the trajectory of PLHIV, including: (a) diagnosis, (b) linkage to care, (c) ART initiation, (d) retention in care, and (e) viral suppression (Kirby Institute, 2018). UNAIDS 90-90-90 targets broadly map onto what is currently considered to be the three key priorities within the Cascade; namely diagnosis, treatment and viral suppression. Region-specific estimates of Cascade components vary, and often depend upon the region's policies and guidelines with respect to access to care and the process of monitoring. Many authors (Drew et al., 2017; Kay, Batey, & Mugavero, 2016; Levi et al., 2016; Lourenço, Hull, Nosyk, Montaner, & Lima, 2015), have noted the lack of consistency in the definition and measurement of aspects of the Cascade, in particular retention in care, and have highlighted the potential difficulties this presents in comparing similar regions, and monitoring global targets. At a practical level, accurate and consistent definitions and estimates of Cascade components such as retention

have vast implications for resource allocation and funding. Figure 1 shows the most recent Australian HIV Care and Treatment Cascade, which demonstrates consistently high estimates (95%) of retention in care.



	Living with HIV	Living with HIV and diagnosed	Retained in care	Receiving antiretroviral therapy	Supressed viral load
2015	25543	22583	21454	19164	17505
2016	26578	23644	22462	20413	18945
2017	27545	24646	23414	21560	20412

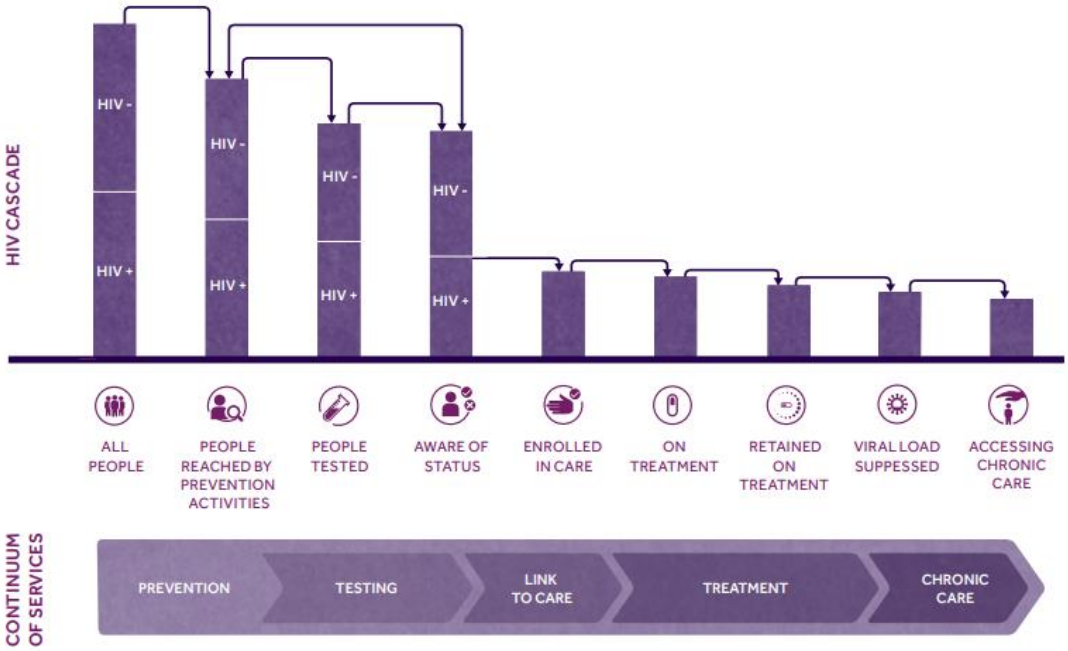
1.10.1 Figure 1: The HIV Care and Treatment Cascade, Australia (Kirby Institute, 2018)

1.10.2 Do current targets represent optimal service delivery?

Arguably, current global 90-90-90 targets should represent the benchmark for optimal care. However, some authors have queried these targets; Auerbach recently asked the important question *"What about the other 10-10-10?"* (Auerbach, 2019, p. S99). This question is central to the idea of optimal care delivery, and suggests that our focus should arguably be shifting towards the remaining 10-10-10. This author also, importantly, noted challenges with comparing the Cascade to 90-90-90 targets,

although the latter should broadly map onto the former. She notes that that the denominator for the second and third '90' targets are derived from the preceding target (i.e. 90% of people diagnosed are on treatment); in contrast, the Cascade denominator throughout is the total number of PLHIV (Auerbach, 2019). Thus, comparison between the two is not straightforward. In addition, Auerbach notes the importance of understanding as much as possible about the 'missing' 10-10-10, and most importantly that the 'final 90' is not and should not be considered the end of efforts to improve clinical outcomes (Auerbach, 2019). Recognition of the importance of expanding targets (including reporting requirements) to include QoL is also discussed. Viral suppression is clearly a primary outcome – however *sustained* viral suppression is the result of a host of biological and psychosocial factors coming together across time, and therefore requires recognition of more than blood results alone.

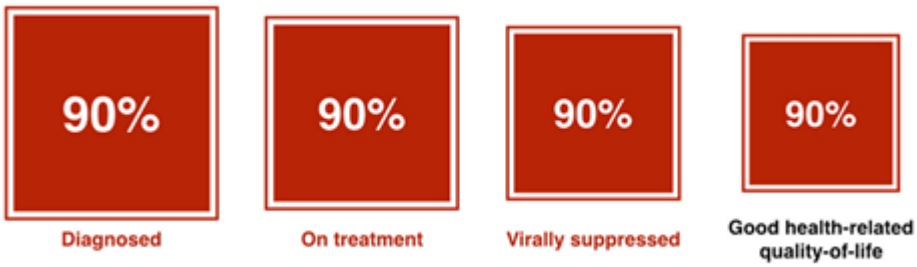
Interestingly, the recent WHO HIV Strategy 2016-2021 also recognises 'accessing chronic care' as a key element in their 'continuum of HIV services and retention cascade' (Figure 2). What this again highlights is an increasing global recognition of the importance of chronic care management and accessing regular care, which arguably surpasses viral suppression alone; however, this appears yet to be reflected in regional guidelines and reporting requirements.



1.10.3 Figure 2: The continuum of HIV services and retention cascade (World Health Organization, 2016b)

1.11 Optimal holistic care: Moving beyond viral suppression to include 'a fourth 90'?

In light of these arguments, the Cascade in its current form arguably does not represent best practice holistic care. Some authors have suggested expanding the Cascade, and indeed the UNAIDS 90-90-90 targets, to include a fourth '90' – 'health-related quality of life', with the explicit purpose of expanding *"the continuum-of-services paradigm beyond the existing viral endpoint of viral suppression…*[which] *entails attention to two domains: comorbidities and self-perceived quality of life"* (Lazarus et al., 2016, p. 1). Figure 3 shows the proposed targets outlined by Lazarus and colleagues.



1.11.1 Figure 3: Inclusion of the "Fourth 90" (Lazarus et al., 2016)

This has since been expanded to more closely map to the Cascade. As Auerbach noted, the denominator of each 90-90-90 target is derived from its predecessor, versus the Cascade which instead considers all PLHIV (Auerbach, 2019). In this way, Figure 3 above suggests 'good health-related quality of life' only for those who are virally suppressed; in fact, this should be the target for all PLHIV. An updated figure by these authors is shown below (Figure 4).

1.11.2 Figure 4: Updated model including the "Fourth 90" for all PLHIV (Safreed-Harmon et al., 2019)

The benefit of including a 'well-being' target is that it recognises that simply managing HIV infection at a medical level neglects to account for its associated medical and/or psychosocial comorbid factors, which can ultimately complicate its management. In addition, it recognises that viral suppression alone does not constitute overall wellness or QoL, and that our aspirations for optimal HIV management should extend to these considerations in addition to viral suppression. The authors specifically call for the global public health community to advocate for a new paradigm *"beyond viral suppression"* (Lazarus et al., 2016, p. 3). Such a perspective is innovative in its inclusion of factors beyond medical alone, not just at a practice level but also at the level of policy and reporting guidelines, and its recognition of the need for broader considerations to optimally support and treating our existing PLHIV community. As discussed in section 1.8.1, this paradigm shift is required primarily as a result of ageing among PLHIV, and the increased risk of comorbidity which can and will impact overall functioning, including effective HIV medical management.

This topic is so pertinent that it was the recent subject of a Lancet HIV special series *"HIV outcomes beyond viral suppression"* (published on 25th November 2019), which questioned whether health systems are prepared to meet the needs of ageing among PLHIV. In addition, the Editorial piece clearly notes that, while viral suppression is important, it should not be considered the only endpoint, and that people should be 'living well' with HIV, not just living with HIV (The Lancet HIV, 2019). Authors within this series noted that PLHIV often present with disproportionately high rates of comorbidities, when compared to the general population, and further suggested that

HIV-infection might exacerbate such conditions (Safreed-Harmon et al., 2019). These authors also conclude that a key priority for future research and policy is to identify mechanisms to monitor progress towards new goals, beyond viral suppression (Safreed-Harmon et al., 2019).

1.11.3 Quality of Life (QoL)

QoL can be *"shaped by the* absence *of negative factors (e.g. ill health and poverty) and the* presence *of positive ones (e.g. social relationships and contentment"* (International HIV/AIDS Alliance, 2018, p. 4). This internationally recognised document also notes that holistic care is necessary to achieve QoL, and includes (a) treatment for HIV, (b) treatment for non-HIV comorbid factors, and (c) recognition of well-being and wider social, cultural and economic rights, and that QoL eventually feeds back into sustained medication adherence and ultimately viral suppression (International HIV/AIDS Alliance, 2018). The first two items within that list are the responsibility of health care providers. In addition, it has been suggested that the impact of stigma and/or discrimination is inherent in any study of QoL (Zeluf-Andersson et al., 2019b), with some suggesting that self-stigma specifically impacts QoL by impacting social interactions (Nobre, Pereira, Roine, Sutinen, & Sintonen, 2018). Tran and colleagues noted that improved health-related QoL was associated with improved ART adherence, while stigma was negatively associated with adherence (Tran, Fleming, Do, Nguyen, & Latkin, 2018). Thus, QoL is necessary not only for individual well-being, but also ultimately to support the individual for lifelong effective HIV management.

Measuring QoL ultimately entails recognition and monitoring of comorbidities; in their study, Langebeek and colleagues noted that PLHIV presented with significantly worse mental and physical QoL compared to their HIV-negative counterparts, and that the greater the number of comorbidities, the worse the report of physical QoL in particular (Langebeek et al., 2017). If the Cascade and corresponding targets were to be expanded to include QoL and associated comorbidity, it would be important to consider *how* this could be monitored and captured in our reporting estimates. Within the existing Cascade, *'retention in care'* is certainly a means by which to achieve this, by allowing opportunity for regular holistic monitoring of all factors beyond VL alone. At present, however, its full potential is not realised.

1.12 What is 'retention in care' and why does it matter?

Successfully achieving and maintaining an UDVL requires consistent medication adherence, as well as regular monitoring to ensure the medications continue to manage virus replication and maintain viral suppression; it requires that PLHIV remain *retained in care*. At its most basic level, retention is necessary to ensure regular VL monitoring; crucially, however, it also affords care providers the opportunity to monitor other potentially modifiable factors which might impact the whole person, their well-being, functioning, and QoL in the context of holistic care and an interdisciplinary approach to health. Sustained viral suppression assumes medication adherence; to support this, understanding its context is imperative. For example, some studies have found that mental illness or substance use can negatively impact

medication adherence (Blashill et al., 2015; Robinson, Knowlton, Gielen, & Gallo, 2016; Yehia et al., 2015a). Solely focussing on biomedical endpoints such as VL without consideration of the factors which influence them could, therefore, be considered short-sighted. In this way, retention can be considered necessary for:

1. Monitoring ART adherence
2. Monitoring the comorbid factors which might impact ART adherence
3. Monitoring comorbid factors which might impact well-being/QoL (i.e. providing optimal holistic care)

Despite this, existing definitions do not account for this broader context and instead focus solely on biomedical endpoints, the first point above.

Current definitions of retention in resource-rich countries vary significantly. In the U.S, retention is defined as attending a medical HIV review (with phlebotomy tests an acceptable proxy) *at least twice per 12-months, spaced at least 90 days apart* (Centers for Disease Control and Prevention, 2018). In Australia and the U.K, retention is defined as *attendance to a medical appointment at least once per 12-months*, often with phlebotomy visits serving as a proxy (British HIV Association, 2018; Kirby Institute, 2018). Consequently, retention estimates in Australia and the U.K, for example, are significantly higher, both currently estimated to be 95% (Kirby Institute, 2018; Public Health England, 2018), compared to 57.2% in the U.S. (Centers for Disease Control and Prevention, 2018). Data on European countries estimate retention rates of

approximately 68% (Drew et al., 2017). The discrepancies could be impacted, in part, by universal healthcare which is available in Australia and the U.K, but not the U.S.

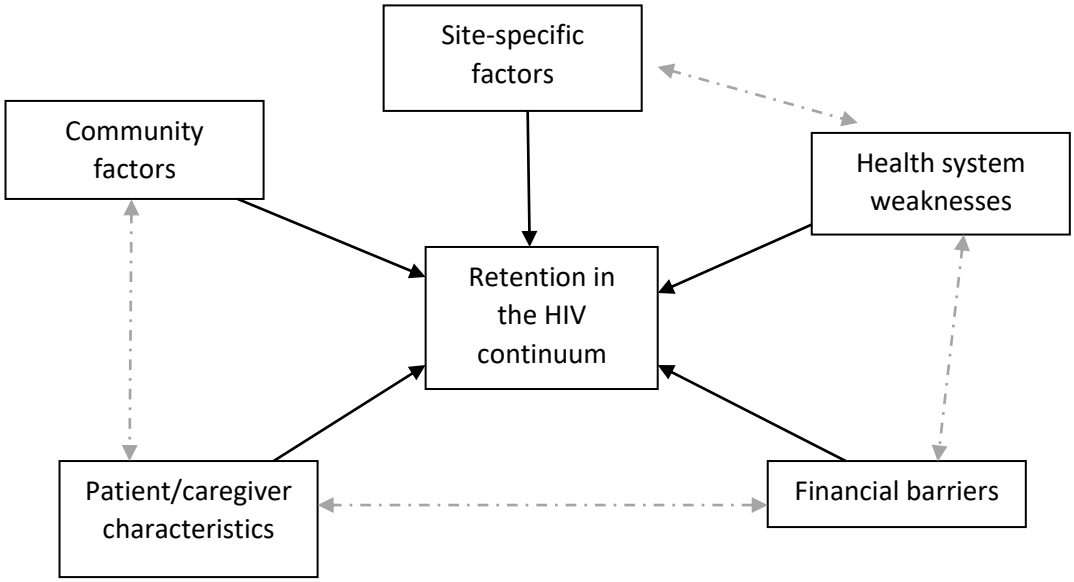
Such definitions only measure VL to the exclusion of other important factors, some of which could be modifiable. In addition, they are likely appropriate for those with a relatively straightforward medical profile and few complicating comorbidities, but might be considered inadequate for the individual with complex psychosocial needs which have the potential to detrimentally impact their well-being, QoL, and ultimately their management of HIV. Definitions of retention have the potential to support the management of complex clinical presentations, which can ultimately impact viral suppression; however the present focus on biomedical endpoints alone does not allow for this. Retention can be considered a marker of 'quality of care' (Umeokonkwo et al., 2019), however current definitions only account for VL in the same way that global 90-90-90 targets favour the same; arguably this does not constitute optimal care.

Recent WHO guidelines have suggested a more progressive approach to considering retention, accounting for the changing nature of HIV and the increasing role of comorbidity which might impact disease progression; their definition of retention is a person attending medical review appointments *"appropriate to* [the] *need"* (World Health Organization, 2017, p. 26). More specifically, this document states *"retention is used to describe a cohort of people living with HIV who are alive and receiving routine HIV care, including ART, at a specific time after enrolling in HIV care or starting ART specifically"* (World Health Organization, 2017, p. 26). The document suggests 'ART

retention' is the most meaningful estimate of success, continuing the trend of biomedical metrics being used to measure treatment success. However, the comment *"including ART"* implies a definition broader than the provision of medication alone. Other WHO documents also define retention from a more holistic perspective, noting *"continuous engagement…in a package of prevention, treatment, support and care services"* (World Health Organization, 2012, p. 3), and *"ensuring that the client continues to receive appropriate services (from both the client and provider perspective) throughout the continuum of HIV care and support"* (World Health Organization, 2012, p. 61). Likewise, the WHO Global Health Sector Strategy on HIV 2016-2021 notes *"The goal: To end the AIDS epidemic as a public health threat by 2030, within the context of ensuring healthy lives and promoting well-being for all at all ages"* (World Health Organization, 2016b, p. 23).These expanded definitions certainly move beyond the biomedical domain, to encompass the other elements of HIV management, and imply the need for other metrics for 'success'.

An argument could be made, therefore, that overly narrow definitions of retention - which focus on VL alone - fail to account for the role of psychosocial and other medical comorbidity in impacting biomedical HIV management as well as health-related QoL. As a result, local, State and Federal government funding may be allocated elsewhere in the Cascade (e.g. prevention and testing). In order to move towards optimal holistic care delivery for PLHIV who are ageing, we need to invest time, research and resources into retention as our means to effectively monitor and treat comorbid factors to improve overall QoL outcomes, not just VL.

The WHO has also developed a model to explain the factors indicated in retention in care (World Health Organization, 2012, p. 17). Although originally developed from a paediatric perspective, there is no reason this cannot be extended to adult populations. The model (Figure 5) suggests an interaction of factors beyond client characteristics alone which might impact retention, including community factors, site-specific factors, health-system factors, caregiver characteristics and financial barriers (World Health Organization, 2012). Client characteristics, in particular, are a focus of the present study series.



1.12.1 Figure 5: WHO proposed interaction of factors which impact retention in paediatric and adolescent cohorts (World Health Organization, 2012, p. 17)

Given the lack of consistency in the measurement and definition of retention, some (e.g. Drew et al., 2017) have suggested retention is now a redundant component of the Cascade and have called for its removal. However, if accurate retention estimates are

not captured, the sector misses the opportunity to evolve with the changing nature of the HIV epidemic and re-focus its attention towards other broader factors which can impact HIV management. While the HIV sector recognises the important role of psychosocial, as well as medical, comorbidity and its impact on disease progression and well-being/QoL, this has not translated into formal policy change or reporting requirements. An existing means by which to monitor and report such comorbidity exists within the Cascade, namely retention in care. Rather than de-valuing it, the time has come to expand retention definitions and standardise its reporting requirements to effectively capture holistic monitoring targets in the service of supporting people to '*live well with HIV*'. In the context of holistic monitoring, removing retention from the Cascade would be a mistake, and the present study series aims to provide results to support this assertion.

1.13 Comorbidity in the context of VL and Retention

Comorbidity is a universal concern in chronic illness treatment and literature. Understanding the nature of and relationships between comorbidities, many of which are modifiable, is important to identify their impact on health outcomes. In the context of HIV, historically this has been attaining and sustaining an UDVL; however, as has been discussed, by itself this is arguably an outdated metric of treatment success. Retention is necessary for three key outcomes: to monitor VL and any changes as a result of adherence difficulties; to monitor associated comorbidity which might impact the individual's overall well-being and QoL; and to monitor comorbidity which might ultimately impact sustained viral suppression. Interestingly, there is likely a

bidirectional relationship between comorbidity and retention; comorbidity certainly has the potential to impact retention, which in turn is necessary to effectively monitor comorbidity. This will be discussed in more detail in section 9.1.2.

Previous studies have investigated the association between these factors and have found that suboptimal retention is associated with a range of adverse health outcomes, including delayed viral suppression (Crawford, Sanderson, & Thornton, 2014; Mugavero et al., 2012a). Likewise, the presence of comorbidities has also been associated with viraemia (Syed et al., 2016), with certain psychosocial factors such as substance use and mental illness thought to specifically impact medication adherence (Blashill et al., 2015; Robinson et al., 2016; Yehia et al., 2015a).

As a result, in addition to providing optimal holistic care and the capacity to monitor all and address the modifiable factors associated with HIV, retention also has the potential to impact viraemia. Furthermore retention, which allows for regular monitoring of psychosocial as well as medical comorbidities, might provide an avenue for early identification of and intervention for certain factors which might impact medication adherence, and ultimately viral suppression. This is in addition to the overall benefit of having comorbid factors monitored and treated, in the context of well-being and overall QoL.

Retention is, therefore, an important component in the movement to expand reporting requirements beyond the biomedicalised perspective of HIV, to encompass broader well-being targets. Many have argued for expansion of the Cascade and global targets to include factors beyond viral suppression; the present study series seeks to specifically address one component of the Cascade in this context - retention in care. Understanding the specific comorbidity antecedents, and the nature of the relationship between these variables, is a necessary foundation to realising this goal.

1.14 Theoretical underpinnings

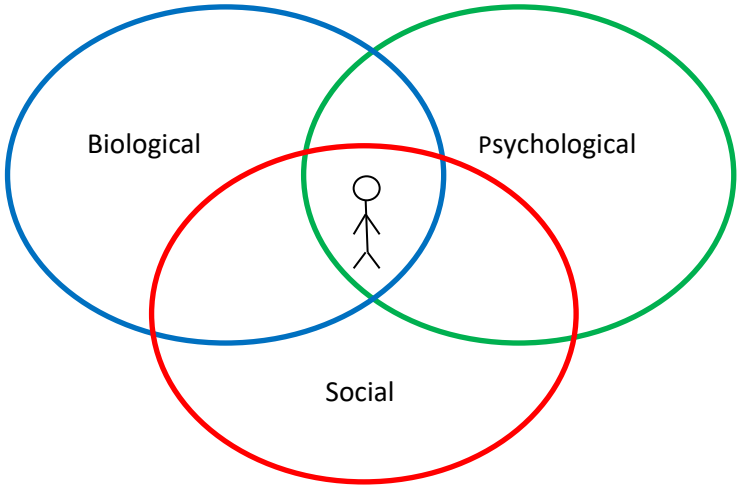
Thus far, this chapter has reviewed the literature and practice in the context of the history of the epidemic. It is necessary now to consider these concerns from relevant theoretical perspectives, specifically accounting for the role of medical and/or psychosocial factors in retention in care.

A number of theories exist to explain and understand the mechanisms of comorbidity and adherence. Theories relating to the latter generally focus on medication adherence, however models also exist specifically related to appointment adherence. What follows is a review of three key theoretical models by which to understand the present study series: the Biopsychosocial Model (Engel, 1980), which details *which variables* are considered to impact chronic disease; the Syndemic Model of comorbidity (Singer, 1994), which outlines *how variables interact* to increase the burden of illness; and finally the Andersen Behavioral Model of Health Service Use

(Andersen, 1995; Andersen, Davidson, & Baumeister, 2014), which considers *how such factors and relationships between variables impact treatment compliance*, specifically the use of health services.

1.14.1 The biopsychosocial model and chronic disease

The biopsychosocial model (Figure 6) of healthcare delivery was constructed specifically to address the gap left by the biomedical model alone, and considers the interplay between the biological, psychological and social determinants of health, with the individual at the centre (Engel, 1980). This model does not seek to negate the role of the medical approach, but rather seeks to extend and broaden this to encompass other relevant factors (Havelka et al., 2009). It would be too simplistic to assume biological factors alone could account for all variation of outcomes; this would be a limited means of explaining human behaviour. Indeed, Engel noted that the biopsychosocial model extends the previous biomedical model by accounting for these previously neglected areas (Engel, 1980). The model also seeks to recognise the role of the individual, their context and behaviour in explaining chronic illness, rather than focussing on symptom profile alone (Havelka et al., 2009). In the context of chronic disease, the model has a vast evidence-base among a range of diseases, including diabetes (Habtewold, Islam, Radie, & Tegegne, 2016), chronic pain (Kamper et al., 2015), and arthritis (Sumner & Nicassio, 2016). Some authors have also argued for an expansion of Engel's original model to encompass a focus on wellness/health in addition to illness, to understand the intricate interplay between the biological, psychological and social variables, and to pay special attention to the role of support networks and connectedness in chronic disease (Lindau, Laumann, Levinson, & Waite, 2003).



1.13.1.1 Figure 6: The Biopsychosocial Model

In the context of HIV, this approach is often used to assist the management of associated comorbidity which often accompanies HIV-infection, for example pain and substance use (Miller, Halkitis, & Durvasula, 2018). In order to fully understand HIV in the ART-era, where the biomedical aspects of HIV management are relatively well controlled, an exploration of the key biological, psychological and social factors which might impact that management is necessary. The following discussion seeks to elucidate the range of biological, psychological and social factors which are known to impact HIV management.

1.14.1.2 Biological Factors

There are a number of biological or medical comorbidity variables which continue to impact PLHIV.

1.14.1.2.1 Viral Hepatitis

Viral hepatitis (inflammation of the liver) is generally found in three main forms; Hepatitis A (HAV), Hepatitis B (HBV), and Hepatitis C (HCV), all with differing modes of transmission and varying degrees of severity. In the U.S, PLHIV are disproportionately affected by viral hepatitis, with nearly 75% of PLHIV reporting a history of injecting drug use being co-infected with HCV (National Center for HIV/AIDS, 2017). In recent years, as treatment for HCV-infection has evolved, a large proportion of previously infected individuals have now undergone treatment and 'cleared' the virus. However, when untreated, HCV and HIV co-infection can accelerate cirrhosis in those whose HIV is not well managed (Bonacci, Lens, Marino, & Forns, 2016).

1.14.1.2.2 Sexually Transmitted Infections (STIs)

Sexually transmitted infections (STIs) are those which are transmitted via sexual contact. HIV is considered to be both an STI and a blood borne virus (BBV) because of the multiple modes of transmission. The most prevalent STIs in Australia are Chlamydia, gonorrhea, syphillis, and human papillomavirus (HPV) (Kirby Institute, 2018), and a recent survey of PLHIV suggested 28.6% of respondents had been diagnosed with an STI in the preceding 12 months (Power et al., 2019). If untreated, the presence of an STI can increase the risk of HIV transmission.

1.14.1.2.3 Tuberculosis (TB)

While largely managed in resource-rich countries due to vaccination programs, the prevalence of Tuberculosis (TB) in resource-limited countries is high. The WHO

estimates that TB is the leading cause of death among PLHIV, with the WHO African region accounting for 84% of deaths in 2017 (World Health Organization, 2018b).

1.14.1.2.4 HIV-related Cancers

During the early days of the HIV epidemic when the immune systems of PLHIV were significantly weaker, HIV-related cancers were common and often considered an AIDS-defining illness. Although the risk of developing HIV-related cancers is now lower than previously, the prevalence remains higher than the general population. The most common, which can impact those with well-managed HIV, are Kaposi's sarcoma, non-Hodgkin Lymphoma, and cervical cancer (associated with HPV) (National Cancer Institute, 2017). In addition, PLHIV are also at higher risk of developing other forms of non-HIV-related cancers; for example, they are 19 times more likely to be diagnosed with anal cancer compared to the general population (Hernández-Ramírez, Shiels, Dubrow, & Engels, 2017). One possible explanation for the overall increase in non-HIV-related cancers is the introduction of ART which has contributed to longevity in PLHIV, and ultimately ageing among PLHIV.

1.14.1.2.5 Diet/Nutrition

Nutrition is an important part of overall health, well-being and immune functioning in the general population, and this can be even more pronounced for PLHIV given their compromised immune systems (U.S. Department of Health and Human Services, 2018). Likewise, HIV-related infections and ART medications can create nutrition-related difficulties for PLHIV (e.g. impairing the capacity to swallow), such that this should be monitored.

1.14.1.2.6 Cardiovascular Disease (CVD)

As the average lifespan of PLHIV increases, so too does their risk of developing diseases related to ageing at a similar rate to the general population. Cardiovascular Disease (CVD) is one such condition, with PLHIV considered to have higher rates of risk factors (e.g. smoking) than the general population (Deeks & Phillips, 2009). There is some suggestion, however, that the rates of CVD are higher in PLHIV as a result of the infection itself and/or medication, even when age and risk factors are controlled for (Deeks & Phillips, 2009; Friis-Møller et al., 2003).

1.14.1.2.7 HIV-Associated Neurocognitive Disorders (HAND)

HIV-Associated Neurocognitive Disorders (HAND) continue to be diagnosed, despite advances in ART. Existing along a spectrum of severity and functional impairment, they remain a cluster of disorders for which HIV specialists should monitor and screen (van den Dries et al., 2017). Cognitive impairment has the potential to severely impact HIV management (e.g. medication adherence) if adequate supports are not in place. Some classes of ART have the capacity to cross the blood-brain barrier and thus control the degree of virus found in the central nervous system (CNS), which is known to impact cognitive function (Atluri et al., 2015). For this reason, consistent ART adherence and regular monitoring of cognitive impairment are necessary to detect any changes in functioning as early as possible.

1.14.1.2.8 Physical health factors relating to ART toxicity

There are toxicity factors associated with long-term ART use. While the medications are highly effective at treating HIV and toxicity has significantly reduced since the

1990's, problematic aspects remain and require monitoring. In particular, the impact of ART on liver and kidney function, bone disease, CVD, and disorders of the CNS should be monitored (Chawla et al., 2018).

1.14.1.3 Psychological Factors

In addition to the biomedical aspects of HIV, the psychological sequalae cannot be ignored, especially in the context of marginalisation, stigma and discrimination, as well as diagnosable mental health conditions, and the presence of psychiatric symptoms in the absence of diagnoses. It is widely understood that the prevalence of psychiatric disorders, including substance abuse, is higher for PLHIV than the general population (De Hert et al., 2011; O'Cleirigh, Magidson, Skeer, Mayer, & Safren, 2015). There is also a suggestion that people with a pre-existing psychiatric condition may be at higher risk of sexual risk-taking, and therefore contracting HIV (O'Cleirigh et al., 2015). Likewise, it is possible that the relationship exists in the reverse, or is bi-directional; in other words, chronic illness and lifelong medical treatment may impact psychological functioning.

1.14.1.3.1 Mood Disorders

Some estimates indicate the lifetime prevalence of mood disorders to be twice as high for PLHIV compared to the general population (American Psychiatric Association, 2012a; Ciesla & Roberts, 2001; Heywood & Lyons, 2016). It is worth noting that some ART medications can also detrimentally impact mental health in some individuals, and drug-drug interactions must be monitored closely if a person is accessing psychopharmacological treatments (American Psychiatric Association, 2012a). There is also evidence to suggest chronic depression, stress and trauma can negatively impact

HIV disease progression (Leserman, 2008). In Australia, 22.3% of respondents to a recent survey reported a current diagnosis of more than one mental health condition, with depressive and anxious disorders the most common (Power et al., 2019).

1.14.1.3.2 Substance use disorders

There is evidence for a strong association between substance use and HIV-infection, either as a precursor to infection (e.g. sexual risk-taking or sharing injecting equipment), or as a means of coping with a diagnosis and chronic illness (American Psychiatric Association, 2012d). Prevalence estimates suggest nearly 50% of PLHIV report past or current substance use disorders (Durvasula & Miller, 2014). In a recent survey of PLHIV in Australia, analgesics, sleeping pills, amyl nitrites and marijuana were the most commonly reported substances used for non-medical purposes (Power et al., 2019). Recent estimates in Sydney, Australia suggest 65.4% of MSM participants reported some form of substance use in the preceding six months, with recreational 'party drug' use reported by 20.8% of the cohort (Broady et al., 2018). In addition, participants were more likely to report substance use, and disproportionately more likely to report crystal methamphetamine (CMA) use compared with HIV-negative men (27.4% vs. 8.7% respectively) (Broady et al., 2018). This figure corroborates the experience of many clinicians working in the HIV-sector in Sydney, NSW.

1.14.1.3.3 Anxiety disorders

Anxiety, along with depression, is thought to contribute to greater disease progression and poorer health outcomes in PLHIV (Heywood & Lyons, 2016). A recent study in Australia estimated that 35% of HIV-positive MSM presented with elevated anxiety

scores on a range of measures, a prevalence which is considered greater than in the general population (Heywood & Lyons, 2016), and which is consistent with other estimates (American Psychiatric Association, 2012b). It is important to note the cluster of anxiety disorders includes Posttraumatic Stress Disorder (PTSD), which is considered common among PLHIV (Durvasula & Miller, 2014; McCall, Lauridsen-Hoegh, Unger, Phillips, & Kille, 2018; Sales, Swartzendruber, & Phillips, 2016); in addition, the potential role of 'complex trauma', *"…exposure to multiple, often prolonged or extended traumas over time"* (Briere & Scott, 2015, p. 516) in PLHIV must be considered in the context of marginalisation, stigma and discrimination.

1.14.1.3.4 Psychotic disorders

There is some evidence that individuals with severe mental illness (SMI), such as Bipolar Affective Disorder and Schizophrenia, are at significantly greater risk of HIV infection, as well as other BBVs such as HBV and HCV (American Psychiatric Association, 2012e; Ayano et al., 2018; Diduch, Campbell, Borovicka, Cunningham, & Thomas, 2018; Firth et al., 2019). Furthermore, for those with comorbid HIV and SMI, especially if also associated with substance use, service engagement and medication adherence can be of concern. In the context of substance use, the impact of drug-induced psychotic disorders must also be considered; while the symptoms can be short-term, prolonged substance use can lead to repeated psychotic episodes (Mills et al., 2011).

1.14.1.3.5 Personality disorders (PD)

High prevalence rates of personality disorders (PD) among PLHIV have been well-documented, with 'Cluster B traits' (characterised by interpersonal difficulties, and

emotion dysregulation) most prevalent (Durvasula & Miller, 2014). A recent audit of PLHIV attending the psychology unit within a publicly funded HIV service in Sydney, Australia found that 63% of participants reported symptoms consistent with a PD, with the most common being Borderline Personality Disorder (57%) (Van Heyst et al., 2018). The chronicity of PD, and interaction with multiple other psychiatric disorders such as substance use and complex trauma, makes it difficult to treat.

1.14.1.3.6 Stigma and discrimination

As a marginalised community, PLHIV have long battled stigma and discrimination. Whether an extension of the early days of the epidemic, where fear regarding transmission was rife, or related to judgement regarding perceived route of infection remains unclear (Chambers et al., 2015; Reidpath & Chan, 2005). Some authors have documented the impact of anticipated stigma on physical health outcomes, mediated by stress, with factors such as social support considered protective (Earnshaw, Lang, Lippitt, Jin, & Chaudoir, 2015). The impact of stigma often transcends psychological distress, and can also be something which precludes PLHIV from accessing care and services (Chambers et al., 2015).

1.14.1.4 Social Factors

Beyond the biological and psychological realms, the impact of social/welfare factors on a person's overall well-being and QoL cannot be discounted and are increasingly gaining attention. These include financial stress/socioeconomic status, isolation/loneliness, housing, ethnicity, sex, and education. The most important of these, according to the National Research Council and Institutes of Medicine, are

socioeconomic status/financial stress, ethnicity and education (National Research Council and Institute of Medicine, 2013), although the role of social isolation is increasingly gaining traction as an important variable (Holt-Lunstad, Smith, Baker, Harris, & Stephenson, 2015). The interaction of these variables can work to heighten existing biological and psychological stressors and are likely to be more pronounced in marginalised populations.

In 2011 during the World Conference on Social Determinants of Health, the WHO noted *"the bulk of the global burden of disease and the major causes of health inequities, which are found in all countries, arise from the conditions in which people are born, grow, live, work, and age"* (World Health Organization, 2011, p. 7), and identified these conditions as the *Social Determinants of Health*, which include social, economic, political, environmental and environmental factors.

There is increasing evidence to underscore the important role of social determinants in health outcomes and to move away from purely biomedical models of health (Cockerham, Hamby, & Oates, 2017). These authors also note that social factors often play an important role in the onset and course of many health conditions, including infectious diseases, such that their influence cannot be discounted (Cockerham et al., 2017).

1.14.1.4.1 Social connection

Isolation and loneliness, *"the distress that exists between actual and desired relationships"* (Greene et al., 2018, p. 1476), have long been considered to have a

significant impact on health, through psychosocial, behavioural and physiological pathways (Umberson & Montez, 2010). These authors suggest that the presence or absence of social ties can impact positive and unhelpful health behaviours respectively. Likewise, they suggest that supportive social connections improve mental health by reducing stress and nurturing meaning and purpose in a person's life (Umberson & Montez, 2010). Other authors (Wallston, Alagna, De Vellis, & De Vellis, 1983) also suggest that social support has a positive impact on physical health by moderating the impact of stress. Physiologically this can lead to reduced blood pressure and stress hormones, among other factors, which facilitate healthy physical functioning. In addition, the role of service-level care and support must not be discounted, with non-ART clinical services contributing to reduction in illness and QoL for PLHIV (UNAIDS, 2016), as well as often providing practical support such as reminders and assistance to attend appointments.

Recent meta-analyses have identified that in the general population there is between 26% and 29% increased risk of mortality for loneliness and social isolation respectively (Holt-Lunstad et al., 2015), and a 50% increased likelihood for survival for those with stronger social relationships, adjusted for age, sex, health status and cause of death (Holt-Lunstad, Smith, & Layton, 2010). Such results suggest that supportive connections can not only improve the quality of a person's life, but also their longevity.

In the context of HIV, the impact of emotional and social support has been identified as important in overall QoL since the early days of the epidemic (Friedland, Renwick, & McColl, 1996), and continues to be the case today, with the presence of a support network positively correlated with reduced anticipated HIV stigma (Earnshaw et al., 2015). Isolation is prevalent in older cohorts in the general population (Hawton et al., 2011), and can potentially be more pronounced in older cohorts of PLHIV, among people who are often marginalised and will likely have lost connections through the course of the epidemic (Greene et al., 2018).

1.14.1.4.2 Financial stress/socioeconomic status

Some Australian studies have found social welfare payments to be associated with suboptimal ART use (Mao, de Wit, Kippax, Prestage, & Holt, 2015; Siefried et al., 2017), regardless of the fact that ART was heavily subsidised in Australia until 2015, when access became free for citizens, permanent residents and some other visa types. This is also in the context of access to universal healthcare and specialised HIV services at no cost, unlike other resource-rich countries (e.g. the U.S.). One possible explanation is the difficulty of many to pay for public transport, in a country where the cost of living continues to rise in some cities (e.g. Sydney, NSW).

1.14.1.4.3 Housing

A recent systematic review documented the concerning association between a lack of stable housing and poor engagement in care, poor ART adherence, suboptimal viral suppression and subsequent increased risk of transmission to others for PLHIV (Aidala et al., 2016). Another study noted that those accessing government-run housing for

PLHIV in New York were more likely to remain retained in care than other PLHIV (Terzian et al., 2015). The WHO have also broadly noted the importance of stable housing on physical health, especially in the context of ageing among PLHIV (World Health Organization, 2018d). They also comment that poor accessibility to housing appropriate to need can pose a number of physical health risks (e.g. falls risk), as well as psychosocial sequalae (e.g. isolation) (World Health Organization, 2018d).

1.14.1.4.4 Education

It is widely considered that education is a key determinant in positive health outcomes, likely related to the capacity to build knowledge, critical appraisal skills, and reasoning (Hahn & Truman, 2015). In particular, education is thought to be important in population health, with benefits including developing individual skills to access and navigate healthcare, and increasing access to economic and social resources (Zimmerman, Woolf, & Haley, 2015). A recent systematic review in the context of HIV extended this idea to include the role of health literacy in managing a chronic illness such as HIV (Reynolds, Smoller, Allen, & Nicholas, 2019). These authors, however, found studies often used education literacy as a proxy for health literacy, thus noting that those with low education literacy may have difficulty with aspects of healthcare such as medication adherence and accurate knowledge regarding HIV, including transmission risk (Reynolds et al., 2019).

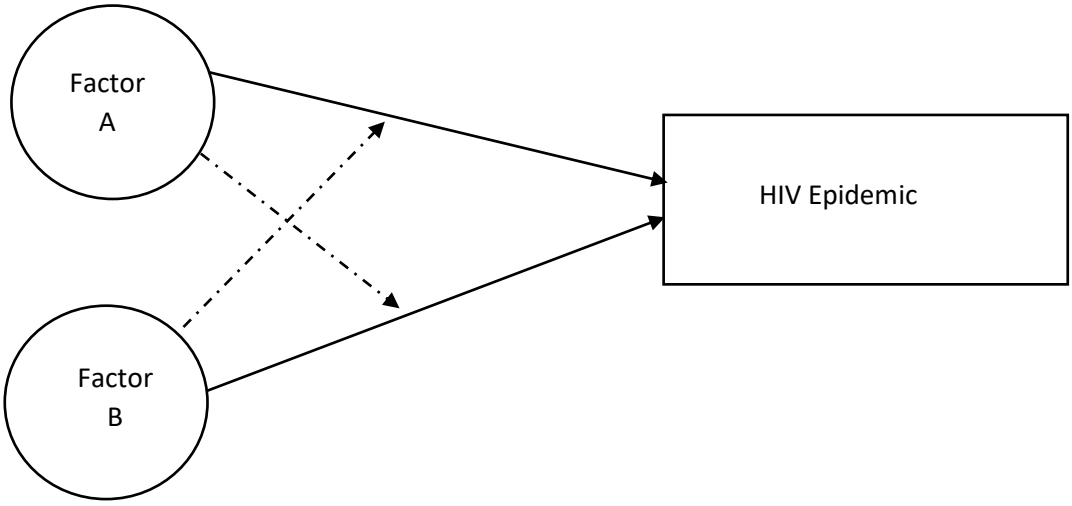
1.14.2 Syndemic Theory

A framework within which to consider the relationships between comorbidities is that of *syndemics*, the adverse interaction of biological, psychological and social conditions

in a way which increases the burden of illness (Singer, 1994; Singer, Bulled, Ostrach, & Mendenhall, 2017). Singer first discussed this theory in the context of the HIV epidemic in 1994 to conceptualise the complex synergistic interaction of factors which increased health disparities and adverse health outcomes. Originally conceptualised from an anthropological perspective, syndemic theory has been applied to social, medical and psychological literatures as a means of explaining comorbid relationships in healthcare. The model extends the Biopsychosocial Model by considering not only which factors are relevant, but *how* they interact, and the deleterious impact such interactions may have on health outcomes.

Syndemic theory considers the complex synergistic interaction between two or more co-occurring health conditions, in the context of their combined impact on disease progression (Singer et al., 2017). Important in the concept of syndemic theory is that it moves beyond a simplistic view of comorbidity, which is often considered to be additive; rather, it recognises the *interaction* between psychosocial, environmental and economic factors which can worsen outcomes. The theory can be considered one of population health, as it focuses on comorbidity trends in populations rather than at the individual level (Tsai, Mendenhall, Trostle, & Kawachi, 2017). By contrast, the norm for clinical trials is to exclude comorbidity, which is not representative of everyday clinical experience where comorbidity in some form is the norm. Therefore, a theoretical model which accounts for, rather than excludes, comorbidity is important in our understanding of population health characteristics.

Syndemics often reduce treatment efficacy and increase treatment cost (Singer et al., 2017); therefore, for long term efficient management of chronic disease, understanding the specific role of syndemics is imperative for individual and public health reasons. Figure 7 below shows the model in the context of the HIV epidemic, highlighting two synergistic factors and their effect on the HIV epidemic (Tsai et al., 2017). The dashed lines show that each factor has a greater impact on the HIV epidemic in the presence of the other.



1.14.2.1 Figure 7: The Syndemic Model (Tsai et al., 2017)

The process of identifying a syndemic is complex and the present study series aims to reflect on comorbidities through this lens. Considering comorbidity from this perspective allows for extensive consideration of not only the key factors involved, but *how* they might interact to impact retention. The present research series aims to begin the process of assessing the possible role of comorbidity on retention in care, through the lens of syndemic theory.

1.14.3 The Andersen Behavioral Model of Health Service Use

Many models of health behaviour exist; for example the Health Beliefs Model (Rosenstock, 1974) which accounts for individual beliefs about health which predict health behaviours; the Theory of Planned Behavior (Ajzen, 1985) which focusses on individual attitudes which shape behaviour; and the Stages of Change Model (Prochaska & DiClemente, 1983) which assesses readiness to act on new behaviours. While these models all account for the underlying processes involved in health-related behaviours, they do not specifically address the issue of health service utilisation (i.e. appointment adherence, or retention).

A recent review of social-behavioural models specific to medication adherence outlined their benefits, including the recognition of a wide range of individual, environmental, cultural and contextual factors in impacting treatment compliance (Amico et al., 2018). The authors reviewed a number of models and concluded that no single model necessarily 'fits' for all situations. Instead, they suggested service providers consider which resonates with their cohort and use the model as a broad guideline for understanding compliance. This includes tailoring the model according to specific factors and specific population characteristics (Amico et al., 2018).

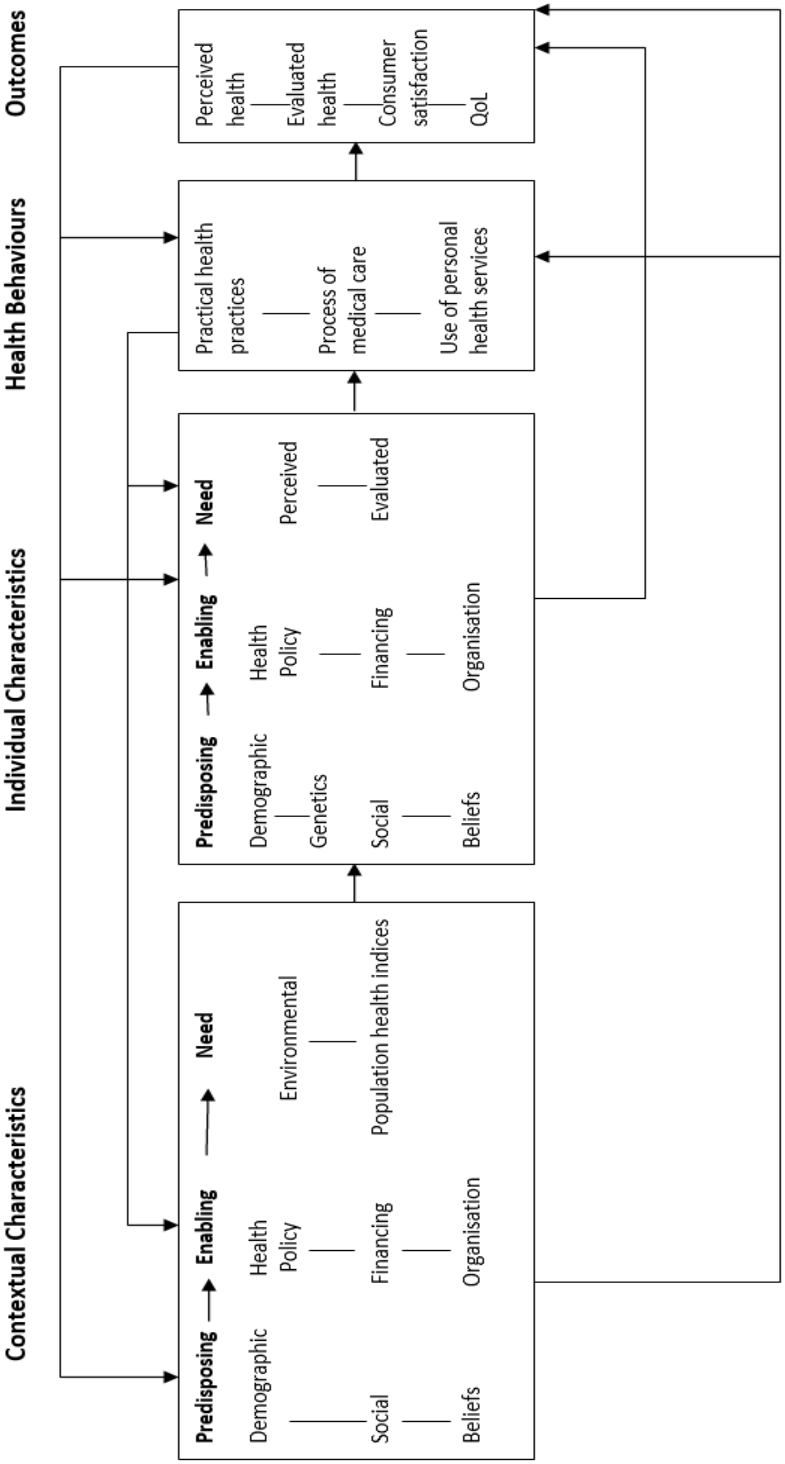
With this in mind, in the context of the present study series and its focus on the complex interaction between biopsychosocial comorbidities and their impact on retention in care, the Andersen Behavioral Model of Health Service Use (ABM) seems

most appropriate to consider here (Andersen, 1995), particularly in the context of accessing medical care. In addition, this model has been used in other studies of HIV retention in care and to classify the barriers identified (e.g. Holtzman et al., 2015). These authors argue that the ABM is more comprehensive than other theoretical models of adherence and health behaviours as it considers not only individual factors but also those relating to the environment and context, all of which can interact to impact retention and adherence. Thus, it also broadly complements the Biopsychosocial and Syndemic models discussed earlier.

The original model, developed in 1968, considered utilisation of healthcare services in the context of individual predisposing and protective factors, as well as needs. This incorporated factors such as health beliefs and motivation, as well as comorbidity and demographic variables to assess their impact on accessing medical care (Andersen, 1995). Since its inception, the model has undergone a number of revisions, and is presently in its 6th version. Figure 8 depicts the most recent version of the model (Andersen et al., 2014). This latest version recognises that improving health service utilisation is best accomplished by focussing on contextual, as well as individual, determinants.

Key components of the model include contextual and individual predisposing, enabling (which facilitate or impede access), and need factors, conceptualised by some as comorbidity requiring intervention (Amico et al., 2018). Examples include cultural norms

(contextual predisposing), health policy (contextual enabling), incidence of disease (contextual need), demographics and social factors (individual predisposing), access to transport (individual enabling), and comorbid conditions (individual need). The model also further describes the dimensions of access (potential versus realised), and whether that access is equitable or not on the basis of the relevant factors (Andersen et al., 2014). Indeed, access can be further determined as effective or efficient according to the model; these additional components beyond contextual and individual factors, while relevant, are beyond the scope of the present study series. Interesting in the review of 'need' is a further categorisation of perceived need (by the client) and evaluated need (by the clinician) in determining health service utilisation. This points to an acknowledgement of the benefits of clinician assessment of comorbid clinical factors. In the context of the present study series, retention in care would be classified as a 'health behaviour', with virological suppression an example of a 'health outcome' (Figure 8).



1.14.3.1 Figure 8: The Andersen Behavioral Model of Health Service Use (Andersen et al., 2014)

1.15 The present study series

The history and literature reviewed thus far highlight the importance of psychosocial, as well as medical, comorbidity in monitoring and evaluating the continued public health response to the evolving HIV epidemic, as well as the significance of retention in care within the Cascade. In the interest of expanding definitions and reporting guidelines which measure treatment success to include factors beyond VL alone (i.e. health-related QoL, or living well with HIV), it is hoped that an increased focus on retention in care specifically will serve as a foundation to address this. Currently, only VL is favoured among retention reporting guidelines and policies; we suggest that such definitions and guidelines should be expanded *'beyond viral suppression'*, especially in the context of ageing among PLHIV where comorbidity is often rife.

While others have focussed more generally on the Cascade and 90-90-90 targets, the present study series specifically focuses on the role of retention in this context. In the service of expanding the Cascade beyond viral suppression, it is argued that we need to invest in retention research to understand its predictors and sequelae. Retention is an existing means by which we can expand monitoring beyond viral suppression to include an assessment of the factors which impact QoL and also have the potential to impact VL. However, retention is arguably not realising its full potential at present. To achieve this, the definitions of retention should be updated in line with the changing nature of HIV, and increased attention should be focussed regarding the factors which impact it in order to optimally address these. Therefore, the focus of this research series is to: (a) understand the comorbidities which impact retention; (b) understand

the nature of the relationship between comorbidity and retention; and (c) review disparities between definitions and estimates to aim for a more standardised assessment which recognises the role of individual differences, psychosocial factors, and health-related QoL. The present study series aims to synthesise the available research to date on this topic and address disparities in the literature.

First, a thorough review of the literature in both resource-rich countries and LDCs is warranted to assess the current landscape. The first study in Chapter 2 (Bulsara, Wainberg, & Newton-John, 2018) reviews the literature on the factors which impact retention, considering holistic care and the biopsychosocial model (Engel, 1980). The series then moves to focus its attention locally to Australia and its epidemic, as one of the countries with the highest reported retention rates. A qualitative study is the second in the series (Chapter 4), capturing the perspectives of clinicians and PLHIV clients attending a large, publicly funded interdisciplinary HIV service in Sydney, Australia, which can be considered representative of other such clinics in the country. The purpose of this study is to gather information regarding perceived barriers to retention, as well as potential solutions to address these, from frontline staff and those impacted by the virus. This study also considers the issue of comorbidity and clinical complexity in impacting retention in care (Bulsara, Wainberg, Audet, & Newton-John, 2019b).

The focus of the third study in the series (Chapter 6) is to consider the context of clinical decision-making which determines clients' retention schedule. The purpose is

to quantify the components of experienced clinician assessments to understand the key comorbidity factors which are present and contribute to complex clinical presentations which can impact retention and effective HIV management. This study gathers data from HIV medical specialists and, using a risk prediction model, identifies the key components; these are weighted according to relevance to generate a complexity screening tool specifically for HIV, the first of its kind to be published to our knowledge (Bulsara et al., 2019a).

The final study (Chapter 8) synthesises the above to consider the potential impact of the identified biopsychosocial comorbidity, in the context of the changing nature of HIV, in redefining region-specific definitions of retention in care (Bulsara et al., under review). These results also seek to test the syndemic model of disease interaction. A case is made for the importance of this aspect of the Cascade to remain central to government policies and guidelines, rather than simplifying Cascades to exclude retention.

The primary purpose of the series is to contribute to the literature recognising the role of comorbidity in complex clinical presentations, and to highlight the need for expanded definitions of retention in care to allow for optimal monitoring of these factors. Ultimately, we aim to demonstrate that neglecting to attend to these factors risks impacting QoL and ultimately medical outcomes of HIV markers. Further, we make a case for the expansion of reporting guidelines and markers for 'successful' treatment beyond medical markers alone. The results presented will be discussed in

the context of the three theoretical models reviewed in this chapter. The study series seeks to translate research to practice, and it is hoped it will inform practice guidelines and policy decisions regarding the Cascade in Australia. Practical applications of the series will be discussed throughout.

1.16 Study 1

The subsequent study is a systematic literature review of the factors which impact retention in care, in countries with advanced economies and LDCs. This paper was written in 2016, therefore references older WHO guidelines which suggested retention be considered as attendance to clinical visits every 3-6 months for those stable on medication, compared to more recent guidelines which suggest attendance 'appropriate to need'. The paper was published online in 2016, and in print in 2018 in *AIDS & Behavior*. The journal referencing format was Vancouver; for the purpose of formatting, this has been adapted to APA in its current form, although the content remains the same as published. Likewise, spelling has reverted from U.S. English (for publication) to U.K. English, for consistency.

1.17 Chapter 1 References

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Chapter 2 – Predictors of adult retention in HIV care: A systematic review

Bulsara, S.M., Wainberg, M.L., & Newton-John, T.R.O. (2018). Predictors of adult retention in HIV care: A systematic review. *AIDS & Behavior,* 22(3): 752-764. doi: 10.1007/s10461-016-1644-y.

2.1 Abstract

Introduction: A systematic literature review was conducted to identify predictors of poor adult retention in HIV medical care in developed and developing countries.

Methods: An electronic search was conducted with MEDLINE (OVID), PubMED, EBSCO, SCOPUS, and Cochrane databases, as well as manual searches. Original, quantitative, adult studies in English, published between 1995 and 2015 were included. Only those with a focus on predictors of retention in care were reported on.

Results and discussion: Of the three hundred and forty-five articles identified, thirty were included following an independent assessment by two raters. In developed countries, the most frequently cited predictor of poor retention was active substance use. In developing countries, physical health factors were most frequently associated with poor retention in care.

Conclusions: The results from this review suggests primary concerns for poor retention include substance use and physical health factors. Other psychosocial factors, such as psychiatric illness and social/welfare factors, were also found to be relevant.

Keywords: Retention in care, HIV, predictors, adult, treatment cascade, developing countries, developed countries

Chapter 3: Synthesising the literature to understand barriers to retention in Australia

3.1 Results from the systematic literature review

The results from the preceding study highlight the complexity of factors which can impact retention. It is clear that there is no single factor, or group of factors, which consistently impact retention; rather, a complex interplay of factors, unique to the individual, will likely impact ongoing HIV management, including retention (Bulsara et al., 2018). It stands to reason that PLHIV will present with more than one factor, given comorbidity is common in the chronic disease literature and often complicates treatment of a primary condition (Nicholson et al., 2019). Importantly, however, there were no studies reviewed which implicated stigma, discrimination, or QoL, highlighting how infrequently these factors are explicitly measured.

The greater recognition of psychosocial factors in resource-rich countries, versus more practical and logistic factors in LDCs, points to the disparity in HIV management in resource-rich versus resource-limited regions. In LDCs, in a context where access to medication and care can be limited, the factors which impact HIV-management and retention rates will naturally lean towards the practical and biomedical aspects (Bulsara et al., 2018). Countries with advanced economies, on the other hand, which are comparatively resource-rich, have access to advanced medication and often holistic care; it is possible that PLHIV in these regions have the capacity to focus more on the

psychosocial than basic biomedical management of the illness. The results support both the Biopsychosocial and Andersen Behavioral Models (ABM), in that they highlight a range of individual and contextual factors which research has determined impact retention in care (considered a 'health behaviour' in the ABM).

Understanding the global context is important, however to truly appreciate the factors which are relevant to local populations, a review of the local context is warranted. To do this, an assessment of the perspectives of clinical specialists and PLHIV is a logical subsequent step.

3.2 Epidemiological differences in countries with advanced economies

The majority of the research from resource-rich countries reviewed in the preceding chapter is U.S-based, highlighting a paucity of retention research in Australia. There are large disparities between healthcare systems in such countries. In the U.S, there is no universal access to free healthcare, although PLHIV do have other means of accessing free treatment (U.S. Department of Health and Human Services, 2019c). This system continues the trend that optimal care is available for those who can afford it, with likely long waiting lists and non-attendance a possible consequence for those who cannot.

Other resource-rich countries such as the U.K, countries within Europe, and Australia have healthcare systems which provides universal access to free healthcare to citizens,

residents, and some other visa types. While some specialist services are subsidised by private health insurance, in the case of HIV free access to high quality specialist services is readily available throughout Australia. Such differences in access to healthcare have significant implications for the Cascade and 90-90-90 targets, especially in the context of retention in care.

3.3 The local epidemic and the public health response

The HIV epidemic in Australia continues to impact some populations disproportionately to others, with 63% of new infections attributable to male-to-male sexual contact in 2017 (Kirby Institute, 2018). In the early days of the epidemic, Australia's response was considered one of the most rapid and sustained in our history of public health (Brown et al., 2014). This included not only significant policy changes (e.g. the introduction of needle and syringe programs) and education, but also the inclusion of peer involvement in all initiatives which were developed and proposed. There was an investment in epidemiological research, and the development of HIV-specific services geographically located in the centre of Australia's epidemic, Sydney NSW. Even in the early days of the epidemic, there was a recognition of the role of factors beyond the biomedical as impacting HIV management.

The Albion Centre (Albion) is one such centrally located service and opened its doors in 1985 as an HIV specialist service in Surry Hills, Sydney NSW. It incorporated not just medical and nursing specialities, but also psychology/counselling and volunteer/social

work support from its inception, and nutrition services soon afterwards. Albion was designed as a 'one-stop shop' to provide all aspects of HIV care under one roof and has been the model for other healthcare services throughout Australia and the Asia-Pacific region. A model such as this highlights a recognition from the beginning of the epidemic regarding the role of allied health, as well as medical, services in optimally managing HIV-infection.

In 2019, the acknowledgement of allied health as well as medical services for HIV is commonplace, with the majority of HIV centres in Australia offering auxiliary services either onsite or within reach. In particular, there is a growing recognition of the role of mental illness in PLHIV, with the prevalence of psychiatric disorders higher for PLHIV than the general population (De Hert et al., 2011; Nedelcovych et al., 2017; O'Cleirigh et al., 2015). In the context of universal access to specialist care in Australia, public health HIV-specialist services have the capacity to treat HIV holistically for everyone. However, private HIV services also exist, with some local general practitioners (GPs) undertaking specialised training in HIV treatment and management.

There is anecdotal evidence from within the public health system in Australia that increasingly complex clinical presentations are becoming the norm. As HIV is now largely manageable from a biomedical perspective, it is possible this has allowed more space for the emergence of other psychosocial factors which also impact PLHIV. Despite advances in the management of this chronic illness and improvements in the

stigma and discrimination experienced by PLHIV, this remains a marginalised cohort of people, and one whose QoL is often implicated. Those who are impacted by social/welfare issues in particular are likely more inclined to access public health services than private GP clinics because of the cost associated with attendance to the latter. As such, the complications of social/welfare factors with other psychosocial factors can be more commonplace in publicly funded services.

3.4 The role of comorbidity

For the first time since the beginning of the HIV epidemic, an ageing cohort of PLHIV is emerging; as such, the presence of medical and/or psychosocial comorbidity is increased as lifespan increases, which can complicate already complex clinical presentations. Even in well managed PLHIV without comorbidity, life expectancy is lower than the general population (Legarth et al., 2016), although this is approaching parity. Some authors have found that a higher number of comorbidities in PLHIV was independently associated with poorer QoL (Langebeek et al., 2017; Millar, Starks, Gurung, & Parsons, 2017), highlighting the importance of monitoring and treating associated comorbidity as well as HIV-infection itself. Nedelcovych and colleagues warn that comorbid psychiatric presentations can also impair clinical outcomes for PLHIV (Nedelcovych et al., 2017). These authors also highlight the bidirectional relationship between HIV infection and certain comorbid presentations, such as depression and active substance use, in the context of neuroinflammation and the stress responses in PLHIV. Thus, accurately identifying comorbidity in PLHIV and managing it appropriately

has implications not only for QoL, but also has the potential to impact effective and sustained medical management of HIV. As discussed in section 1.12.1, some of the common comorbidities include:

Biological

- Viral hepatitis
- Sexually transmitted infections (STIs)
- Tuberculosis (TB)
- HIV-related cancers
- Diet/nutrition
- Cardiovascular disease (CVD)
- HIV-Associated Neurocognitive Disorders (HAND)
- Physical health factors relating to ART toxicity

Psychological

- Mood disorders
- Substance use disorders
- Anxiety disorders
- Psychotic disorders
- Personality disorders
- Stigma and discrimination

Social

- Social connection
- Financial stress/socioeconomic status
- Housing
- Education

3.5 Accessing expert local opinion

The preceding study reviewed relevant international literature regarding the factors which impact retention in care. This chapter shifts the focus from global to local management of HIV; that is, within Australia. The next step, therefore, in understanding this issue is to collaborate with local experts; clinicians in the field, as well as PLHIV. The following study is a qualitative review of local HIV clinicians and specialists to assess the factors which might impact retention in care. Consistent with a biopsychosocial model of healthcare delivery (Engel, 1980), in the context of holistic HIV care, medical and allied health clinicians were approached to be involved. In addition, this study was framed by the ABM (Andersen et al., 2014) in monitoring not only individual and contextual factors, but also making an assessment of evaluated need, as determined by specialist clinicians.

3.6 Study 2

The subsequent study aims to synthesise the results from the preceding chapter to capture the local context, in the form of qualitative appraisals of clinicians and clients regarding their perspectives on barriers to retention. The paper was published in *AIDS Patient Care & STDs* in 2019, using the Vancouver referencing style; for the purpose of formatting here, this has been adapted to APA. However, the content of the article remains the same as that which was published. Likewise, spelling has reverted from U.S. English (for publication) to U.K. English, for consistency.

3.6.1 Goals

Consistent with a Biopsychosocial Model of optimal healthcare delivery (Engel, 1980), the following study aims to gather information from experts in the field: clinicians and PLHIV. The importance of hearing from medical clinicians as well as allied health workers is recognised, such that the study will include medical doctors, nurses, clinical psychologists and social workers. The perspectives of PLHIV were paramount and ensure a client-centred focus to this research.

3.6.2 Research questions

Research questions asked participants to identify the key factors which, in their opinion, were barriers to retention, as well as some potential solutions to overcome these. Follow up questions relating to the specific role of comorbidity were asked, where indicated by the discussion.

3.6.3 Methodology

Given the difficulty recruiting clients for research who struggle to attend appointments, the questions above were modified slightly to include a caveat: that clients could draw on their experience now, or on previous personal experience, acknowledging that their present attendance rates may not always have been possible. In addition, the question was further expanded to allow participants to draw upon the experiences of others, if this was de-identified and broad in nature. The focus group facilitator was mindful of ensuring this occurred.

3.6.4 Analysis

Clinician and client focus groups were conducted to access relevant opinion regarding the barriers to retention in care. The broad model for qualitative analysis determined by Braun & Clark (Braun & Clark, 2012) was followed.

The data were analysed according to broad themes, while also looking at overlapping ideas between clinicians and clients within each theme. This was determined to be the most appropriate method of analysing the data in the context of the research questions of interest.

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Chapter 4 - Retention in HIV care in Australia: The perspectives of clinicians and clients, and the impact of medical and psychosocial comorbidity

Bulsara, S. M., Wainberg, M. L., Audet, C. M., & Newton-John, T. R. (2019). Retention in HIV Care in Australia: The Perspectives of Clinicians and Clients, and the Impact of Medical and Psychosocial Comorbidity. *AIDS Patient Care & STDs*, *33*(10), 415-424. doi: 10.1089/apc.2019.0094.

4.1 Abstract

Significant advances in our understanding and treatment of HIV have led to improvements in the medical management of the illness, as HIV-infection has evolved from an acute to a chronic illness. Increasing our understanding of the medical and/or psychosocial comorbidities, which can interact to determine 'clinical complexity' and impact HIV management, will further strengthen this process. Retention in care is a critical step of the HIV Treatment Cascade which facilitates effective management of these comorbidities and their impact on HIV medical management. The present study sought to build on literature regarding medical and/or psychosocial comorbidity which impacts retention in care, and often leads to clinically complex presentations, by gaining the perspectives of people living with HIV (PLHIV), and medical and allied health clinicians in the field in Sydney, Australia. A total of 16 clinicians (medical doctors, nurses, clinical psychologists and social workers) and 14 clients participated in a series of focus groups and were asked to comment on the perceived barriers to retention, and potential solutions to overcome

these. The results indicated a significant degree of overlap between clinician and client perspectives, and identified 'service-specific factors', 'logistic/practical factors', 'medical/physical factors', and 'psychosocial factors' as potential barriers to retention. Results are reviewed in the context of similarities and differences in perspectives between clinicians and PLHIV, and limitations regarding the generalisability of findings are discussed. The broader context of comorbidity and clinical complexity is also examined.

Keywords: HIV, Qualitative, Retention, Comorbidity, Medical, Psychosocial

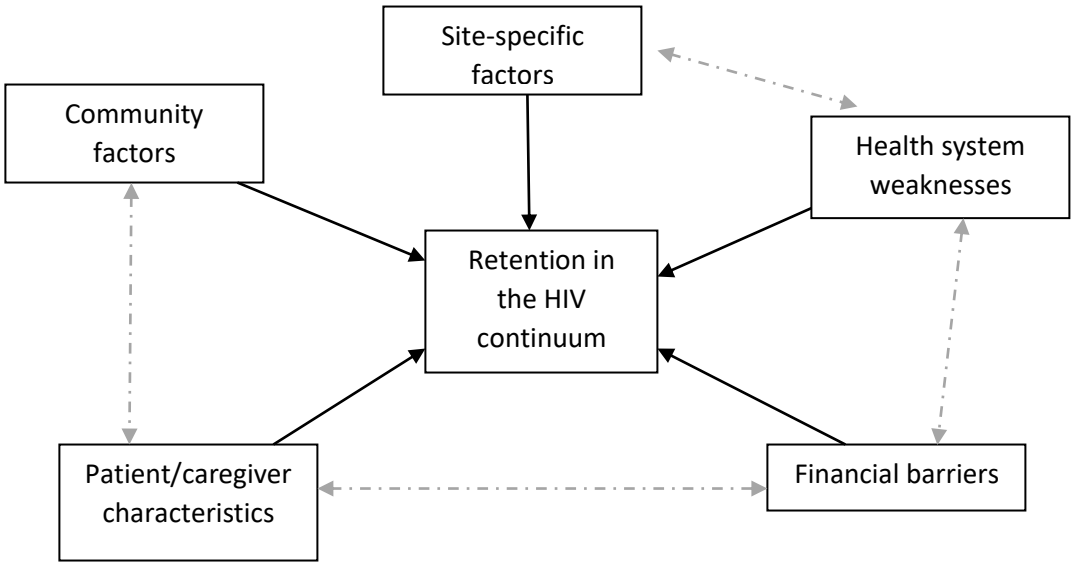
Chapter 5 – Identifying clinical complexity to assess its impact on retention

5.1 Results from the preceding study

The preceding qualitative study offers insight into the barriers to retention from the perspectives of clinicians and PLHIV, with a specific focus on the impact of comorbidity. The study complements the systematic literature review outlined in Chapter 2, in highlighting that there is no single factor or group of factors which impacts retention; rather there is a complex interplay of medical and psychosocial factors which have the potential to affect retention rates (Bulsara et al., 2019b). This relationship points to the role of comorbidity, and the complex clinical presentations which often ensue.

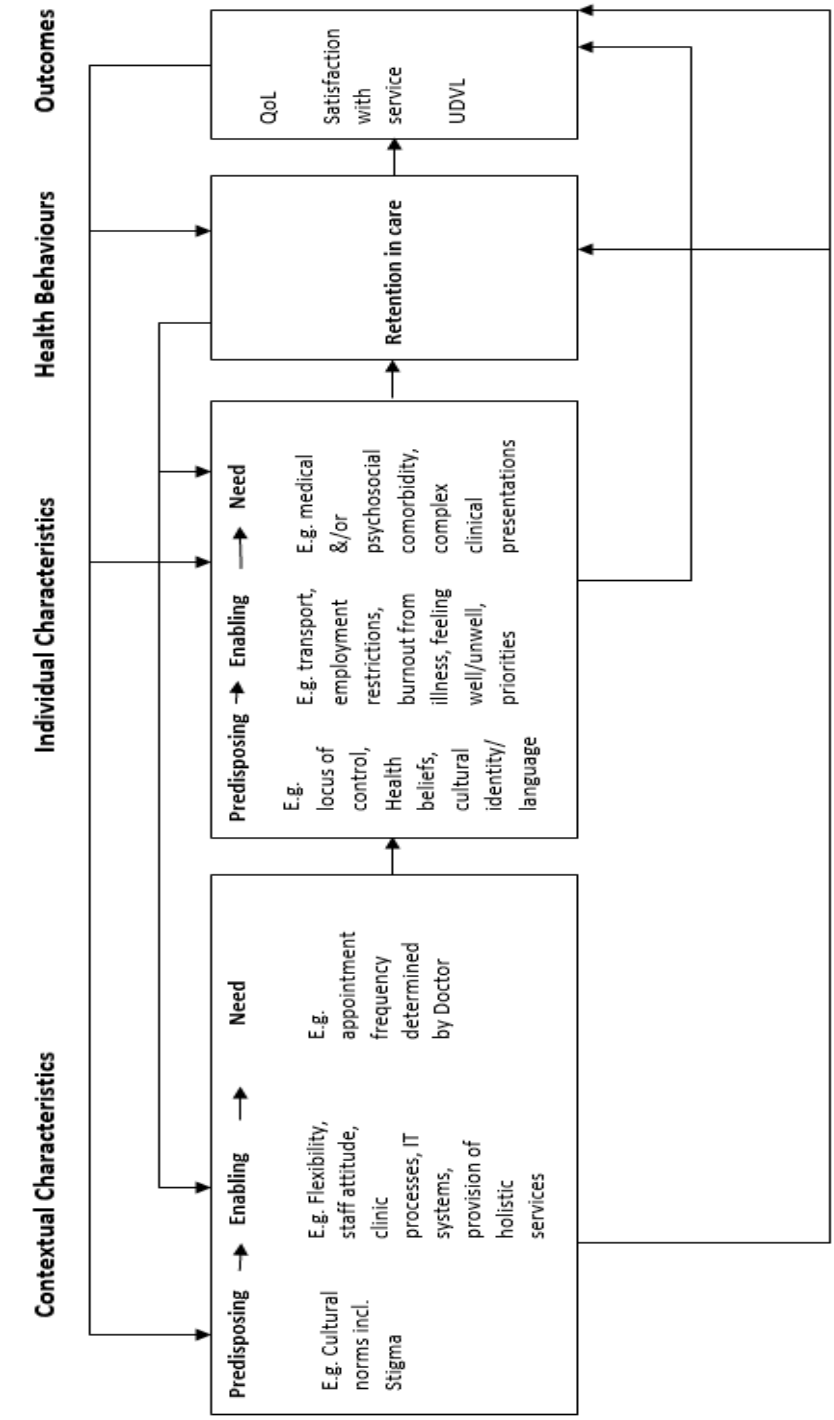
The preceding study's results also complement an existing model of factors which are considered to impact retention in care, albeit in the context of paediatric and adolescent groups. Figure 1 depicts this model (World Health Organization, 2012, p. 17), and is similar to the model suggested in Chapter 4. The WHO model suggests a complex interaction of factors, beyond client characteristics alone, which might impede retention. There is nothing to suggest this model cannot be extrapolated to other populations, including adult PLHIV. It is worth noting that people disengage from care for a number of reasons; transfer to another service (of which care providers are either aware or not), serious illness/death, as well as disengagement due to client characteristics (World Health

Organization, 2012). The latter is the area about which we have as yet been unable to quantify; the specific client characteristics, or comorbidity, which might negatively impact retention.



5.1.1 Figure 1: WHO proposed interaction of factors which impact retention in paediatric and adolescent cohorts (World Health Organization, 2012, p. 17)

This model is also consistent with the ABM (Andersen et al., 2014) in that it acknowledges and accounts for the role of multiple client-specific factors, organisation factors, and contextual factors in impacting health service utilisation and retention in care. Figure 2 places the results from the previous study in the context of the ABM, combining clinician and client identified factors. Interestingly these results are similar to those described in previous studies, using the ABM to map barriers to retention in HIV care (Holtzman et al., 2015).



5.1.2 Figure 2: Results of the previous study in the context of the Andersen Behavioral Model of Health Service Use (Andersen et al., 2014)

The preceding two studies have outlined global literature and local perspectives on barriers to retention, and both have highlighted the role of comorbidity and the complex clinical presentations that ensue. It is important, therefore, to develop standardised ways to assess this comorbidity with a view to ensuring appropriate monitoring and intervention.

5.2 Comorbidity

Comorbidity research has strong underpinnings in the chronic disease literature and its impact on individual health outcomes as well as health care resources and costs is well recognised (HIV Outcomes Coalition, 2017; McPhail, 2016). Particular factors which complicate this include social and economic disadvantage and ageing, and the impact on overall QoL can also not be ignored (Lazarus et al., 2016; McPhail, 2016; Zeluf-Andersson et al., 2019a). In the context of QoL in particular, recognition of this is important not only for individual well-being, but also because this likely feeds back to impact medical outcomes such as adherence and ultimately VL (International HIV/AIDS Alliance, 2018).

Anecdotal evidence suggests that comorbid and complex clinical presentations are not uncommon especially in the public health system. However, the presence of comorbidity itself is not necessarily a concern which warrants immediate attention (Schaink et al., 2012); many with comorbidities often manage these without functional impairment, including

the potential impact on medical HIV management. Such presentations require regular and consistent monitoring for change, and if not managed well have the potential to impact on functioning across domains, including HIV management. They may also warrant an interdisciplinary team response, for optimal service delivery.

Central to the study of comorbidity is the recognition that the ensuing relationships are more complex than simply additive; an isolated person with a diagnosed mental illness is not necessarily twice as 'complex' as an isolated person in the absence of mental illness. Rather, there is a complex interaction of effects, which is unique to each individual based on temperament, personal history and experiences, as well as comorbidities consistent with the factor categories outlined in the ABM (Andersen et al., 2014). While this is difficult to quantify in the realm of research and standardised assessment and treatment delivery, it is imperative that healthcare workers and policy makers keep this at the fore of clinical decision making.

5.2.1 Syndemics

As discussed in section 1.12.2, recognition of the synergistic effects between diseases/conditions was first discussed by Singer in 1994, interestingly in the context of HIV. He described a conceptual framework and used the term *syndemic* to describe the presence of two or more diseases or conditions which interact to increase the burden of illness (Singer, 1994; Singer & Clair, 2013). A syndemic framework differs from a traditional

assessment of comorbidity in that it accounts for the social context and recognises that those who are vulnerable tend to experience more health adversity (Hart & Horton, 2017; Mendenhall, 2017). The timely recognition and addressing of comorbid factors which contribute to a syndemic is also noted, to minimise the escalation of medical, psychological and social challenges (Mendenhall, 2017).

5.2.2 Clinical complexity

Considering the interaction of comorbidity and its potential impact on retention through the lens of syndemic theory, understanding the nature of relationships is important. In practice, clinicians often observe that when these variables interact, they can impair functioning and regularly require intervention from multiple sources; in this context, the interdisciplinary team is often paramount. These complex clinical presentations frequently herald vulnerability and are often evident in marginalised populations, such as PLHIV.

5.2.3 Measuring comorbidity/complexity using a screening tool

Existing scales specific to PLHIV and used to predict comorbidity and mortality are well documented, however tend to focus on biomedical aspects alone; for example, a frailty index to predict HIV disease severity (Guaraldi et al., 2015), and an index of HIV mortality for Veterans (Justice et al., 2013). To date, there have been no screening tools to assess the interaction of medical and/or psychosocial comorbidity in PLHIV, despite a burgeoning recognition that optimal holistic care involves addressing psychosocial as well as medical

factors associated with HIV-infection (Pratt, Hibberd, Cameron, & Maxwell, 2015; Sampalli, Dickson, Hayden, Edwards, & Salunkhe, 2016).

Screening tools have a long history in the health literature and are important adjuncts to others forms of assessment for several reasons. First, they are central to preventative medicine as they allow for early identification of difficulties, which can accelerate appropriate interventions (Iragorri & Spackman, 2018). A common occurrence in resource limited services, like the public health sector, is a 'reactive' approach to client presentations; that is, responding when the client presents in crisis, rather than proactively identifying complex clinical presentations and establishing appropriate supports.

Second, they are necessary to heighten awareness of common difficulties to allow for adequate resource allocation and optimal care delivery. Understanding trends in clinical presentations from a population health perspective, particularly those associated with adverse outcomes, is a central component of epidemiological research. The capacity of such information to guide resource allocation should also not be discounted.

Third, the development and delivery of brief screening tools can be a cost-effective way of monitoring potential comorbidity in large populations (Iragorri & Spackman, 2018). While

not diagnostic, they have the capacity to assess for key markers of comorbidities with relatively low cost and effort, and can inform treatment and resource allocation appropriately.

The use of screening tools in clinical practice is not without its challenges, however their success depends largely on provider compliance; balancing clinically meaningful screening with clinically workable tools is important, as busy clinicians favour brevity. The risk of false positives and false negatives is also a concern (Iragorri & Spackman, 2018). As screening tools lack the rigor of diagnostic assessments, there is a risk of low accuracy. Thus, all screening tools should possess a caveat to be overridden by clinical judgement or assessment. To overcome this, stringent sensitivity/specificity analyses are necessary to minimise prediction error. The limitations of screening tools should, therefore, always be considered prior to their use.

5.2.4 Challenges to measuring comorbidity/complexity

In certain situations, the presence or absence of comorbidity can impact engagement with services. For some, it can improve retention in care as there may be more points of connection within a service (Crawford, 2015), whereas for others comorbidity can be associated with 'treatment fatigue', feeling overburdened and disengaging from care (Corless et al., 2008). It might be a fair assumption, therefore, that both scenarios might be true for clients within the same service. In the case of the latter, accessing those clients for

the purpose of research and understanding their profile of comorbidity may prove challenging.

This is especially relevant in the context of comorbidity and retention in care research. Ideally, studies investigating retention rates and its predictors should be prospective in nature to compare characteristics between two cohorts of interest: those who attend their appointments (and are retained in care) vs. those who do not. However, by definition, those who are not retained in care do not attend their appointments, and thus accessing this cohort for data collection purposes often proves difficult.

Prospective research in this field has been conducted (e.g. Tobias et al., 2007), but requires a major financial investment to overcome the logistical problems outlined above. It would be necessary to employ research staff to access and obtain consent to participate in research from a cohort of non-retained clients. This is beyond the scope of most clinical research activity. Potentially as a result of this, many retention studies have performed retrospective cohort studies utilising data from routinely collected variables. Thus, the quality of the data is clinic-specific and depends upon the quality of the variables routinely collected. Many studies tend, therefore, to comment on socio-demographic variables alone and may lack the capacity to analyse other more psychosocial variables. Identifying

appropriate workarounds to access the relevant information is therefore a key component of the present research series.

Comorbidity measures have historically either favoured a binary approach (indicating '1' if a condition is present, and '0' if not), or a weighted system, which accounts for the varying influence of different factors (e.g. Austin, Wong, Uzzo, Beck, & Egleston, 2015; Justice et al., 2013). The risk with cumulative scores or 'counts' of comorbidities alone is the potential to underestimate the influence of specific factors or overestimate the additive impact of two or more conditions. Thus, for the purpose of the present research, a weighted system was favoured in order to account for the varying degrees of impact of variables on retention.

5.3 The pros and cons of clinician assessment

The mode of assessment also requires consideration. Self-report measures of relevant conditions would clearly be an effective way of accessing such information about comorbidity; however, this would likely require clients to complete multiple assessment measures and be present within the clinic for the process which, as has been discussed, can be challenging for those who are sub-optimally retained – i.e. the target group. It would also require clients to possess and impart accurate knowledge about physical and psychosocial comorbid factors. Precedents exist for clinician-assessed comorbidity/complexity measures, with a recognition of the unique and specialist

perspectives care providers have regarding their clients (e.g. Grant et al., 2011). However, this method of assessment can be conceived as subjective, not only in the context of appraisals about client complexity but also regarding the provider's own persona and/or professional history which might impact their assessments. It also assumes clients are open and honest with clinicians, which might not always be the case (e.g. in the case of potentially stigmatising factors such as substance use).

In clinical practice, however, clinician assessment rather than client self-report is most commonly used to guide decision-making. During clinical consultations, clinicians make assessments regarding clients' comorbidities, their interactions and complexity, and these assessments inform clinical decision-making including treatment planning, referrals, and schedules of visits. Indeed, clinical treatment guidelines often contain the caveat that encourage providers to exercise 'clinical judgement', as there is a recognition that guidelines cannot possibly account for all combinations and eventualities of comorbidity, and thus clinician judgement is necessary (Treadwell, 2015). Likewise, clinician assessment is at the core of many theoretical models, including the ABM (Andersen et al., 2014) which highlights the role of 'evaluated need' (i.e. comorbid factors identified by clinicians which require intervention).

5.3.1 Quantifying clinician assessment

In public health specialist HIV services in Australia, such as Albion, holistic care is highly valued. Specialist HIV medical care providers determine appropriate treatment, schedules

of visits and referrals during clinical consults, and often account for a range of psychosocial as well as medical/physical health factors in this decision-making process, either alone or in collaboration with the interdisciplinary team. This involves an assessment of the impact of key comorbidities on a person's functioning, which research and clinical experience suggest might affect PLHIV. Identifying these factors, and quantifying this assessment in some way, is an important next step to addressing comorbidity and the ensuing clinical complexity. Such quantification would also benefit less experienced or isolated (e.g. rural & remote) clinicians working in the field. In the context of retention, identifying complexity/comorbidity as a first step to understanding its impact on retention is therefore paramount to optimal holistic HIV management.

5.4 Study 3

The following study presents data on the development and validation of a clinician-rated client complexity rating scale, specifically for PLHIV. This paper was published in *International Journal of STD & AIDS* in 2019, using the Vancouver referencing style. For the purpose of formatting here, this has been altered to APA, however the content remains the same as that published. Results will be explored in the context of the three theoretical models outlined in Chapter 1, however it should be noted that the remaining two studies particularly focus on the individual component of the ABM, in addition to the Biopsychosocial and Syndemic Models.

5.4.1 Rationale for developing the scale

As previously discussed, comorbidity characterised by a complex interaction of medical and/or psychosocial factors is thought to increasingly be the focus of public health services in Australia serving the HIV community. As the sector has improved its management of HIV-infection biomedically, the complex impact of psychosocial factors on overall HIV management and QoL has become more apparent. At Albion, it was anecdotally estimated that approximately 20% of PLHIV attending the service did so in the presence of comorbid factors which often led to complex clinical presentations and impacted their functioning and resource allocation within the service. Accurately identifying this complexity, and the specific factors which comprise it, became a priority to ensure appropriate allocation of resources to best support the most vulnerable and marginalised clients within the service.

5.4.2 Consumer Engagement

Consumer engagement is gaining traction as a central component of optimal healthcare delivery (Graffigna & Vegni, 2017). Consistent with local guidelines and policies, the importance of consumer engagement in developing the screening tool was considered. South East Sydney Local Health District (SESLHD), a large district within NSW Health within which Albion is located, have developed a community partnership strategy which determines the degree of involvement of consumers in changes to clinical practice (South East Sydney Local Health District, 2015). In accordance with this, the development of the proceeding complexity rating scale was raised with Albion's Consumer Advisory Group in

December 2017. Feedback from the group was overall positive and the purpose behind the development of the screening tool was acknowledged.

5.4.3 Early development of the scale

An existing complexity rating scale used in local alcohol and other drug services was identified, with a view to modifying it for use with PLHIV (The Clinical Complexity Rating Scale [CCRS] Deacon et al., 2016). This scale identified common comorbidities for their cohort, although focussed on the presence/absence of the variable. This was altered for our use by (a) modifying the list of variables to suit a population of PLHIV, and (b) adjusting their definitions and scoring system to reflect the issue of *functional impairment*, as was relevant to our cohort.

While the specific Methods regarding the development of the rating scale are described in the proceeding chapter, what is not discussed in the published manuscript is that early development of the scale involved exploratory and confirmatory factor analyses to determine the most appropriate combination of variables. However, in the service of a 'weighted' scoring system which would account for the unique contributions of each variable to the assessment of clinical complexity, this process was abandoned in favour of the development of a risk prediction algorithm.

5.5 Chapter 5 References

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Chapter 6 - The development of an HIV-specific complexity rating scale

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6.1 Abstract

As treatment for HIV improves, an ageing population is experiencing comorbidity which often leads to complex clinical presentations requiring an interdisciplinary care approach. This study sought to quantify clinician assessment of the level of clinical complexity, through the development of a rating scale for people living with HIV (PLHIV), to improve client care through an interdisciplinary care model.

An existing alcohol and other drug complexity rating scale was selected and modified for use with PLHIV. HIV-specific items were included through consultation with an interdisciplinary team. A risk-prediction model was developed and validated using clinician ratings of clients attending The Albion Centre (Albion), a tertiary HIV clinic in Sydney, Australia, resulting in the development of the Clinical Complexity Rating Scale for HIV (CCRS-HIV).

Multivariable logistic regression models identified eight characteristics based on clinician assessment of complexity in PLHIV: financial instability; social isolation; problematic crystal methamphetamine (CMA) use; mental illness and/or other problematic substance use; cognitive/neurological impairment; polypharmacy; current hepatitis C (HCV) infection and/or cancer; and other physical health comorbidity. A weighted risk-prediction model was developed and validated. The final model accurately predicted 85% of complex clients, with a sensitivity of 80% and specificity of 91%.

This study developed an HIV-specific clinician-rated complexity scale. Further investigations are required to validate the CCRS-HIV with broader HIV populations. This simple complexity screening tool is a promising adjunct to clinical assessment to identify clients with complex physical and psychosocial needs who may benefit from interdisciplinary care interventions and allocation of resources.

Keywords: Complexity, screening tool, HIV, interdisciplinary, comorbidity

6.2 Introduction

HIV medical treatment has advanced significantly, reshaping HIV management. These advances improve viral suppression, such that life expectancy for people living with HIV (PLHIV) is approaching that of the general population (Samji et al., 2013). With the potential to manage HIV as a chronic health condition, comorbidity from other challenging chronic medical and psychosocial conditions can have a significant impact on retention in care and quality of life (QoL) (Salter, Lau, Go, Mehta, & Kirk, 2011).

Concurrent chronic physical (e.g. other physical diagnoses and associated treatments), and psychosocial (e.g. psychological, social and economic circumstances, and stigma) conditions complicate client presentations, particularly within the public health domain (Grant et al., 2011). HIV primarily impacts marginalised and often stigmatised communities where the mental health burden is higher than the general population (Chaponda et al., 2018; Heywood & Lyons, 2016), and HIV can compound this inequity (Petrak & Miller, 2002). Discrimination, stigma, poor mental health, substance misuse and QoL, and social isolation have all been shown to have a negative impact on HIV health outcomes, including poor adherence to antiretroviral therapy (ART), poor retention in care and mortality (Bolsewicz, Debattista, Vallely, Whittaker, & Fitzgerald, 2015; Gonzalez, Batchelder, Psaros, & Safren, 2011; Korthuis & Edelman, 2018; Leserman, 2008; Sayles, Wong, Kinsler, Martins, & Cunningham, 2009; Smart, 2009).

Older age has also shown to be a significant factor affecting HIV outcomes and is associated with poorer clinical outcomes and a higher mortality rate, with a 16-times risk of death within first year of diagnosis in those aged 50 years or older (The Lancet HIV, 2017). Ageing in PLHIV, is associated with social isolation, loneliness, stigma and increased risk of mental illness (Rueda, Law, & Rourke, 2014). Identifying risk factors for comorbidity and frailty, and easy identification of client complexity, has become a clinical care priority. It is evident, therefore, that PLHIV, particularly those with past prolonged immunodeficiency, have complex care needs as they age.

Studies of client complexity in HIV care have suggested that primary care providers are better able to identify client complexity compared with rule-based systems, such as identifying the number of comorbid diagnoses (Grant et al., 2011). Multifactorial interactions of comorbid diagnoses can impact a person's capacity to effectively manage HIV-infection, including adherence to ART or appointment attendance. Two issues arise from complexity issues within HIV care. First, clients who disengage from care have difficulties suppressing HIV and are at risk of life-threatening HIV complications (Brinkhof, Pujades-Rodriguez, & Egger, 2009) and transmitting the virus. Second, QoL can be adversely affected irrespective of HIV suppression if comorbidity issues are not addressed.

Current research reflects a general consensus that interdisciplinary care improves outcomes for clients with chronic and/or comorbid health conditions (Korner et al., 20116; Mitchell et al., 2015). The investigation of the clinical and economic effectiveness of interdisciplinary care for complex health conditions is an emerging research field. A recent Cochrane review (Reeves, Pelone, Harrison, Goldman, & Zwarenstein, 2017) concluded that there is currently insufficient evidence to definitively interpret the impact of interdisciplinary interventions, however, compared with usual care, interdisciplinary care of complex clients can improve elements of disease control and service delivery at a modestly increased cost (Mitchell et al., 2015), supporting the development of a holistically healthy population of PLHIV. In terms of the experience of interdisciplinary care, clients report enhanced satisfaction and improved health outcomes while health workers report enhanced job satisfaction, greater role clarity and enhanced well-being at work (Mickan, 2002). Much of the literature reviewed here was conducted in the United States (US), and there is a paucity of Australian–based research. Furthermore, there is no validated clinician-administered rating scale to identify clinical complexity in HIV.

Risk prediction models offer a mechanism to identify risk factors and their role on potential outcomes (Wand et al., 2018). To determine effective treatment plans, including developing an appropriate schedule of attendance, clinicians routinely make assessments about the degree of intervention and resource allocation required based on clinical complexity of clients. There is also benefit in proactively identifying potential risk factors

rather than reacting once comorbidity has already impacted on HIV-management. The primary aim of the present study was to quantify the components of specialised HIV-clinician assessments, to develop and validate a simple screening tool. Clinicians determine treatment plans and appointment schedules based upon their assessment of clients' health care needs and capacity to adhere to a regime. Inherent in this assessment is an estimation of the degree and impact of client comorbidity and clinical complexity. This methodology has been used in previous studies (Grant et al., 2011) seeking to quantify clinician assessment to improve patient outcomes.

6.3 Methods

6.3.1 Development Phase

The Albion Centre (Albion) cohort of 1,125 regular PLHIV clients was divided into a development database (n=189) and a validation database (n= 936). During the initial phase of the study, two attending medical officers (AMOs) at Albion assessed their clients who had attended for a medical review over a 9-month period. Both AMOs had over 20 years' experience working with PLHIV. Each client was assessed as 'complex' or 'not complex' by their respective AMO, based on the clinician's long-term knowledge of the clients. For the purpose of the present study, 'complexity' was defined as "*the presence of comorbidity currently impairing functioning, and potentially warranting an interdisciplinary team response"*.

An existing rating scale comprising nine items and used in drug and alcohol settings, the Clinical Complexity Rating Scale (CCRS) (Deacon et al., 2016), was adapted. This scale had a mixed binary and non-binary scoring system and was not specifically assessing functional impairment; therefore, the scoring was modified to ensure it was binary, to have consistency across variables, and the definitions were adapted to specifically address the issue of functional impairment. Clinicians from different disciplines (medical, nursing and psychology) independently identified further HIV-specific items which were of conceptual interest. An additional eight HIV-specific items were added to form a composite scale. All 17 items are listed in Table 1.

Scale	Variable
CCRS	Substance Use
	Physical health
	Mental health
	Cognitive impairment
	Social network
	Home stability
	Financial stability
	Children < 5 years
	Recent prison
Adapted scale	**CCRS items above *PLUS***
	Crystal methamphetamine (CMA) use
	Detectable Viral load (VL)
	Hepatitis C (HCV)
	Polypharmacy
	Neurological impairment
	Diabetes
	Cardiovascular disease (CVD)
	Cancer

6.3.1.1 Table 1: List of variables used to assess clinical complexity in the present study

Of this cohort, 16% were considered 'complex' according to clinician assessment and were subsequently rated across the 17 variables (Table 1). Definitions of each variable can be found in Appendix A. An age- and sex-matched 'non-complex' cohort was identified and rated in the same way.

The AMOs rated *functional impairment* according to each of the 17 variables as a binary code. Non-binary variables from the original CCRS scale were re-coded in the analyses, such that '0' denoted 'the variable did not cause functional impairment' and '1' denoted 'the variable caused functional impairment'. The only exception to this was 'polypharmacy', for which clients received a score of '1' solely for the presence of this factor (i.e. being prescribed at least 5 medications). For the purpose of this study, *functional impairment* was considered to be a loss of functional capacity, as a result of the variable in question, in the context of their everyday life. AMOs agreed that functional impairment was evident when any of the complexity items in question were inhibiting the client's ability to fully engage in social, occupational or physical activities, or the AMO believed the extent to which the client could function in these domains was significantly reduced as a result of complexity. For example, AMOs agreed that mental health or substance use issues that impacted the client's ability to regularly engage in employment or led to the repeated request for medical certificates was deemed 'functional impairment'. Given scores can, and should, be modified over time in response to changing

client characteristics, receiving a score of '1' denoted functional impairment *at the time of assessment*.

Multivariable logistic regression models were used to create a predictive model and identify the key variables of interest. After fitting the univariate logistic regression models, variables were entered into the multivariate model if they had a p-value of less than 0.10 in the univariate analysis. The final multivariate model was obtained using a forward stepwise approach and included statistically significant covariates ($p<0.05$). The resulting scale, the Clinical Complexity Rating Scale for HIV (CCRS-HIV; Appendix B), comprised eight variables, four psychosocial and four physical health variables. The model's goodness of fit was assessed using the Hosmer–Lemeshow goodness-of-fit test (Hosmer, Lemeshow, & May, 2008). High p-values (>0.05) were considered a reasonable fit.

After the final model was identified, a weighted risk-prediction screening tool was developed by rounding each regression coefficient (β-coefficient) to the nearest integer and multiplying by 10. This scoring procedure has been used in multiple other studies, with statistically acceptable robustness (Wand et al., 2017; Wand et al., 2018). The total CCRS-HIV score for each client was derived by summing the individual weighted risk factor scores. There are precedents and rationales for the use of summary comorbidity measures which use weighted scores to assess the presence of comorbidity (Austin et al., 2015).

Statistically and clinically relevant 'cut-offs' to identify clinically complex individuals with acceptable robustness and accuracy were determined using the development dataset. The predictive power of these cut-offs was assessed using the validation dataset, using standard statistical measures to determine sensitivity/specificity and the area under the receiver-operating curve (AUC) to assess the accuracy of the model and the discriminative power of the risk-prediction screening tool.

6.3.2 Validation of the screening tool

The purpose of the validation phase of the study was to confirm whether factors identified during the development phase could still be considered significant predictors of the primary outcome of interest, clinical complexity. Following identification of the statistically and clinically relevant variables during the development phase, data for the remaining clients accessing Albion for medical care (n = 936) were collected using the same methodology described above. During this phase, the remaining AMOs within the service assessed their clients according to the variables identified.

Validation of the screening tool was conducted using the original eight variables and cut-offs determined during the development phase. All analyses were conducted using Stata statistical software v14.0 (College Station, TX, USA).

6.4 Results

The total sample (N = 1125) was comprised of 1024 (91%) males and 101 (9%) female clients of Albion. The mean age of clients attending Albion is 48 years (range 19-88 years). The profile of sex distribution shown here is consistent with other HIV services in Australia. Results from the coding across all 17 variables during the development phase (n = 189) are presented in Table 2. The distributions of these variables were analysed to provide unadjusted odds ratios to show the strength of the associations with the primary outcome, clinician-assessed 'complexity'.

	Characteristics N (%)	Unadjusted Odds Ratio 95% CI)	p-value
Age			
<45 years	53 (27.32)	1	
45-54 years	77 (39.69)	1.07 (0.53, 2.15)	0.858
55+ years	64 (32.99)	1.04 (0.50, 2.16)	0.920
Substance Use			
No	166 (85.57)	1	
Yes	28 (14.43)	4.46 (1.72, 11.57)	0.002
Physical Health			
No	89 (46)	1	
Yes	105 (54)	5.18 (2.79, 9.61)	<0.001
Mental Health			
No	104 (53.61)	1	
Yes	90 (46.39)	11.51 (5.84, 22.67)	<0.001
Cognitive impairment			
No	143 (74.48)	1	
Yes	49 (25.52)	15.4 (5.75, 41.26)	<0.001
Social Network			
No	147 (76.56)	1	
Yes	45 (23.44)	13.0 (4.84, 34.90)	<0.001
Home Stability			
No	166 (86.46)	1	
Yes	26 (13.54)	15.67 (3.58, 68.48)	<0.001
Financial Stability			
No	151 (78.65)	1	
Yes	41 (21.35)	32.16 (7.48, 138.28)	<0.001
Recent prison[a]			
No	181 (94.27)	-	
Yes	11 (5.73)	-	
Children < 5 years			
No	181 (94.27)	1	
Yes	11 (5.73)	2.81 (0.72, 10.96)	0.135

[a]Model did not converge

6.4.1 Table 2: The distribution of all variables in the development dataset. Shaded items denote HIV-specific items added to the original scale

	Characteristics N (%)	Unadjusted Odds Ratio 95% CI)	p-value
CMA Use			
No	169 (88.02)	1	
Yes	23 (11.98)	8.16 (2.34, 28.50)	0.001
Detectable VL			
No	150 (78)	1	
Yes	42 (22)	0.54 (0.27, 1.10)	0.083
HCV			
No	171 (89.06)	1	
Yes	21 (10.94)	5.05 (1.62, 15.82)	0.005
Polypharmacy			
No	130 (67.71)	1	
Yes	62 (31.29)	6.27 (2.94, 13.32)	<0.001
Neurological impairment			
No	159 (82.81)	1	
Yes	33 (17.19)	7.50 (2.75, 20.41)	<0.001
Diabetes			
No	179 (93.23)	1	
Yes	13 (6.77)	2.38 (0.71, 8.00)	0.162
CVD			
No	162 (84.38)	1	
Yes	30 (15.63)	1.37 (0.63, 3.01)	0.428
Cancer			
No	180 (93.75)	1	
Yes	12 (6.25)	5.47 (1.16, 25.65)	0.031

6.4.1 Table 2 contd: The distribution of all variables in the development dataset. Shaded items denote HIV-specific items added to the original scale

6.4.2 Deriving the complexity screening tool

Multivariable regression models were conducted during the development phase to determine the final model which included four psychosocial factors: financial instability [adjusted Odds Ratio (aOR): 14.78, 95% CI: 2.62, 83.51)]; problematic CMA use (aOR:7.05, 95% CI: 1.25,39.65); mental illness and/or other problematic substance use (aOR:4.22, 95% CI: 1.45,12.27); and social isolation (aOR:10.78, 95% CI: 2.47,47.14), and four physical health factors: cognitive/neurological impairment (aOR: 6.19, 95% CI: 1.94, 19.81); polypharmacy (aOR: 4.27, 95% CI: 1.43, 12.76); current (problematic) HCV infection and/or cancer (aOR: 5.65, 95% CI: 1.47, 21.79); and other physical health comorbidity (aOR: 5.33, 95% CI: 1.69, 16.76). The data from the development and validation phases for the resulting eight variables comprising the CCRS-HIV are outlined in Table 3, and the scale is provided in Appendix B.

Variable	Development dataset [AUC (95% CI): 94% (91%, 97%)]			Validation database [AUC (95% CI): 94% (95% CI: 91%, 96%)]		
	Adjusted Odds Ratios	p-value	Score β*10	Adjusted Odds Ratios	p-value	Score β*10
Financial Instability						
No	1			1		
Yes	14.78 (2.62, 83.51)	0.002	27	6.86 (3.35, 14.06)	0.000	19
Problematic CMA use						
No	1			1		
Yes	7.05 (1.25, 39.65)	0.027	20	26.57 (10.07, 70.07)	0.000	33
Mental illness and/or other problematic substance use						
No	1			1		
Yes	4.22 (1.45, 12.27)	0.008	14	3.83 (2.20, 6.67)	0.000	13
Social isolation						
No	1			1		
Yes	10.78 (2.47, 47.14)	0.002	24	10.72 (5.66, 20.63)	0.000	24
Cognitive/neurological impairment						
No	1			1		
Yes	6.19 (1.94, 19.81)	0.002	18	3.66 (1.19, 10.67)	0.023	13
Polypharmacy						
No	1			1		
Yes	4.27 (1.43, 12.76)	0.009	15	4.12 (1.98, 8.57)	0.000	14
Current HCV infection and/or Cancer						
No	1			1		
Yes	5.65 (1.47, 21.79)	0.012	17	8.95 (3.26, 24.62)	0.000	22
Other physical health comorbidity						
No	1			1		
Yes	5.33 (1.69, 16.76)	0.004	17	4.53 (2.51, 8.21)	0.000	15

6.4.3 Table 3: Results from multivariable logistic regression analyses for the development and validation datasets

Re-fitting these variables for the remaining 936 participants during the validation phase was shown to have good predictive value. High p-values (0.325 and 0.182 for the development and validation models respectively) indicated reasonable model fits for both development and validation cohorts.

Given the consistent results observed between the development and validation datasets, it was decided to maintain the model derived during the development phase as the final model, as this was validated during the second phase of the study.

6.4.4 Performance of the complexity screening tool

Analyses were conducted to assess the performance of the model for various cut-offs to identify complexity. The development and validation dataset results are summarised in Table 4, and show that high cut-offs resulted in high specificity, but relatively low sensitivity. On balance, a cut-off of 40 (total CCRS-HIV score) was used to determine 'complex' presentations with an acceptable level of statistical precision. Table 4 shows the final model to determine complexity, balancing appropriate sensitivity with specificity. During the validation phase of the study, the data were fitted according to the cut-offs determined during the development phase and were shown to have good predictive ability. The final model accurately predicted 85% of complex clients, with a sensitivity of 80% and specificity of 91%. The overall AUC was 95% (95% CI: 92%, 98%) for the final model, demonstrating high discriminative power.

Clinicians were consulted regarding the clinical utility of the scale to identify complexity and target interventions. Accordingly, a three-tiered 'traffic light' system was developed to categorise complexity. As per results in Table 4, a score of 40 or above was used to classify someone as 'complex' (Red) which determined that this cohort required additional interdisciplinary interventions, more frequent follow-up and more frequently reviewed care plans. The remaining two tiers were developed to classify those as 'not complex' (Green, score 0-29), and those with 'some complexity evident' (Orange, score 30-39), requiring monitoring and care plans of lower intensity.

			Development Model				Validation Model		
			AUC[a]: 95% (95% CI: 92%, 98%)				AUC[a]: 95% (95% CI: 92%, 98%)		
Complexity Label	Range	Cut-offs	Sensitivity (%)	Specificity (%)	% correctly classified	Sensitivity (%)	Specificity (%)	% correctly classified
Green (not complex)	0-29	> 25	98	78	88	90	87	87
Orange (some complexity evident – requires monitoring)	30-39	> 30	98	79	89	82	91	90
		> 35	85	89	87	76	93	90
Red (complex – requires integrated care and support)	≥ 40	> 40	80	91	85	72	95	83
		> 45	76	91	83	66	95	80
		> 50	67	95	81	60	96	77

[a]AUC: Area Under the Curve for score as a continuous variable

6.4.5 Table 4: Performance of the development and validation models (shaded line denotes chosen cut-off)

6.5 Discussion

The present study is the first, to our knowledge, to quantify experienced HIV-clinician assessment of clinical complexity and determine the individual variables which comprise such an assessment. Higher scores on the CCRS-HIV were associated with increased prevalence of complexity, which provides a platform for a more coordinated, enhanced and targeted interdisciplinary care team approach. The scale also potentially provides the opportunity to separately identify physical and psychosocial comorbidity, which could be useful in directing interdisciplinary care.

PLHIV now have a similar life expectancy to that of the non-infected population due to ART but the incidence of non-AIDS comorbidity and malignancies amongst PLHIV is increasing (Weber et al., 2013). Reasons include: mental health and other psychosocial factors; ageing; ongoing immune activation and inflammation despite virological suppression (Phillips, Neaton, & Lundgren, 2008); high rates of modifiable risk factors (e.g. smoking); and the long term effects of ART (Friis-Møller et al., 2003). In addition, PLHIV are vulnerable to stigma, social isolation and mental health issues. As Albion is publicly funded, it also has a significant number of clients who are from culturally and linguistically diverse (CALD) backgrounds, are isolated, homeless, and/or have mental health and/or alcohol and other drug problems.

Specific rates of non-AIDS comorbidity in our clinic population are published elsewhere (Chan et al., 2018) and are similar to the rates within the Australian HIV Observational Database (an observational cohort study of more than 4,000 PLHIV across Australia under routine clinical care), including rates of psychological disorders such as depression (35%) and anxiety (18%) (Petoumenos et al., 2017a). This highlights that contemporary HIV management has moved away from treating the virus alone to encompassing the psychosocial and lifestyle factors of clients. Thus, it is important to have available a validated complexity screening tool to identify those clients who require more intense interdisciplinary care, support and follow-up. Not only does this attend to all the health needs of the client but it also feeds back into the maintenance of virological suppression by ensuring clients' adherence to ART and prevention of transmission of HIV.

This study has developed a valid and standardised scale of clinician-rated complexity in PLHIV that can be used to guide interdisciplinary HIV management. The scale allows any member of the clinical team to detect complexity with accuracy similar to that of a specialist HIV physician. By identifying specific, measurable factors, the scale may further assist in the development of interventions that will potentially maximise retention in care. As all members of the clinical team can see a client's complexity score, it provides more opportunity for interdisciplinary engagement. For example, if a client with a high score attends to see the Triage Nurse, their score would trigger an alert to other relevant clinicians; this allows more opportunistic engagement of vulnerable clients.

Specific potential intervention strategies are likely to include: 1) Tailored monitoring programs guided by the specific factors identified for individual clients; 2) Development of individualised interdisciplinary case management plans; and 3) Referral for specific medical and/or psychosocial interventions. The development of a risk prediction model such as this has the benefit of minimising prediction error; it does not, however, provide evidence of a causal relationship between variables and the outcome which might be more useful in determining prevention and intervention strategies. Further research is needed to identify whether the combined use of this scale, and related intervention strategies, contribute to a significant increase in retention in care and other client outcomes. Arguably, effective use of such a scale may prevent negative outcomes of complexity by alerting the need for intensive care needs as soon as a client enters a service. In addition, the use of such scales in conjunction with improved interdisciplinary care coordination models should improve QoL and well-being.

To our knowledge this is the first complexity rating scale in HIV to be based on an Australian population from a large, publicly funded HIV clinic in metropolitan Sydney. The present clinical setting and diversity of client presentations lends itself to a more predictive and appropriate model of client complexity. The scale has now been incorporated in the state-wide electronic medical record, allowing clinicians to input data directly into the model during the client consultation, identifying areas of need that can be addressed by other members of the interdisciplinary team. This model can also be used to

further quantify the impact of clinical interventions over time; for example, to measure changes in a client's complexity rating following an intervention. These are some of the advantages of quantifying complexity and progress within HIV management, as opposed to prior methods of qualitatively describing progress.

It is worth noting that similar biomedical models have been developed for the clinical assessment and management of HIV clients. Consequently, precedents do exist for this form of clinician administered rating scale (Grant et al., 2011), even to the extent of using summary (additive) comorbidity measures (Austin et al., 2015), which some have suggested are not ideal (Schaink et al., 2012). An important and contemporary example of a clinical tool that is applicable to ageing PLHIV is the 'frailty index' validated by Guaraldi *et al.,* (Guaraldi et al., 2015) which predicts survival and risk factors for incident comorbidity that are independent of viral load and CD4 amongst PLHIV. Likewise, the Veterans Ageing Cohort Study (VACS) index (Justice et al., 2013) predicts mortality in a cohort of veteran PLHIV. The present study, however, is unique in its development of a tool to screen for complexity in PLHIV within Australia, and also for its inclusion of psychosocial as well as medical/physical health factors. This is especially important to develop a coordinated and collaborative interdisciplinary response to holistic care needs.

There are limitations to this research. First, the specific scoring criteria are not clearly defined for every item on the tool, which is largely a nominal measurement scale (i.e. requiring yes/no responses). For example, the exact clinician-reported threshold of what constitutes social isolation may not itself be uniform. Second, it is unclear how representative the sample population is in relation to the entire Australian HIV population, given that our clients are predominantly Caucasian men who have sex with men, living in metropolitan Sydney. However, Albion is one of the largest publicly funded HIV clinics in the state, with at least 40% of the service's clients come from across the state and from different socioeconomic and CALD backgrounds (Chan et al., 2018). It is therefore reasonable to infer the tool is sufficiently validated to be used throughout New South Wales.

A third limitation of the present methodology is that it is subjective in nature, inherent in quantifying clinician assessment. Comparing clinician ratings in specific domains against clinicians' broad assessment of whether a client is 'complex' or 'not complex' can be argued to be problematic. This, however, is the reality of clinical consultations, where the clinician is required to make such assessments regarding a person's complexity in order to determine a course of treatment, visit schedule and appropriate referrals. The scale developed in the present study aims to quantify such an assessment, however future studies should seek to validate these assessments against other more objective measures of complexity. Likewise, clinician assessment of *functional impairment* is also subjective in

the present study. Future research should consider more objective measure of a loss of functional capacity.

The scale primarily identifies accumulative scores of issues to represent complexity and may not account for other factors around clinician engagement, chronicity and acuteness of other comorbidity and available supports and resources. Complex trauma and other psychological conditions and their related behaviours may also be considered the actual drivers of the symptoms being presented as contributing to complexity. It is therefore possible that the present scale does not accurately assess all the relevant factors that impact PLHIV. Future modifications of the scale could seek to adapt and modify the variables assessed, as well as assessing the correlation between clinician and self (client) reported concerns.

In the present context, ratings relied upon prior knowledge of existing clients for clinicians to appropriately estimate the extent of their comorbidity. However, it is also possible for the scale to be utilised during an initial consult and can be used to target clinical assessment questions accordingly.

6.5.1 Conclusions

This study demonstrates promising results for the development and use of a complexity rating scale for PLHIV. Use of this scale to target clinical interventions, with an increasing

move towards proactive early intervention for non-AIDS comorbidity, is an important next step. The tool, while validated in its current form, requires ongoing modification and review informed by evolving data. It does, however, provide clinicians with a simple and brief means of assessing the most relevant non-AIDS comorbidity, with a view to targeting resources and interventions accordingly, and can readily be inserted into an electronic medical record. What makes this model unique in the field of interdisciplinary HIV care is that it has potential advantages for both the individual (improvement of general health outcomes) and public health (enabling adherence to ART and thereby reducing onward transmission of HIV).

6.5.2 Ethical approval

This study has received quality assurance or quality improvement (QA/QI) approval from South East Sydney Local Health District (SESLHD) Human Research Ethics Committee (HREC) in 2017, as well as HREC approval from the University of Technology Sydney (UTS) in 2018.

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6.6 Appendix A

Definitions of each of the 17 variables assessed during the development phase of the study. Scoring denotes evident functional impairment based on various factors at the time of assessment.

Variable	Definition
Substance Use	Active substance use impacts functioning
Physical health	The presence of physical health conditions impacts functioning
Mental health	The presence of symptoms of mental illness impacts functioning
Cognitive impairment	Cognitive impairment impacts functioning
Social network	Social isolation impedes functioning
Home stability	Lack of stable housing impedes functioning
Financial stability	Lack of financial stability impedes functioning
Children < 5 years	The responsibilities for the care of young children impede functioning
Recent prison	Recent incarceration impedes current functioning
Crystal methamphetamine (CMA) use	Current CMA use is associated with functional impairment
Detectable Viral load (VL)	Current detectable VL impacts current functioning
Hepatitis C (HCV)	Current and untreated HCV infection impacts functioning
Polypharmacy	The client is prescribed ≥ 5 medications
Neurological impairment	Current neurological impairment impacts current functioning
Diabetes	Current Diabetes diagnosis impacts current functioning
Cardiovascular disease (CVD)	Current CVD impacts current functioning
Cancer	Current Cancer diagnosis impacts current functioning

6.7 Appendix B – The Clinical Complexity Rating Scale for HIV (CCRS-HIV)

Instructions

Consider whether the presence of each variable impacts functioning

The items can be considered in any order

Items 1, 2, 4, and 5 below are Psychosocial (PSY) items.

Items 3, 6, 7, and 8 are Physical Health (PH) items.

Weighted scores are to be added to receive a Total score

		Yes (1)/ No (0)	Weighted Score
1	Is there problematic Crystal Methamphetamine (CMA) use which impacts functioning?		20
2	Does mental illness (including other problematic substance use, not CMA) impact functioning?		14
3	Are there any cognitive/neurological concerns (including HAND) which impacts functioning?		18
4	Does social isolation impact functioning?		24
5	Does financial instability impact functioning?		27
6	Does the client take 5 or more medications (polypharmacy)?		15
7	Is there a current Hepatitis C (HCV) and/or Cancer diagnosis which impacts functioning?		17
8	Does any other physical comorbidity (not HCV or Cancer) impact functioning?		17
		TOTAL	

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Chapter 7 – The role of comorbidity and clinical complexity in understanding and defining retention

7.1 Understanding results from the preceding study

The preceding chapter outlines the process for the development of a clinician-assessed complexity screening tool specifically to screen for comorbidity and clinical complexity in PLHIV. While there are limitations to the research, it serves as an initial step to developing a more robust and clinically rigorous assessment of complexity and comorbidity than relying on unquantified clinician judgement. In the context of all three theoretical models described in Chapter 1, the results are promising. The factors identified by clinicians in the development phase are wholly consistent with the Biopsychosocial Model. It is worth noting that it was beyond the scope of the rating scale to assess for contextual factors, as highlighted in the ABM, and thus only the individual component of that model is relevant here, as previously discussed. Likewise, while these results do not specifically test the Syndemic Model, the inclusion of weighted scores instead of binary additive scoring certainly lends this model to be tested in the future.

7.1.1 Strengths and limitations

As discussed in Chapter 6, the CCRS-HIV has a number of benefits. First, it provides clinicians with a brief screening tool to 'flag' clients with complex presentations who might benefit from additional resources and/or an interdisciplinary team approach. While it is currently being used with existing clients at Albion, it also has the benefit of being useful

for new clients to the service. For example, in the case of a new client who presents to see the triage nurse or intake psychologist, the assessing clinician can use the items included within the CCRS-HIV to expand upon or guide their initial assessment; it serves as a guide for targeted questioning about factors which we know tend to impact our client base. In this way, early identification of potential problematic areas allows for early intervention and allocation of resources/appropriate referrals at the point of entry to the service, rather than waiting for these risk factors to reveal themselves during a crisis. This shift from 'reactive' to 'proactive' care was central to the inception of the CCRS-HIV.

Second, the screening tool is a brief way of harnessing years of clinical experience in clinicians within the HIV sector for those who are new to the field, or potentially do not have the benefit of interdisciplinary team support. The CCRS-HIV was developed with clinicians with over 30 years of clinical experience working with PLHIV in the public sector, throughout the various stages of the epidemic. As such, their knowledge of clinical 'trends', informed by the evidence-base within the literature as well as clinical experience, and variables which might negatively impact a person's well-being, functioning or QoL is exceptional. For clinicians without experience in this field, or for those in rural and remote settings without much support from an interdisciplinary team, this knowledge is invaluable. In addition, the brevity of the screening tool makes it a workable adjunct to clinical assessment. In developing the tool, we were conscious of balancing the clinically meaningful with something which was also clinically workable; that is, it needed to include

all relevant variables while not being too onerous to complete that clinicians avoided doing so. The resulting scale, we believe, balances these aspects well.

However, the limitations cannot be ignored. As discussed in Chapter 6, the scale is subjective and makes use of clinician knowledge of the client. This obviously requires/is dependent upon a strong engagement between client and treating clinician, which studies have shown is important to successful management of HIV-infection (Chen et al., 2013), however is consistent with Andersen's concept of 'evaluated need' as being clinician assessment of client factors which require monitoring and/or intervention (Andersen et al., 2014). Results from a recent multi-national survey (including Australia) indicated that the majority (71%) of respondents reported feeling comfortable raising issues with their primary HIV specialist (ViiV, 2018), suggesting these doctors have a unique insight into the lives of their clients and supporting the concept of clinician-assessment, which has precedents within the HIV literature (e.g. Grant et al., 2011). For new clients where the relationship is not established, however, the items in the scale remain a valuable assessment guide.

In addition, there may be some criticism of the methodology of comparing clinician assessment of individual variables to clinician assessment of 'complexity'; however, this was intentional to try and replicate the current qualitative process during clinical consultations where clinicians synthesise the information from the client to make

assessments of complexity to guide treatment planning, appointment schedules, and referral options. Although the tool requires further validation in the context of more objective measures of these areas, it certainly provides a promising foundation for work in this field, particularly in the context of those who are sub-optimally retained.

7.1.2 The role of stigma and QoL

One important psychosocial factor, which was beyond the scope of the CCRS-HIV to assess, is HIV-related stigma. Despite advances in treatment and improvements in the public perception of HIV, stigma remains an issue for many and certainly can, and does, impact retention (Christopoulos et al., 2019; Yehia et al., 2015b). Christopoulos and colleagues also found that stigma was associated with viraemia, suggesting a role in medication as well as appointment adherence (Christopoulos et al., 2019). The stigmatising nature of living with a chronic illness and being dependent on services and medications have also led some authors to suggest that this stigma might impede optimal retention, given medication and appointment adherence can serve as reminders of the illness (Hutchinson & Dhairyawan, 2017).

While the importance of HIV-related stigma is acknowledged, unfortunately it was not included in the CCRS-HIV development for a few reasons. First, stigma, unlike mental illness, or HCV-infection, is unlikely to be routinely assessed by clinicians unless it is raised through the course of psychology or social work discussions. Second, the purpose of the screening tool was to assess medical, behavioural, psychological and social factors which

are readily quantifiable and modifiable with clinical interventions. The premise behind the CCRS-HIV was to develop a brief screening tool with the most relevant, routinely collected, variables which impact the functional impairment of PLHIV; thus, including stigma was beyond its scope. Its exclusion, however, does not minimise the important role of stigma, and any future prospective research should aim to address this explicitly.

Likewise, the preceding scale did not assess, as a predictor or outcome, the role of well-being and/or QoL. This is largely due to the fact that the scale was developed by clinicians regarding their knowledge of clients, although without direct contact with clients to inform its development. At present, the key outcome of HIV treatment 'success' remains a sustained UDVL, although this has been suggested as being outdated in isolation of other factors (Guaraldi, Milic, & Wu, 2019). Rather, many have suggested a QoL outcome/metric is *as* relevant as VL, and may in fact also feed back into medical outcomes such as VL and medication adherence (International HIV/AIDS Alliance, 2018). This might feasibly also extrapolate to retention in care. While QoL was not explicitly assessed here, it should be a focus of future research in the field, and might be an important inclusion to any future versions of the scale which include a client-rating component.

7.2 Changes to clinical practice as a result of the development of the CCRS-HIV

In practice, the development of the CCRS-HIV was one part of a broader clinical redesign project at Albion aimed at improving interdisciplinary care for clients with complex presentations, which is described in more detail in Chapter 10.

7.3 How identifying complexity assists retention

Understanding the profile and characteristics of common comorbidities impacting PLHIV is incredibly useful clinical information, with the logical progression being ascertaining whether particular profiles impact retention. The following discussion and study aim to address this.

Identifying complex comorbid presentations has obvious benefits to enhancing optimal clinical care, but how does this relate to retention? In the context of holistic care, which is characteristic of public health HIV services in Australia, the role of psychosocial as well as medical factors which can interact to increase the burden of illness (Singer et al., 2017) is increasingly well understood. Such comorbidity has the potential to negatively impact retention rates; conversely, retention is necessary for ongoing monitoring of all comorbidities, thus suggesting a bidirectional relationship. In facilitating optimal holistic care and working towards well-being and QoL for PLHIV, clinicians must consider all potential factors. An HIV medical specialist routinely monitors and assesses for other

aspects of the client's functioning and presentation beyond their biological status alone, such as mental illness, substance use, and housing/welfare concerns. Likewise, psychologists working in the HIV/sexual health sector are trained to recognise the signs of possibly concerning medical factors which might warrant referral to medical and/or nursing specialists. However, this monitoring can only occur if the client presents for review. For clients who do not attend regularly, this ongoing holistic assessment is elusive, and thus best practice is not achieved.

The hypothesis that clients with multiple comorbid presentations might be sub-optimally retained in care, as a result of the interaction of these presentations on their functional capacity, is central to the subsequent study. In order to understand the profile of clients who are not retained in care, one must first be able to identify comorbidity/clinical complexity in the cohort, to then monitor its impact on retention rates.

7.4 Understanding retention

To begin, an in-depth analysis of retention definitions is necessary. Interestingly, no standard or consistent definition prevails, even in regions with similar demographic profiles such as the U.S. and Australia. One might consider a global definition difficult to achieve, although the WHO appear to have done so; what is unclear, however, is why this is not adopted worldwide. As noted in section 1.11, the WHO stipulates that a person is

considered retained in care if they attend for medical review *"appropriate to* [the] *need"* (p.26, World Health Organization, 2017). This is in contrast to the U.S. which determines retention as attendance twice in 12-months, 90-days apart (Centers for Disease Control and Prevention, 2018), and the U.K. and Australia which determine retention as attendance once in 12-months, with VL used as a proxy (British HIV Association, 2018; Kirby Institute, 2018).

Interestingly, despite a seemingly more inclusive definition than those determined by specific regions, the WHO still favours 'ART retention' as the *"most accurate and meaningful measure of treatment success"* (World Health Organization, 2017, p. 26). However, when taken in conjunction with WHO statements on retention in other documents, a more comprehensive description ensues. For example, in a WHO meeting report, retention is defined as *"…continuous engagement from diagnosis, in a package of prevention, treatment, support and care services"* (World Health Organization, 2012, p.3), and *"ensuring that the client continues to receive appropriate services (from both the client and provider perspective) throughout the continuum of HIV care and support"* (World Health Organization, 2012, p.61).

When regarded in this context, the WHO definition outlined above can be considered to (a) recognise the role of the clinician in providing expert guidance regarding appointment

schedules, (b) recognise the importance of individualised care approaches rather than 'one-size-fits-all', and (c) account for the complexity of comorbidity, such that people are not 'missed'. A person, for example, who is stable and managing well can afford to see their doctor once or twice a year. For others with complex care needs, this will be inadequate. Individualising this metric therefore appears to make the most sense. The WHO also note the importance of retention in care to minimise 'leakage' at each step of the Cascade; in fact, promoting retention is a key component of the WHO 2016-2021 Strategy, albeit from a primarily biomedical perspective (World Health Organization, 2016c), which is directly at odds with those who have suggested it is redundant (e.g. Drew et al., 2017).

In addition, recognition of the role of specialist HIV clinician assessment is paramount, as these clinicians determine a course of treatment (including a schedule of visits) based on a thorough assessment of the client's individual needs. To ignore this component would be to generalise among a cohort where individual differences should be accounted for. When determining clinical guidelines for groups of people or disease profiles, the caveat of recognising 'clinician judgement' is often stipulated to ensure optimal and individualised care and treatment (Treadwell, 2015). As the WHO definition is open to interpretation regarding which perception of need it relates to, it was considered that attendance 'appropriate to need' relates to the need determined by the clinician, in the context of

individualised assessment, to account for the role of all factors which might impact HIV management in the present research.

The disparity in definitions between regions is one reason some authors have advocated for retention in care to be removed from the Cascade (e.g. Drew et al., 2017). However, it is argued that this would be a mistake. As discussed, retention is the only aspect of the Cascade which has the potential to monitor PLHIV holistically, thereby accounting for all medical and/or psychosocial comorbidity. In an age where the role of psychosocial factors in HIV management is becoming increasingly important, continuing with a Cascade which only captures biomedical endpoints would be retrogressive and arguably would not constitute best practice. Instead, expanding the Cascade as suggested by some authors (e.g. Lazarus et al., 2016) to include an explicit measurement of QoL seems more progressive, and more consistent with the delivery of optimal healthcare. Region-specific estimates in the Cascade often determine funding and resource allocation. If the only aspect which allows for the monitoring of comorbidity, well-being and QoL (i.e. retention in care) is removed, and overly simplistic schedules of retention which do not account for complex comorbidities are relied upon, we risk inflating retention estimates and biasing funding to public health services. As the PLHIV population continue to age, these characteristics will become increasingly clinically challenging; thus, inadequate funding to manage these is a dangerous step for improving the QoL of PLHIV.

Further, if biomedical endpoints such as viral suppression remain the sole focus, we neglect the factors which impact them. Viral suppression assumes medication adherence; poorly monitored or managed mental illness or substance use, for example, has the potential to significantly impact medication adherence (Blashill et al., 2015; Robinson et al., 2016; Yehia et al., 2015a). Focussing on viral suppression alone without paying attention to the context which surrounds it is, again, a false economy. A case can be made, therefore, for expanding current definitions of retention to explicitly include the role of monitoring of medical and/or psychosocial factors which might impact all aspects of HIV management, including retention. Likewise, it seems an appropriate next step to expand existing metrics of 'success', which currently focus on VL alone, to include other client-centred outcomes such as monitoring and treatment of comorbid conditions, and a focus on well-being and QoL (Guaraldi et al., 2019; Lazarus et al., 2016). Furthermore, explicit recognition of the role of specialist clinician assessment may also be warranted.

This is not to suggest, however, that all people with identified mental illness, or social/welfare concerns will be sub-optimally retained or have difficulties with medication adherence; in fact, the majority of clients with comorbidities currently manage well. A recent Australian survey of PLHIV found most respondents reported good general health overall (Power et al., 2019). It is important, though, to recognise such variables as 'risk factors' or areas which warrant monitoring and attention, as although they may not be impacting functioning at present, without appropriate care and support the likelihood of

that happening increases. This is especially relevant to ageing among PLHIV. An interesting question here is, if we identify concerns early and provide extra support where necessary, could future crises be diminished in intensity, or even averted?

7.5 Testing syndemic theory

The study of syndemics relates to population level trends rather than individual specifics (Tsai et al., 2017), which is consistent with the present study series. In order to assess whether a syndemic is present, a number of factors need to align. A central premise is to ascertain whether the disease burden in combination is greater than alone; that is, it must explain a synergistic interactive impact of elements rather than a cumulative additive impact alone (Tsai & Venkataramani, 2016). According to these authors, such methodological requirement have not been followed in previous research purporting to relate to the study of syndemics, and risk diluting the importance of understanding such synergistic effects (Tsai & Venkataramani, 2016). Thus, the subsequent study will aim to assess this, with the methodological rigour described by these authors.

In the event that syndemic relationships are not discovered, the aim of the study will be to understand whether cumulative (additive) relationships between variables exist, in the context of their impact on retention in care; such information remains valuable in expanding our understanding of the factors which impact retention.

7.6 Study 4

The following study reviews estimates of retention based on Australian and WHO definitions, and aims to assess the role of various medical and/or psychosocial comorbidity factors in impacting retention rates. As previously discussed, prospective research in this area is fraught with difficulties, specifically the issue of accessing clients who are not retained for the purpose of data collection. While previous studies, including a combination of prospective and retrospective research designs, have identified some factors (discussed in Chapter 2), there is limited information regarding Australian cohorts. Furthermore, as previously discussed, prospective research requires a significant financial investment in the context of staff to manage participant attrition, and retrospective designs generally favour routinely collected demographic variables, with few able to comment on comorbid presentations. The following study aims to address this gap. The specific question regarding syndemic relationships will also be addressed.

This paper is currently under review in *AIDS Care* using the APA referencing style, and the content remains the same as that which was submitted.

7.6.1 Study goals

Current estimates of retention in care in Australia are extremely high (95%), and have been relatively consistent in recent years (Kirby Institute, 2018). However, considering the complexities of understanding retention, including whether definitions account for all PLHIV especially the most vulnerable and marginalised, comparison against the WHO

metric will also occur. As discussed, the WHO definition of *"attendance appropriate to* [the] *need"* will be operationalised as adherence to a schedule of visits determined by an HIV medical specialist. To our knowledge, no studies have compared region-specific definitions with the WHO definition, which we sought to address. There are two central questions to this study:

- Is there a cohort of people who are considered retained according to the Australian metric, but who are not attending as needed/recommended?
- Are there particular characteristics about this cohort, with a specific focus on medical and/or psychosocial comorbidity?

7.6.2 Initial study design

A prospective cohort study was initially designed to assess the role of various comorbid factors on retention rates. However, as discussed in section 5.2.4, this was unsustainable. Inherent difficulties with prospective research in this area relates to the difficulty accessing a cohort who are sub-optimally retained who, anecdotally, might present with more complex comorbidities; such contact is often opportunistic in the context of unscheduled visits to the clinic, and would require funding to support a research assistant. Unfortunately, this was not possible and despite eight months of attempts, only data for those who were optimally retained could be gathered.

As such, the study design had to be reconsidered. Given the capacity to provide some assessment of comorbid factors, albeit clinician-assessed via the CCRS-HIV, it was decided

to conduct a retrospective cohort study assessing the impact of these factors on retention. While not ideal, this should provide a basis for future research in the area.

7.6.3 Relevant methodological issues within the present study design

In designing this study, we sought to ensure our measurement was as robust as possible. Multiple metrics to measure retention exist in the literature, and there is no explanation of 'on time' attendance. For the purpose of the present study, the most relevant metric and definition of 'on time' attendance had to be developed in a way that was meaningful to the study.

7.6.3.1 Measures of retention in the literature

Two studies (Mugavero, Davila, Nevin, & Giordano, 2010; Mugavero et al., 2012b) have reviewed the process of measuring retention and considered different options such as measuring missed appointments, using VL as a proxy for attendance, and measuring appointment adherence; both studies concluded that there are pros and cons to each method, and no clear 'gold standard' could be identified. Rather, they noted the measurement should be tailored to the study.

Given the present study involved measuring retention against the most recent WHO standard of attendance 'appropriate to need', measuring appointment adherence appeared the most meaningful estimate. This metric involves considering the number of appointments attended 'on time' as the numerator, with the total number of

recommended/scheduled visits as the denominator, providing an individualised proportion of visits attended on time for each participant. This method means each participant naturally has a different denominator to determine the proportion of appointment adherence, however this measurement is consistent with WHO guidelines of monitoring individualised schedules of attendance appropriate to need, and other studies in the area (Mugavero et al., 2010). Therefore, measuring the proportion of *their* scheduled visits attended is appropriate in this context, and is comparable to others with a different schedule.

7.6.3.2 Timeframe definitions

Previous literature regarding retention has measured attendance against existing region-specific estimates (e.g. U.S. or Australia) where the definition is clear. To our knowledge, there are no studies assessing retention against the WHO metric of attendance 'appropriate to need'. As such, there is no clear precedent of operationalising retention against which to measure (i.e. the timeframe within which attendance is considered 'on time'). For example, it is important to operationalise whether a client who attends a week late for a scheduled visit is still considered 'on time', versus someone who is 3 months late for their appointment. Such measurement is inherently difficult to undertake and to compare, and there are no precedents in the literature to support this process. In particular, identifying a timeframe within which attendance is considered 'on time' is a key concern. As such, these parameters had to be defined here.

In contrast, defining 'lost-to-follow-up' (LTFU) has occurred, with the WHO recognising this as 90 days after the last scheduled appointment (World Health Organization, 2012). While it might seem to make sense to use this metric here, it is important to note that the two are measuring quite different things; LTFU assesses the timeframe of non-attendance after which a person can be considered to have dropped out of care, whereas the present study series is more concerned with ways in which to measure optimal appointment adherence, in the context of a recommended schedule of visits by a specialist HIV clinician.

An initial review of one month of the data was conducted to determine (a) the proportion of visits which needed to be included within that timeframe, and (b) the timeframe within which on time attendance would be considered. The data suggested very little difference between those who attended 75% of their appointments vs. 80% or 90% of their appointments; therefore, a conservative proportion of 75% was chosen. With respect to the timeframe, the initial sweep of the subset of data determined that 56.9% attended at least 75% of their appointments within one month of the scheduled/recommended visit. A further 12.3% attended at least 75% of their appointments within two months of the scheduled/recommended visit. Theoretically, one month was considered a generous length of time within which to reschedule an appointment. As there is no clear precedent in the literature regarding the length of time which constitutes 'on time' attendance, it was therefore decided to define 'on time' attendance as within 1 month/30 days.

7.7 Chapter 7 References

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Chapter 8 – Current definitions of retention in HIV care: The potential role of comorbidity

Bulsara, S.M., Wainberg, M.L., Rogers, K., McAloon, J., Grove, R., & Newton-John, T.R.O. (under review). Current definitions of retention in HIV care: The potential role of comorbidity. Manuscript submitted for publication. *AIDS Care*.

8.1 Abstract

Retention in care is a central component of the HIV Treatment Cascade which facilitates monitoring of medical and/or psychosocial comorbidity. Region-specific definitions of retention differ, and may suit stable and functioning clients, while not providing a valid categorisation of more complex clinical presentations characterised by comorbidity.

A retrospective file review of 363 people living with HIV attending an HIV clinic in Sydney, Australia, was conducted. Retention rates were compared with Australian (attendance once in a 12-month period) and World Health Organization (attendance 'appropriate to need') recommendations to identify a 'target group'; those retained according to the Australian definition, but not attending according to clinician recommendations ('appropriate to need'). The impact of age/sex, viraemia, and clinician-assessed comorbidity on retention were assessed.

Results indicated 97% of participants were considered retained according to the Australian definition, but only 56.7% according to clinician recommendations. There were no significant associations between age, sex or viraemia, and retention. Those with psychosocial comorbidity alone were less likely to be in the target group (*OR=0.51*). The interaction of physical and psychosocial complexity variables was predictive of poor retention (*OR=2.39*), and suggestive of a syndemic relationship. Characteristics of the target cohort are also explored, and recommendations are made accordingly.

Keywords: HIV, Retention, Complexity, Psychosocial, Comorbidity

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Chapter 9 – Adapting definitions and measurement of retention in the context of comorbidity and clinical complexity

9.1 Results from the preceding study

The results from the previous study are mixed with respect to the role of clinician-identified comorbidity and its impact on retention. While it is heartening to see the limited impact of comorbidity on VL - likely indicative of the huge medical strides in ART efficacy, tolerability, and simplicity - a relationship between comorbidity and retention was demonstrated (Bulsara et al., under review). These results must be interpreted with caution, given (a) often low cell numbers and therefore low power, and (b) the infancy of the screening tool used. However, they do provide an important signpost for future research to develop.

9.1.1 Discrepancies in estimates of retention

One of the more interesting findings of the previous study was the discrepancy between estimates of retention, dependent on the definition. Estimates using the Australian definition were 97%, consistent with overall estimates in Australia (Kirby Institute, 2018); however, significantly fewer (56.7%) attended appointments consistent with specialist clinician recommendations.

It is, of course, possible that clinicians are overly cautious in recommending a schedule of visits; however a more likely scenario is that they are, in fact, considering all aspects of the client's presentation which warrant monitoring. In this way, failing to adhere to this schedule might not (immediately) negatively impact HIV disease progression, however it arguably does not constitute optimal holistic care of the individual.

An important consideration here is the allocation of Government resources and funding, which are determined by the estimates and definitions of retention. In Australia, consistently high estimates of retention likely signal a funnelling of resources to other areas of the Cascade such as testing and prevention, potentially at the expense of retention. If the definition of retention on which the estimates are based is flawed, this is problematic. It could be argued that existing definitions and metrics of retention in Australia are overly specific in their focus on VL alone, and suit relatively stable and functioning clients, where one VL test per 12 months might be considered adequate care. This metric does not, however, suit more complex clinical presentations which require far more frequent and intensive holistic monitoring than one phlebotomy test per year.

9.1.2 Understanding comorbidity and its impact on retention

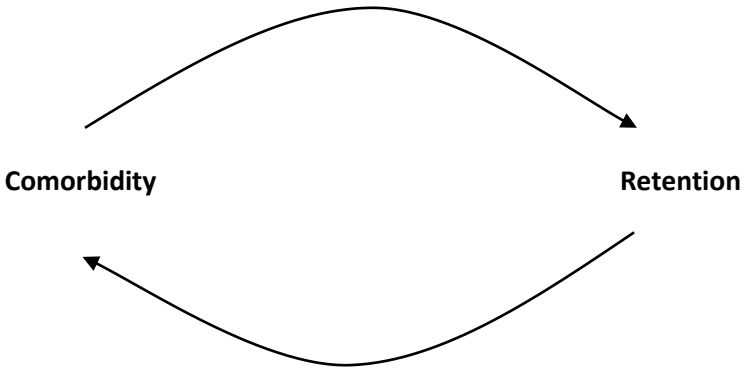
The preceding study also highlighted particular comorbidities which might impact retention. Interestingly, those with only clinician-identified psychosocial (PSY) comorbid presentations were *more* likely to adhere to a schedule of visits determined by their HIV

specialist, potentially indicative of the particular variables which comprised that domain. There is a body of literature on 'frequent attenders' which highlights that individuals presenting with factors such as social isolation, financial instability and mental illness might attend health services more frequently than normative counterparts (Bulsara et al., 2019b; Chua & Johnson, 2019; Crawford, 2015). Indeed, when compared to this group, those with no comorbidity were significantly more likely to be in the target group (i.e. sub-optimally retained), potentially pointing to clients feeling well and not prioritising appointments (Bulsara et al., 2019b). Some authors have suggested that additional comorbid conditions are easier to accommodate if individuals can identify a 'cognitive link' between them (Morris, Sanders, Kennedy, & Rogers, 2011). Thus, this could account for the finding that psychosocial comorbidity alone might not impact retention (based on the similarity of variables), but the combination of that and physical factors might prove too different to accommodate and therefore negatively impact retention. Further research is required to fully understand this result, especially the mechanisms by which psychosocial comorbidity alone actually improves retention.

Perhaps of most interest in the context of comorbidity and complex clinical presentations is the significant interaction between the physical health (PH) and PSY complexity domains. This showed that, when compared to PSY comorbidity alone, the interaction of PH variables with PSY highlighted a significantly higher odds of being in the target group. This finding is significant in the context of understanding the role of comorbidity and its

impact on retention. Interestingly, the significant 2x2 exploratory interaction analysis contained variables from the PSY domain only (problematic CMA use and social isolation); however, given the low numbers these results must be interpreted with caution. One possible explanation is that the specific variables which comprised the significant PH*PSY interaction was a 3x3 equation. It is therefore likely that the presently identified problematic CMA use and social isolation variables only accounted for two of three relevant variables, with the third being a 'PH' factor. These results can be considered in the context of the Biopsychosocial Model and the individual component of the ABM in their exploration of a range of factors which impact retention. Likewise, they are certainly consistent with the Syndemic Model of disease interaction.

The results also highlight a bidirectional relationship between comorbidity and retention. Comorbidity certainly seems to impact retention; however, retention is required to monitor complex comorbidities. Figure 1 below depicts this relationship.



9.1.2.1 Figure 1: The potential bidirectional relationship between comorbidity and retention

As this figure suggests, the two are inextricably linked, and an assessment of one (e.g. retention) cannot exist without consideration of the other (e.g. comorbidity).

9.1.3 The role of syndemics

Consistent with the model required to test syndemic theory (Tsai & Venkataramani, 2016), the previous study's results highlighted a promising step forward. The following equation was determined by Tsai & Venkataramani to be the only correct method to test a true synergistic syndemic relationship between variables:

$$Y = \alpha + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_1 X_2$$

In the context of the preceding study, the equation is as follows:

$$Y = \alpha + \beta_1 PH + \beta_2 PSY + \beta_3 PH * PSY$$

This fully saturated model, which shows the synergistic interaction of PH and PSY factors in negatively impacting retention rates, suggests that research which focusses on

biomedical aspects of HIV in the absence of psychosocial factors, presents an incomplete assessment. While some authors have recognised the importance of psychosocial underpinnings of a biomedicalised HIV response (Aggleton & Parker, 2015; Kippax & Stephenson, 2012), this remains a relatively uncommon perspective. While VL rates remain low, the biomedicalised approach has pre-eminence. Though not discounting these medical advances and successes, it is impossible not to recognise gaps with this approach. The HIV sector has long recognised the importance of psychosocial factors, yet this has not translated into meaningful policy recognition, changes in guidelines, reporting guidelines, or metrics of success; a prime example of this is the continued medicalised definition of retention in care which can, and should, encompass all aspects of client monitoring. At present, the expectation remains that 'success' is measured by viral suppression alone. As will be discussed in section 11.2.5, a modification of these definitions is warranted to encompass overall well-being and quality of life metrics, as well as VL.

9.2 Implications of the results

The results of the preceding study must be considered in context. Ageing among PLHIV dictates that attention must be paid to their changing needs as they age. This requires an understanding and review of relevant comorbid factors which might impact overall health, functioning, QoL, and adherence to medications and appointments.

If clients are not retained, the risk for poor management of their illness (and the potential for worsening health outcomes and transmission) increases. It is therefore a false economy not to focus on this area, as its neglect may in fact lead to increased future costs. The current NSW Health HIV Strategy recognises the role of psychosocial support and the importance of retention in care, although these are cursory mentions, with the primary focus being testing and prevention methods (NSW Health, 2015). Such public health strategies and policy documents require an overhaul to increase the focus of resources, research, and interventions on supporting PLHIV with complex care needs. Indeed, the significant PH*PSY interaction result in the preceding study, as well as the finding that the majority of those with a detectable VL during the study period were in the target group, certainly highlights the importance of these factors. Early identification of, and intervention for, those at risk are likely to avoid detrimental individual and public health outcomes.

9.3 Chapter 9 References

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Chapter 10 – Research Impact

10.1 Translational research

In developing this study series, the primary focus was translational research. As a clinician who has worked in the HIV sector for 12 years, it was important to develop a research series which would translate into practical clinical changes to improve outcomes for PLHIV. While studies 1, 2 and 4 (Chapter 2, Chapter 4, and Chapter 8 respectively) all provide valuable insights into retention and its predictors in Australia, study 3 (Chapter 6; the development of the CCRS-HIV) is likely to have the most practical utility in terms of clinical practice.

10.1.1 Changes to clinical practice

In practice, the development of the CCRS-HIV was only the first step in practical clinical changes which have occurred at Albion over the past two years. As a result of interdisciplinary discussions which took place at a Strategic Planning Day in 2017, the clinical units at Albion recognised the need to improve services in two key ways: (a) identify clients with complex care needs in a standardised way, and (b) appropriately and effectively provide intervention. It became apparent during this Planning Day that interventions with those with complex clinical presentations were often crisis-driven and reactive; the primary goal was to develop a more proactive means of identifying and responding to clinical complexity.

The process of developing and validating the CCRS-HIV with this cohort has been described in Chapter 6, and therefore need not be repeated here. However, in practice this was only the first step in a clinical redesign project, involving all clinical disciplines, but especially the medical, psychology and nursing units at Albion. The primary goal here was to move from a multidisciplinary clinical service to one which functioned as an interdisciplinary unit; the former involved each clinical unit working in isolation within discipline boundaries and communicating as needed, and the latter was conceptualised as all units working together on the same problem with overlapping disciplinary boundaries. Albion has always been at the forefront in the context of holistic care, has offered a range of medical, nursing and allied health services from its inception, and has often been the model for the creation of similar services in the Asia-Pacific region. HIV has always been conceptualised holistically within the service, and this project (termed 'Interdisciplinary Care' [IDC]) was built on this existing strong foundation.

The practicalities involved a team approach to reviewing all PLHIV on an AMO's clinical 'list' (i.e. the AMO who most frequently sees the client and is responsible for their ongoing care). These teams included an AMO, Nurse, and Clinical Psychologist at a minimum, with Pharmacy, Nutrition, Social Work, and Admin involved as necessary/appropriate. All clients were reviewed by the team, and CCRS-HIV assessment was one component of this assessment. Care plans were developed for those who were identified as having complex care needs, and these were reviewed regularly. Appropriate referrals were also a focus of

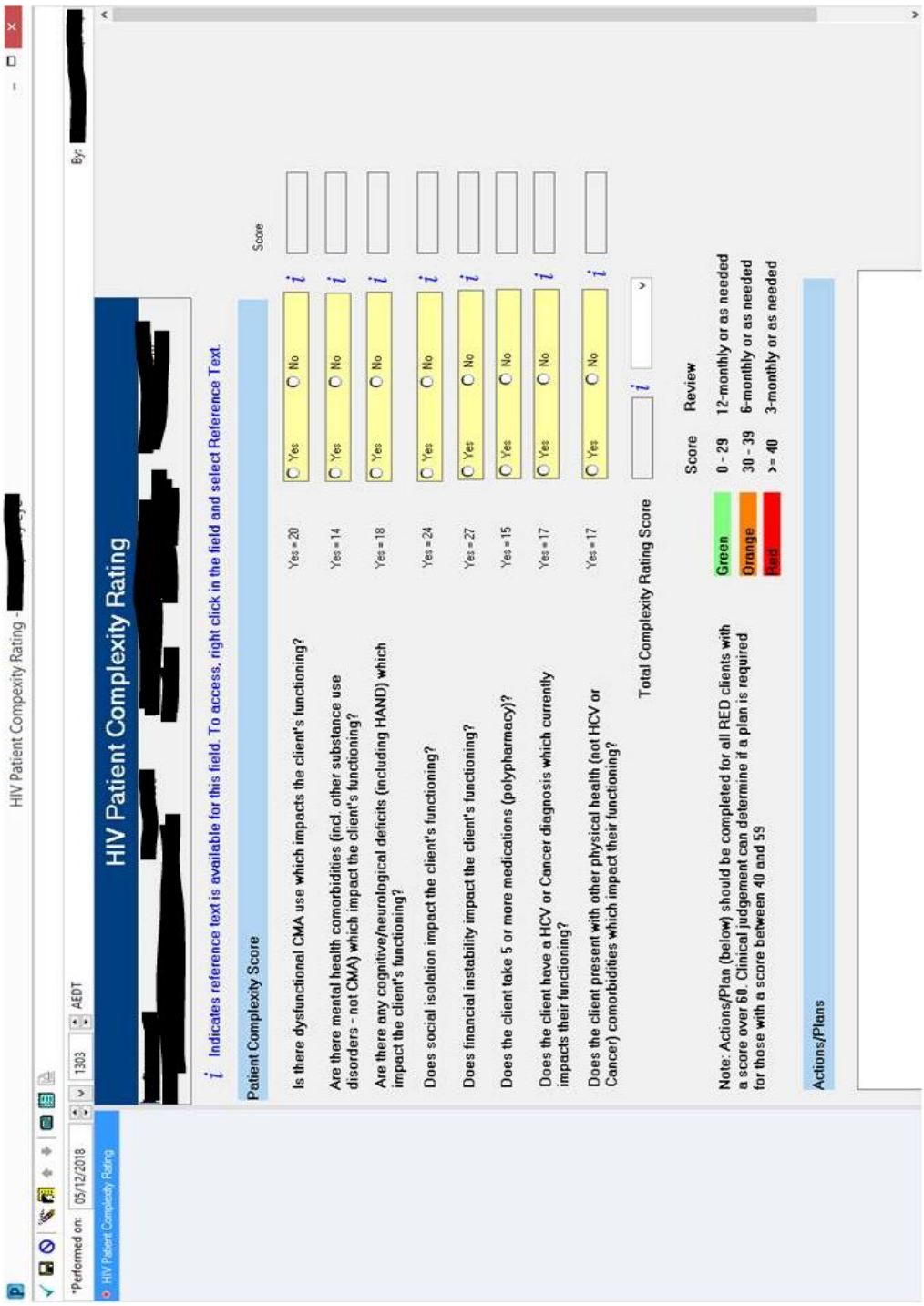
these discussions. Where appropriate and practicable, clients were invited to be part of this process.

This clinical redesign began in 2018 and so is new, however (anecdotally) this process has improved clinician communication and collaboration with a common goal of improved client outcomes. Our current IT systems do not have capacity to provide alerts where clients have not attended; this process of reviewing all clients within the service allowed us to allocate time specifically to review all clients' attendance, medical and psychosocial outcomes, and refer as necessary. As a result of this process, and using the CCRS-HIV to monitor this, we identified that approximately 80% of our client base were managing well (classified as 'Green' on the CCRS-HIV, as discussed in section 6.4.5), with approximately 20% (classified as 'Orange' or 'Red' in section 6.4.5) requiring additional support because of their vulnerability or complex care needs. This was consistent with clinical experience and expectations regarding the rates.

Our system requires ongoing evaluation, as does the screening tool itself. However, we believe the tool is a useful adjunct to clinical assessment and provides an accurate evaluation of the most common complexity factors which impact our cohort.

10.1.2 Integration to Electronic Medical Records (eMR)

A significant achievement during this process was integrating the CCRS-HIV into the Statewide (NSW) Electronic Medical Record (eMR), as a result of its validation with our cohort. Figure 1 is a deidentified screenshot of the CCRS-HIV screening tool on eMR; any clinician within the service who has contact with a client has the capacity to enter data directly into the eMR. The weighted scores and total are calculated automatically, and there is space for a care plan as needed. This information is henceforth readily available to other clinicians within the service who encounter the client and is easily modifiable based on new information and changes in circumstances. It is worth noting that Albion is a 'secure' site on eMR, which means other services within the health district (e.g. Emergency Departments) are unable to access information related to our clients. This is because of the ongoing stigmatising nature of HIV.



10.1.2.1 Figure 1: Deidentified screenshot of the CCRS-HIV on the Statewide electronic Medical Record (eMR)

10.2 Requests from other services for the CCRS-HIV

As a result of conference presentations on this topic, there has been interest from other similar services who have requested access to the screening tool. As the CCRS-HIV is now integrated into eMR, there is no way of knowing exactly how many services are accessing or using the tool. However, to date we have received six requests from other services similar to Albion in NSW, QLD and WA for a copy of the tool. Four of these have been provided the screening tool, the remaining two services (one in NSW and one in WA) had only just made contact at the time of submission. Two presentations to local clinical services (St Vincent's Hospital, and Sydney Sexual Health) were also requested and provided specifically on the development, validation and utility of the screening tool.

Chapter 11 – Discussion

11.1 The problem

The present study series was borne from over a decade of experience working clinically within a public tertiary referral HIV setting, and observing the increasingly complex clinical presentations of PLHIV. Witnessing the difficulty in engaging clients with comorbid presentations, and the ensuing clinical complexity, was a key motivator in developing this research.

11.1.1 The biomedical response to HIV

Since the beginning of the epidemic in the 1980's, service providers and advocates have recognised that the impact of HIV is not purely biomedical, and nor should its treatment be confined to biological factors alone. Optimising holistic HIV care requires recognition of all the factors that impact it. Furthermore, holistic care requires regular monitoring, not only of the traditional biomedical markers of VL and CD4, but also of other medical and/or psychosocial factors which are known to impact disease progression and overall well-being and/or QoL (International HIV/AIDS Alliance, 2018; Zeluf-Andersson et al., 2019a). Despite this recognition the response was, and continues to be, dominated by a medical perspective. A biomedical-only response to HIV was reasonable and critical in the early days to contain the epidemic, but is now an overly restrictive marker of success in isolation of other factors. Outcomes and metrics of success should, in 2019, transcend VL

alone, and should be holistic, individualised and client-centred (Chan et al., 2018; Guaraldi et al., 2019; HIV Outcomes Coalition, 2017). It is important to note that because the medicalised response *has been so successful*, it has allowed us to move to a chronic illness perspective, where our parameters of assessment and monitoring should likewise be expanded. The sector has long recognised that optimal service delivery includes allied health approaches. The paradox, however, is that psychosocial factors are not recognised or captured in reporting data, the evaluation of service outcome/success, nor treatment success.

The issue with continuing to respond in a biomedical context alone is that the sector overlooks the psychological and social underpinnings of sustained behaviour change that are necessary to make biomedical interventions effective (Aggleton & Parker, 2015; Kippax & Stephenson, 2012). One example of this is the 'U=U' campaign, one which focuses on viral suppression to manage transmission risk. While biomedical at its core, it exists on a premise of social and psychological behavioural change (such as sustained medication adherence), which is often not recognised. In 2019, holistic care delivery should be the HIV sector's primary purpose and neglecting to recognise that optimal care goes beyond an UDVL is short-sighted.

This is not to say that the sector does not value and recognise the importance of psychosocial factors; it clearly does, as evidenced by the range of allied health auxiliary

services available for PLHIV. However, this recognition and appreciation for the role of psychosocial factors has not, as yet, translated into meaningful policy change (in the context of reporting requirements), which is an important next step. It is also not the intention of this research to suggest that VL is not a good marker of treatment success; clearly it is. However, it is outdated to consider it the *only* marker of success, and we suggest it should instead be considered alongside other *'health-related QoL'* markers, and that expanding definitions of retention in care and associated reporting requirements is the means by which we can achieve this.

11.1.2 Comorbidity

Comorbidity has always been an issue in chronic illness, and HIV is no exception. However, it is not favoured in research methodologies. Clinical trials often exclude comorbidity in favour of methodological "tightness" and rigour, thus limiting real-world applicability of findings (Singer et al., 2017). A recent retrospective review of an Australian HIV cohort identified that the mix of medical, psychological and social comorbidities lead to complex clinical presentations requiring an interdisciplinary approach (Chan et al., 2018). Other studies have similarly noted the impact of comorbidity on treatment fatigue (Corless et al., 2008), health outcomes and cost (McPhail, 2016), and QoL (Zeluf-Andersson et al., 2019a). It has also been suggested that PLHIV might present with disproportionately higher rates of comorbidity when compared to the general population, and that their HIV-infection may exacerbate some comorbid presentations (Safreed-Harmon et al., 2019). These authors also note the importance of meeting the complex care needs, characterised by comorbidity, of

an ageing cohort of PLHIV, and further suggested that indicators used to monitor optimal progress should expand beyond viral suppression alone (Safreed-Harmon et al., 2019). Interestingly, few studies have assessed the impact of comorbidity on retention specifically, and some have found that comorbid presentations actually improve retention (Crawford, Sanderson, Breheny, Fleming, & Thornton, 2014), potentially in the context of increased points of connection/engagement. Others, however, have suggested that comorbidity can lead to 'treatment fatigue' and therefore disengagement from services (Corless et al., 2008).

11.1.3 Ageing

Ageing in HIV, as with other chronic illnesses, is associated with comorbid medical conditions (Lazar, Kersanske, & Braunstein, 2019). However, the role of psychosocial comorbid factors such as social isolation, stigma, and mental illness can also complicate effective HIV management and must therefore not be ignored (Rueda et al., 2014). As discussed in section 1.8.1, many studies have assessed the role of psychosocial, as well as physical, comorbid factors in older PLHIV. Results suggest a higher degree of comorbidity in older, versus younger, PLHIV, and particularly attended to the role of psychosocial factors such as mental illness, social isolation and financial strain (Erenrich et al., 2018; McGowan et al., 2017; O'Brien et al., 2018). In addition, poorer clinical outcomes and an increased risk of mortality are associated with older age in PLHIV (The Lancet HIV, 2017). The risk of increased psychosocial and medical comorbidity as people age suggests that overall health outcomes will only deteriorate. Indeed, understanding the impact of

comorbidity on QoL is necessary as a result of ageing among PLHIV (Lazarus et al., 2016). As such, even though the results presented in Chapter 8 suggest the presence of such factors might not implicate VL *at this point*, early identification, ongoing monitoring and effective interventions for these factors likely allow for longevity of positive health outcomes, including viral suppression. This can only be achieved through regular monitoring, and thus underpins the importance of appropriate definitions and accurate estimates of retention in care. In the context of an ageing cohort of PLHIV, understanding the potential impact of, and relationships between, biopsychosocial comorbidities on accessing healthcare remains a priority.

11.1.4 The Cascade, retention in care, and optimal service delivery: Beyond viral suppression

The current Cascade and 90-90-90 targets, which focus on biomedical metrics of success alone, are presently considered to represent optimal service delivery. However, as has been discussed, this perspective is arguably outdated. As HIV medical management has evolved, so too has our clinical understanding and appreciation of other comorbidity factors which impact HIV management, and the need to address holistic care needs beyond viral suppression alone with an ageing cohort cannot be ignored (Kall et al., 2019). Additionally, clinical and research perspectives on what constitutes optimal care rarely consider biomedical aspects alone, in isolation of their psychosocial counterparts. As such, the concept of optimal care in HIV is currently undergoing a dramatic change, with many suggesting this should include QoL measurements in addition to traditional biomedical

markers (Guaraldi et al., 2019; HIV Outcomes Coalition, 2017; International HIV/AIDS Alliance, 2018; Kall et al., 2019; Lazarus et al., 2016).

One existing means within the Cascade by which to monitor relevant comorbidity factors is retention in care. While retention has been widely studied, in recent years has lacked the appeal of other elements of the Cascade in terms of funding, resource allocation, and research. Region-specific definitions vary, although all currently point to monitoring of biomedical outcomes, such as viral suppression, rather than broader monitoring of holistic care needs. To expand the Cascade and global targets to include QoL measurements, we need a means by which to monitor and assess this; retention seems the obvious choice, although this too requires expansion in terms of its definition and means of measurement. In order to achieve this, we require a thorough understanding of the factors which impact it.

The World Health Organization recommendations (World Health Organization, 2016a) seeks to provide international guidelines, and therefore consider both countries with advanced economies and LDCs; as such, these guidelines are required to be broader than their more prescribed country- or region-specific counterparts. Many resource-rich countries (e.g. Australia, U.S, and U.K) continue to have a biomedical focus at the core of their definition

of retention, which does not adequately account for the range of factors which can impact PLHIV, including their capacity to attain and maintain viral suppression.

The WHO definition also remains biomedical in its focus and discusses the importance of 'ART retention', noting that *"retention is used to describe a cohort of people living with HIV who are alive and receiving routine HIV care, including ART, at a specific time after enrolling in HIV care or starting ART specifically"* (World Health Organization, 2017, p. 26). The comment *"including ART"* implies however, along with other documents discussed in section 1.11, that they consider the definition to go beyond ART retention alone. As such, their definition of attendance 'appropriate to need' provides a platform for a more inclusive approach to retention and recognises individual differences with respect to the optimal schedule. While it might be possible for some individuals to monitor and respond to this need themselves, it seems most appropriate that this need is determined by specialists in the field, who consider the holistic health perspective of the individual and determine a visit schedule accordingly. Therefore, one interpretation of the WHO guidelines is that it refers to adherence to a schedule of visits, determined by a specialist in the field.

What is clear is that there are no consistent definitions of retention across, or even within, regions. Likewise, consistent measurement of retention remains elusive, with multiple

metrics existing to attempt to capture this aspect of the Cascade (Drew et al., 2017). Examples of measurement include counting missed appointments, attended appointments, and VL testing; given the lack of consistency, the suggestion of tailoring measurement to the context of specific studies seems most appropriate (Mugavero et al., 2012b).

As a result of different definitions and measurements of retention, comparison both between and within regions is difficult. Some have suggested this lack of clarity lends itself to a removal of retention from the Cascade (Drew et al., 2017); however, for many reasons this would likely be a mistake. First, removing retention diminishes its value. Retention is an existing means by which clinicians can review and monitor all factors (biological, psychological and social) which are known to impact HIV and its management. Failing to do so would risk providing sub-optimal care. Second, retention is one of the few aspects of the Cascade which accounts for the management and support of PLHIV which is not solely biomedical in focus. Again, this allows for holistic care. Third, retention is a metric by which resources and funding can be allocated; inaccurate measurement or reporting of retention therefore skews regional responses to the epidemic. For example, in Australia current estimates of retention are approximately 95%. From a resource-allocation perspective, this conveys to policy makers that existing services do not require assistance to support or improve retention rates as there is little room for improvement. Increasingly complex clinical presentations impede the capacity of HIV tertiary services to effectively

holistically monitor and care for PLHIV. As discussed in section 1.11, there are three key benefits to retention remaining in the Cascade. Retention facilitates:

1. Monitoring of ART adherence
2. Monitoring comorbid factors which might impact ART adherence
3. Monitoring comorbid factors which might impact well-being/QoL (i.e. providing optimal holistic care)

From a well-being and QoL perspective, HIV management should transcend UDVL alone, a perspective recognised by many (e.g. Chan et al., 2018; Guaraldi et al., 2019). We should be focussing our attention on how well someone is living with HIV, and the degree to which their illness impacts functioning across other domains. This is not only clinically relevant now in the context of holistic management, but also signals potential difficulties which might impact medical HIV management in the future. Some authors have suggested that the Cascade and global 90-90-90 targets should, in fact, be expanded to include a 'Fourth 90 – living well with HIV' (Lazarus et al., 2016). These authors draw on the WHO Global Health HIV Strategy 2016-2021 and note that viral suppression is not the (sole) ultimate goal of treatment – *"The goal: To end the AIDS epidemic as a public health threat by 2030, within the context of ensuring healthy lives and promoting well-being for all at all ages"* (World Health Organization, 2016b, p. 23). This expansion of policies, guidelines, and reporting requirements beyond the paradigm of viral suppression alone is a critical next phase for the global HIV sector. Failing to do so risks missing an important opportunity to

provide optimal care to the global PLHIV community.

Precedents exist for the expansion of public health approaches to healthcare delivery; early approaches to disease management were considered too narrow and necessitated broadening from a biomedical to a biopsychosocial model (Havelka et al., 2009). We have also recently witnessed the sector being responsive to new information, evidenced by the recent shift in health promotion materials to account for rising infection rates among people who report heterosexual contact. In this way, so too does the definition of retention, and reporting requirements to measure the same, require expansion to encompass more, including health-related QoL.

The present study series provides a series of novel and translational results in the field of comorbidity and retention in care and provide direction for improving existing models of care and policies which drive the same. The purpose is to expand our knowledge about potential comorbidity barriers to retention, as well as how it is defined and measured, as a first step towards eventually expanding the Cascade and targets to include factors other than viral suppression alone.

11.2 The study series

The aim of the present study series was to review and address disparities in the HIV retention in care literature, with a particular focus on the local landscape. Specific goals were fourfold. First, to understand the international literature regarding barriers to retention. Second, to understand the local landscape. Third, to consider how comorbidity is assessed in PLHIV. Finally, fourth, to review current definitions of retention in the context of comorbidity.

Through a series of four studies, the thesis aims to map the complexity of medical and/or psychosocial factors which impact retention in Australia, and which have the potential to ultimately influence HIV outcomes.

11.2.1 Study 1

The first study (Chapter 2) was a systematic review of global literature regarding predictors of retention. Results of this study suggested a complex interplay of demographic, physical, psychological and social factors across countries with advanced economies and LDCs. In resource-rich countries, a higher prevalence of psychosocial predictors was evident, whereas more practical and biomedical aspects dominated the literature on LDCs (Bulsara et al., 2018). Common to both regions, however, was that no single factor or group of factors predicted difficulty with retention, but rather a complex interplay among and between factors was more likely.

11.2.2 Study 2

The second study (Chapter 4) provided a qualitative analysis of clinician and client perspectives of the barriers to retention. This study purposely had a more local focus, addressing issues in an urban Sydney setting. Once again, interacting factors, or comorbidity, were identified as a key barrier to retention, and suggested solutions included adequately identifying specific comorbidity profiles, as well as enhancing interdisciplinary care to address this (Bulsara et al., 2019b).

11.2.3 Study 3

The third study (Chapter 6) described the development of a brief, clinician-assessed screening tool of clinical complexity (comorbidity) specifically for PLHIV. The risk prediction algorithm that was developed provides clinicians with a useful adjunct to an otherwise qualitative assessment of clinical presentations, and allows for the unique perspective of a treating HIV specialist to understand comorbidity (Bulsara et al., 2019a). The tool, the Clinical Complexity Rating Scale for HIV (CCRS-HIV), provides a brief assessment of functional impairment across eight key variables – four physical health (PH) variables and four psychosocial (PSY) variables. The scale provides a weighted score for each variable, recognising the unequal impact of various factors, and a total score which can determine further intervention by the interdisciplinary team, as necessary (Bulsara et al., 2019a). These results pave the way for a further exploration of potential syndemic relationships.

11.2.4 Study 4

The fourth and final study (Chapter 8) reviews local and international definitions and measurements of retention and assesses the predictors of sub-optimal retention in Australia. Comparisons with Australian and WHO definitions of retention are made, and the characteristics of the 'target group' (those considered retained according to Australian definitions but not adhering to a schedule of visits determined by their HIV care provider, as recommended by the WHO) explored. The results indicated a large disparity between estimates (97% retained according to the Australian definition, and 56.7%, according to the WHO definition, adhering to a schedule of visits determined by their care provider). Those with clinician-identified psychosocial comorbidity alone were more likely to be compliant to the schedule of visits determined by their HIV specialist and, when compared to this group, those with no comorbidity and those with a complex interaction, or syndemic, of physical and psychosocial factors, were less likely to be retained (Bulsara et al., under review). More specifically, results suggested a synergistic interaction of problematic CMA use and social isolation in impacting retention. Retrospective research in this field has the capacity to examine the impact of routinely collected variables alone, often sociodemographic variables, with minimal opportunity for a standardised assessment of comorbidity. This study expands upon that literature to include an assessment of clinician-identified comorbidities.

11.3 Comorbidity, VL, and Retention in the present study series

The results from the present study series raise a number of issues. It is evident that poor retention was not associated with poorer biomedical outcomes (e.g. VL) in the fourth study (Chapter 8). However, as has been discussed, this can be considered an outdated metric of treatment success by itself. The present study series provides preliminary results supporting the assertion that the combination of physical health and psychosocial comorbidity has implications for retention outcomes, when considering retention as adherence to an individualised schedule of visits determined by a clinician, which has been suggested as more appropriate (HIV Outcomes Coalition, 2017). As discussed in section 9.1.2.1, the relationship between comorbidity and retention is likely bidirectional; comorbidity has the potential to impact retention, which in turn is necessary to monitor comorbidity. While not providing definitive evidence, the results certainly highlight the need for further research and for the discussion about retention guidelines to be revisited.

Of particular interest is the fact that the combination of physical and psychosocial comorbid factors were indicative of sub-optimal retention to such a degree that they 'overpowered' psychosocial factors alone in the opposite direction. It stands to reason that an increased burden of illness can contribute to poor health outcomes. For example, comparable comorbid conditions have been considered to be more manageable as a result of their similarities (Morris et al., 2011), suggesting that those which are different might not be so easy to contend with. Likewise, the medication adherence literature

points to the complexity of pill regimens directly impacting medication adherence (Libby et al., 2013). These data, in the context of the present results, suggest the burden of physical on top of psychosocial comorbid factors was so great that it became excessive, over and above psychosocial comorbidity alone.

Comorbidity, by definition, requires the management of multiple treatment priorities. Acute illnesses require effective treatment of the primary condition as a matter of urgency; however, once this is achieved and the illness is considered chronic, clinicians can shift their focus to other secondary conditions. In the context of the present study series and the trajectory of HIV management, now the international sector has largely achieved biomedical management of the virus, it is time its focus turns to the other related comorbidities which are implicated and should not be ignored while the search for a curative treatment continues. A contemporary example is the Diabetes Mellitus literature, which has long recognised that just focussing on blood glucose levels, in isolation of other relevant factors, is short-sighted and likely to compromise health outcomes. Current guidelines in this field recommend a thorough assessment and monitoring of all related medical and psychosocial factors (American Diabetes Association, 2018), as a means of ensuring that barriers to adherence are detected and can be addressed before complications (which in the case of insulin-dependent diabetes can include blindness, skin ulceration and peripheral neuropathy) arise.

Understanding comorbidity is especially relevant in the context of an ageing cohort of PLHIV, which the sector is facing for the first time. As the average age of the population of PLHIV increases, so too does the potential for psychosocial and physical comorbidity including the potential impact of long-term ART use. If, in managing this cohort, we only account for physical factors and neglect to attend to the psychosocial, the potential to miss the interaction of the two and its impact on retention is significant. Again, this is not to suggest that services do not attend to psychosocial factors, but rather that we have reached the point where such factors need to be explicitly measured, monitored and reflected in reporting requirements; retention in care is the means by which we can achieve this, if it too is expanded.

In the final study of this series, sub-optimal retention (i.e. not adhering to schedule of visits determined by an HIV specialist) was significantly associated with having a detectable VL during the study period, albeit with very low numbers given the vast majority (93.4%) of participants maintained an UDVL during the period of study. This finding supports other research which has noted an association between missed clinic visits (as a measure of retention in care) and medical outcomes such as VL (Zinski et al., 2015). This attests to advances in ART efficacy and tolerability (and by extension, adherence). However, it does also suggest that, although medical endpoints remain on track at present, there is an association between retention and VL which should be monitored. Indeed, given only 6.6% of participants in this study had a detectable VL, from

a traditional biomedical perspective it can be argued that neither retention nor comorbidity impacted VL in the present series. This association has been noted in previous research, however, especially the impact of physical comorbidity on the likelihood of having a detectable VL (Syed et al., 2016), and the role of psychosocial factors, such as mental illness and substance use, on medication adherence (Blashill et al., 2015; Robinson et al., 2016; Yehia et al., 2015a); it therefore warrants attention.

While sustained viral suppression remains the cornerstone of treatment success, we have moved beyond the point where it is the *only* marker of success, and understanding and attending to the factors which underpin it is necessary to provide optimal care. As service providers there are two options: to react to these factors when we see a rise in VL, or try to identify risk factors proactively and provide necessary structures and supports as early as possible. In the interest of adopting proactive, versus reactive, clinical monitoring and treatment, vigilance of relevant comorbidities is warranted to provide optimal care. Thus, despite the results in the present series which do not point to detrimental medical outcomes *at this point*, it is argued that this does not represent optimal care as it does not account for all factors, and neglects to recognise that such variables could become increasingly problematic over time especially as clients age, meaning that although clients remain alive much longer, we have limited information regarding how *well* they are living. This is in keeping with other literature suggesting the importance of monitoring *'health-related quality of life'* (Lazarus et al., 2016).

A consideration of the difference between population and individual health needs is also warranted. Delivery of services in the context of population health needs may have been appropriate in the early days of the epidemic, and certainly have a place in the current landscape; however, best practice would likely suggest delivery of services on the basis of assessed individualised need. A contemporary example is mental health services; while such service delivery is guided by population health principles and trends, individualised assessments and treatment plans determine the course of interventions. This currently applies to HIV service delivery in practice, although is not reflected in reporting requirements and metrics for treatment 'success'.

In this context, a more appropriate definition of retention to encompass the capacity to monitor all comorbidity might be *"attendance as recommended"*. This would likely see a decrease in estimates of retention in Australia, and therefore may be unpopular; however, it is important the figures accurately represent frontline clinical experience, in order to allocate funding and resources accordingly. A change such as this would augment support for services who see increasingly complex clinical presentations and are often not resourced adequately to provide optimal care to this vulnerable cohort. Perhaps more importantly, it would also signal the importance of holistic care reporting, which ultimately lends support to (a) recognition that this constitutes optimal care for PLHIV, (b) the value of individualised specialist assessment which accounts for biopsychosocial variables, and (c) the possibility of future changes in guidelines to explicitly include health-

related QoL as a measurable outcome of HIV treatment success. In an era when psychosocial comorbidity is recognised and treated, it seems appropriate that this now translates into meaningful policy change.

11.4 Current results in the context of theoretical models

The theories described in Chapter 1 which are relevant to the study series must now be considered again, in light of the current findings.

11.4.1 HIV and the Biopsychosocial Model

The biopsychosocial approach to optimal healthcare (Engel, 1980) has a long history in the chronic disease literature, as clinicians and researchers alike have recognised the role of all factors in impacting disease progression in a range of illnesses such as chronic pain (Kamper et al., 2015), diabetes (Habtewold et al., 2016), and of course HIV (Miller et al., 2018). A thorough exploration of relevant biological, psychological and social factors which impact HIV is covered in Chapter 1 of this thesis, and a diagram of the model is provided in section 1.13.1.1; suffice to say, the role of all factors need to be considered when planning effective monitoring and intervention strategies.

Results from the present studies have indeed highlighted a range of factors from the biological, psychological and social domains which impact PLHIV in the context of

retention. The literature review presented in Chapter 2 highlighted this is consistent globally, although specific differences are identified between countries with advanced economies and LDCs. Likewise, in Chapter 4 it is evident that clinicians and clients locally identify the same; that a combination of biopsychosocial factors not only impact PLHIV and their healthcare and well-being, but more specifically can interact to impact retention in care.

Chapter 6 showed the development of a complexity rating scale, highlighting again the combination of medical and/or psychosocial factors in contributing to complex clinical presentations. Finally, in Chapter 8, the role of these biopsychosocial comorbidities on retention in care was assessed.

11.4.2 Comorbidity and Syndemic Theory

Throughout the course of the study series, and corroborated by clinical experience, it has become apparent that rarely do factors present in isolation. Comorbidity is well documented in the chronic illness literature, and HIV is no exception. One way in which HIV might differ from other illnesses, however, is the trajectory of attention comorbidity has received. HIV itself is a relatively 'new' illness, with a timeline of approximately 35 years. For the first 20 years of the epidemic the primary focus of research and clinical interventions was to develop effective medication which could manage the virus' replication. While there was a recognition of the impact of HIV on other elements of a

person's life, this was not the focus, and there was little considered about the opposite direction; that is, the impact of psychosocial aspects on HIV medical management.

Advances in ART have allowed a more holistic view of HIV to flourish. There is increased recognition of the role of psychosocial factors, not only as consequences of HIV-infection but also as something which can influence HIV disease progression. In fact, a combination of biological, social and psychological (and sometimes cultural, contextual, and economic) factors are often both the cause and consequence of HIV disease progression.

Singer, in the 1990's, coined the term 'syndemic' to describe the synergistic impact of multiple factors which, when taken together, increase health disparities and poor health outcomes (Singer, 1994). In the context of comorbidity, it is not simply the additive effect of multiple co-occurring illnesses, but rather their interactive (synergistic) effect on the outcome; the syndemic model is provided in section 1.13.2.1. A thorough understanding of syndemics is critical, as syndemics typically reduce treatment efficacy and increase treatment costs (Singer et al., 2017). One focus of the present study series was to ascertain whether any such syndemic is present in this cohort, and to assess its impact on retention in care.

The Clinical Complexity Rating Scale for HIV (CCRS-HIV), developed in Chapter 6, lends itself to the theory of syndemics given it does not assume equal weighting of variables. In

addition, the results highlighted in Chapter 8 highlight the role of syndemic theory in retention in care. These findings point to a synergistic and complex interaction of physical and psychosocial factors which impact retention. The specific 2x2 variable interaction analyses failed to identify which physical health factor was relevant, suggesting that the appropriate syndemic consists of a 3x3 or greater interaction. Unfortunately, due to low cell numbers and power, 3x3 interactions were not possible. What this suggests however is that a likely alternative would be:

[PH variable][problematic CMA use]*[social isolation]*

This might in fact account for the PH*PSY complexity domain interaction, or syndemic.

11.4.3 Retention in care and The Andersen Behavioral Model of Health Service Use

The interacting roles of individual and contextual demographic variables, service factors, and comorbid factors, and their impact on service use, were outlined in the ABM (Andersen, 1995; Andersen et al., 2014). This model (shown in section 1.13.3.1) has also been used in previous studies to conceptualise individual and contextual factors which specifically impact retention in HIV care and ART adherence (Holtzman et al., 2015). Understanding the often-bidirectional effects of variables is particularly pertinent to the present study series, especially in the context of the Biopsychosocial Model and Syndemic theory.

The results outlined in Chapter 2 showed that, globally, a range of individual comorbidities as well as service-specific and demographic factors, impacted retention in HIV care. While differences were identified between resource-rich countries and LDCs, a complex interplay of factors was often identified. Likewise, in Chapter 4, these results were supported within a local context as clinicians and clients identified a number of these factors which interact to impact retention. Section 5.1.2 showed the specific results from this study mapped onto the ABM. Interestingly, the variables identified in the CCRS-HIV (Chapter 6) did not include demographic or service-specific factors, so do not exactly replicate this Model; however, this is largely because the screening tool specifically focused on individual comorbid factors. It could be argued, therefore, that this screening tool provides an assessment of one component of the ABM, 'individual characteristics'. Chapter 8 extended this slightly by including basic demographic variables of age and sex, however a more comprehensive test of this model was beyond the scope of this study series.

11.5 Strengths of the study series

There are a number of strengths of the study series. First, this thesis challenges the status quo. It is tempting to wholly accept current definitions of retention, which boast impressive estimates as a result. On the world stage, Australia seems to be leading the way in achieving global UNAIDS 90-90-90 targets. While not detracting from the very clear gains Australia has made in fighting the HIV epidemic, these data suggest we can do

better. This should be the goal of all clinicians and researchers; not to stagnate when the numbers appear to exceed expectations, but to question methodologies, processes, and policies in an attempt to find the gaps and plug modifiable holes.

The present results suggest, in fact, we have some way to go before we are truly achieving those targets. One such disparity is the lack of any well-being or QoL inclusion in guidelines, policies and reporting requirements, as recommended by some authors (e.g. Lazarus et al., 2016). Recognising these gaps is also imperative to ensure resources are allocated appropriately. Publicly funded services are increasingly at capacity, treating highly complex and vulnerable clinical presentations which both impact HIV disease progression, and are as a result of the same. The three experimental studies described herein access the same cohort, and thus results are comparable across studies. Albion is the largest HIV-specific publicly funded clinic in Australia, and therefore can be considered to be representative. Its model of interdisciplinary care has also been replicated across the Asia-Pacific region.

The present study series also translates research to clinical practice. As discussed in Chapter 10, the development of the Clinical Complexity Rating Scale for HIV (CCRS-HIV; Chapter 6) has led to workable changes in clinical practice to improve recognition of and response to complex clinical presentations characterised by comorbidity. Significant

changes in the way comorbidities are identified (with ongoing and new clients), as well as a coordinated and collaborative interdisciplinary team approach to developing and implementing appropriate care plans as a result, have anecdotally improved client care and outcomes at Albion. It is, as yet, too early to empirically evaluate these outcomes. While there is limited capacity with existing electronic systems to provide alerts when clients do not attend, the integration of the screening tool into routine clinical practice allows for more comprehensive follow-up for those who are not optimally retained.

The integration of the CCRS-HIV onto the Statewide electronic medical record (eMR) has also allowed for significant dissemination of the validated screening tool. This allows for the tool to be accessible by other services, across NSW, with similar cohorts. In addition, as discussed in Chapter 10, services in other States in Australia have also become aware of the screening tool, as a result of conference presentations, and have requested access to it.

The results described here provide a local perspective on the aspects that inform retention in care, in a landscape dominated by international research. This might partly be as a result of such high estimates of retention in Australia which, at 95%, do not invite research or improvement. However, as has been demonstrated by the results outlined in

Chapter 8, these estimates warrant further attention and review, in light of the discrepancies highlighted.

The present research series extends previous research in a number of ways. While recognition of the role of psychosocial factors is growing, their impact on HIV-disease progression remains under-evaluated. The international HIV sector has, in so many ways, been one of the most progressive in the context of chronic illness. Yet one key area the sector lags is in its continued focus on the biomedical metrics of success alone. While achieving and maintaining an UDVL is central to longevity and eventually eliminating HIV-transmission, it is short-sighted to consider this the only worthwhile measure of success. As described in the research series, there is a risk that complex comorbid presentations (many of which are modifiable) might potentially negatively impact VL outcomes (Blashill et al., 2015; Robinson et al., 2016; Syed et al., 2016; Yehia et al., 2015a). Current Australian standards, which suggest only the most basic monitoring (VL testing once a year), suit stable and high functioning clients. As a result, estimates are potentially inflated, QoL and well-being are not measured, and funding is funnelled elsewhere. In practice, complex, vulnerable, marginalised clients who attend publicly funded clinics are not reliably accessing care as they should, as recommended by their care provider. The assessments made by experienced clinicians in the public health workforce, often in collaboration with allied health colleagues, must not be discounted.

To illustrate this point, consider this example. If a specialist provider recommends a client returns in 2-months for review, there is likely to be a rationale behind that. It might be to follow-up with the client regarding their psychiatry referral; it might be to conduct additional lipid tests; it might even be to revisit drug and alcohol rehabilitation options. Regardless of the reason, if clinicians are employed to make those assessments, they must be heard. The client who fails to return for their 2-month appointment to review rehab/lipids/psychiatry is technically not counted as poorly retained, as they will likely return within the 12-months; this does not, however, mean they are accessing or receiving optimal care to address all concerns. It also means clinics who allocate staff hours to assertive follow-up strategies are not funded for these activities; on paper, of course, it appears as though 95% are retained, and therefore this extra funding would not be warranted. It is worth considering, therefore, whether reconceptualising retention as 'optimal service delivery' is warranted.

Clinicians have a duty of care to provide the best treatment possible for clients. This alone should be enough to warrant review of the current status quo. These biopsychosocial factors identified here are likely to, at some point, impact HIV disease progression. In addition, many of the factors implicated can be modified if appropriately assessed, monitored and treated. Even from a purely financial perspective, current guidelines are short-sighted and likely to cost more long-term.

It is hoped that the present study series at least opens this discussion. It by no means provides conclusive evidence, but hopefully provides a signpost to the gaps in care for PLHIV with complex clinical presentations, and some direction regarding future potential research.

11.6 Limitations of the study series

The research series is not without its limitations. Specific limitations of individual studies are discussed in the respective chapters, however overall limitations should also be noted.

One key variable missing from the research conducted herein, especially in Chapter 6 and Chapter 8, is stigma; this is not because its role is not recognised. When developing a clinician-assessed screening tool, the variables included had to be those which clients routinely discuss with their care providers, or which are known and obvious. Unfortunately, despite the important role of stigma in retention, it might not be discussed explicitly with care providers. For this reason, and because this made accurate assessment of the variable impossible, it was excluded. This of course means it was also excluded from the final study. In addition, despite this research advocating for explicit measurement of QoL, this has not been achieved here. Interestingly, the two concepts are inextricably linked, with studies suggesting that measurement of stigma and/or discrimination in PLHIV is inherent in the measurement of health-related QoL (Zeluf-Andersson et al., 2019b).

Unfortunately this was a key limitation of the retrospective study design in the fourth study, however would be an important inclusion in any future prospective studies.

This issue raises another limitation, that of clinician assessment. While precedents exist, especially in assessing complexity, accurate clinician assessment is reliant on open and frank dialogue between clinicians and clients. This might be especially problematic for stigmatising factors such as substance use. However, the clinician-assessed screening tool was designed to quantify current best practice; experienced clinician assessment. As discussed in Chapter 7, prospective research was originally planned to assess the impact of comorbidity on retention, but was unfortunately unsuccessful for reasons described elsewhere. This must be recognised as a significant limitation of the research series, as retrospective research is limited to routinely collected variables.

While recruitment from one site can be considered a strength of the research in the context of comparison and flow between studies, it can also be viewed as a limitation. While broadly representative of the majority of PLHIV living in Sydney, it cannot be said that the results generalise to all PLHIV or HIV services. The current study series was conducted using an urban sample in a relatively well-resourced setting. The service capacity of urban vs rural settings is likely very different, as is the client profile; therefore, the results may not be generalisable. In the context of a less resourced setting, a more medical definition of retention may be much more appropriate and better reflect the priorities of the service. Therefore, results should only be extrapolated to other urban,

well-resourced settings, and recommendations should be modified accordingly. However, this highlights a significant area for improvement in well-resourced urban HIV clinics, ultimately driven by policy directives and funding allocation.

11.7 Practice priorities and future research

This study series has identified a number of potential future research and practice priorities, to expand upon the results described here.

11.7.1 Retention in the Cascade

The present research has developed our understanding of retention, how it is defined, and the barriers to achieving this. Several authors have suggested a simplification of the Cascade, in line with UNAIDS 90-90-90 targets (Drew et al., 2017; Lourenço et al., 2015), which include abandoning retention in care definitions and estimates all together; this seems largely related to the inconsistencies which abound. However, it seems that of all the stages outlined in the Cascade, retention in care is the most relevant to monitor the medical and/or psychosocial comorbidity which increasingly contributes to poor health outcomes in PLHIV and may interact to increase health disparities (Singer, 1994). Therefore, enhancing our understanding of retention appears more appropriate, to develop clear and consistent definitions of retention in line with holistic care goals, its antecedents, and data collection approaches; this will ensure optimal clinical care, as HIV specialists do not only review VL results but also monitor other psychosocial factors, such

as mental illness, well-being, and QoL. In keeping with Lazarus and colleagues' suggestion of expanding the Cascade and global targets, recognition of the role of well-being or *'health-related quality of* life' is warranted (Lazarus et al., 2016). If retention is removed from the cascade, it paves the way to de-value regular monitoring of comorbidities which could lead to poorer health outcomes overall, including HIV-specific biomedical outcomes such as viraemia. It is likely that the majority will continue to function well in the face of comorbidity, but for the complex few for whom interventions should be targeted, by not holding onto retention there is scope and opportunity for clinical deterioration across biological, social and psychological domains; this is avoidable.

11.7.2 Expanding definitions of retention

Instead of removing retention, a more sensible long-term plan would be to increase the attention on this area of the Cascade. If definitions were modified to capture those who are not adhering to a recommended schedule of visits (on the basis of an individualised specialist assessment), more accurate estimates of retention would highlight the gaps in the system; that is, expanding the WHO definition to consider a definition of retention such as *"attendance as recommended"*. Indeed, individualised assessment is highly regarded, with some authors recently noting that *"good medical practice exists at the intersection of general observation with individual experience"* (The Lancet Psychiatry, 2019, p. 713). The HIV sector could take its cue from the Mental Health sector, which has long recognised the value in individualised assessment and treatment plans, rather than reporting treatment outcomes the basis of population health trends. Awareness of these

disparities, rather than overlooking them, will then allow for improvements in best practice holistic care. This would require resources and might involve provisions for improved IT systems which can alert when clients do not attend as recommended, or increased case management positions to provide active and assertive follow-up outside the clinic for those who require it.

Broadening the definitions of retention away from the purely biomedicalised model would therefore provide an innovative means of addressing the issues described here with complex clinical presentations, including the need for an increased focus on well-being and QoL. This would include expanding guidelines and policy directives which currently favour testing and prevention strategies, arguably at the expense of support to assist people to live well with HIV.

11.7.3 Recognising the role of comorbidity

Inherent in this expansion of retention definitions would be an explicit focus on identifying, managing, and treating modifiable comorbidities within an interdisciplinary framework. This recognises the role of complex clinical presentations and their impact on overall well-being and QoL, long-term cost to the health service, and HIV disease progression. In an era where 'Ending HIV' is the goal and the focus is on prevention and testing, there must be an acknowledgement that this cannot occur without providing optimal care for our existing PLHIV cohort and ensuring that no one is left behind. Tsai and colleagues highlighted the need for 'multicomponent interventions' to address syndemics

(Tsai et al., 2017). Expanding the existing syndemic research with greater power and identifying the potentially 'missing' PH variable of interest, would be an important first step.

The CCRS-HIV detailed in Chapter 6 is a promising start to the provision of early identification screening tools for complexity in HIV; however, it requires further development to ensure it can be a widely used screening tool for clinicians to identify risk factors for appointment and medication non-compliance, as well as identifying aspects of the presentation which warrant intervention and referral. This screening tool should be validated with broader populations (e.g. in less resourced settings) and improved in terms of correlating clinician and client responses.

11.7.4 Moving beyond viral suppression for optimal holistic care

The results of this research support previous studies and policy recommendations which have called for an expansion of clinical outcomes *"beyond viral suppression" (*Guaraldi et al., 2019*;* Lazarus et al., 2016*)*. The HIV sector has achieved so much in 35 years, and rather than be complacent, now is the time for us to hone the response further. Comorbidity impacts medical outcomes such as VL, but also more broadly affects QoL (Zeluf-Andersson et al., 2019a); QoL in turn feeds back to impact medical outcomes such as medication adherence and VL (International HIV/AIDS Alliance, 2018). These concepts are inextricably linked, and to separate them, as current guidelines do, and only focus on one outcome

such as VL misses the point of holistic care, which has always been central to HIV service delivery.

Expanding our concept of outcomes and metrics for success necessitates an overhaul of how QoL and the comorbidity factors which influence it are measured, monitored and treated. Retention in care is an existing means by which this can be achieved, if its definitions are also expanded. The HIV Outcomes Coalition recommends individualised care plans and the involvement of the interdisciplinary team for optimal service delivery (HIV Outcomes Coalition, 2017); retention is also necessary to monitor the efficacy of these interventions. In doing this and recognising the importance of biopsychosocial comorbidity, not just in clinical practice but also in policies and reporting requirements, the sector has the capacity to move beyond viral suppression.

11.7.5 Reviewing State and Federal public health HIV strategies within Australia

To update how retention is viewed and defined requires an overhaul of existing State and Federal public health policies and guidelines, and a commitment from policy makers to make this a priority. State and Federal governments have a responsibility in the way they communicate strategic priorities. The current NSW Health HIV strategy speaks minimally about support and care for the existing PLHIV cohort, when in fact this should be front and centre and should be broader to encompass well-being and QoL as an explicit metric of

success – living well with HIV (Lazarus et al., 2016). Leading the way in HIV policy and research is not necessarily having achieved targets, but rather recognising and addressing the gaps in our system.

11.7.6 Future research

There are a number of directions for future research which have been highlighted by the present series. First, further development of the CCRS-HIV would be necessary to address the gaps with this study, including the need for greater objectivity, validation with broader cohorts, and perhaps correlating clinician and client assessments. It would also be ideal to incorporate an assessment of stigma and how this might impact retention, as this is a gap in the present findings. Explicit measurement of QoL and functioning is also important here. Some authors have discussed the role of client self-report in assessing factors such as QoL (Kall et al., 2019). One possibility would be to include client ratings using the PozQol questionnaire in future research, an Australian brief self-report questionnaire validated to assess QoL, including perceived stigma, among PLHIV (Brown et al., 2018). This would serve to explicitly assess well-being/QoL among this cohort and monitor any potential impact on retention. In addition, correlating these reports with client-assessment on the CCRS-HIV would potentially serve to provide a thorough assessment of comorbidity, including QoL and stigma and/or discrimination.

This is only possible in the context of prospective research designs, a second potential area for future research, as discussed in the context of the fourth study. Even the most complex and poorly retained clients usually attend a service at some point. It would be ideal to try and 'capture' their attendance when they do present, as this may be 'ad hoc' and outside the boundaries of scheduled appointments.

If this is not feasible, a further possibility is to change some of the parameters of the fourth study to only target those identified as the most complex within a service (i.e. those who score in the 'medium' and 'high' brackets on the CCRS-HIV) and track their retention. The present results were skewed by the large proportion of clients without problematic comorbidities; while this is encouraging from the perspective of population health and well-being, focussing on those with more complex presentations might yield more useful results regarding those who are most vulnerable.

11.8 Conclusion

We have come a long way since 1981, but now is not the time to be complacent. Seemingly outstanding Australian Cascade estimates should not be a signal for the sector to abandon the pursuit of innovation and improvement. We must move from service delivery appropriate to population health needs, to service delivery appropriate for

individual needs. The public health response to an evolving epidemic must progress, and requires original approaches to achieve this.

There are a number of areas yet to improve in the management of HIV and its associated medical and/or psychosocial comorbidity. Early identification of, response to, and treatment of modifiable comorbidities which have the potential to impact not only the trajectory of HIV disease progression, but also overall well-being and QoL, are imperative. The results in the present study series have demonstrated it is possible to monitor these comorbidities among PLHIV; the next step is to specifically equate these to QoL.

To optimally support the PLHIV community, a broader definition of 'success' is required to ensure best-practice holistic healthcare delivery. Retention in care provides an existing pathway by which clinicians can monitor and review comorbid and complex presentations, and instead of abolishing it, these data suggest it should be expanded. The results described here have highlighted the inadequacy of current retention in care definitions in Australia, and how this limits our capacity to monitor clients based on an individual assessment of holistic needs.

Policies and guidelines which inform resource allocation should 'plan for the worst, and hope the best', which they arguably currently fail to do. At present, definitions which drive

estimates favour stable and functioning clients, while potentially neglecting the more complex and vulnerable cohort. While these current results are cautiously optimistic in the context of current health outcomes for PLHIV, we require clinical services to prepare for a time when this might not be the case, especially with an ageing cohort of PLHIV; this is the essence of proactive and holistic optimal healthcare delivery.

The present study series provides promising results to open this discussion and set a path for future research to expand upon. State and Federal policy makers in Australia have a responsibility to review current research and practice guidelines to ensure best practice holistic management for PLHIV, to ensure no one is left behind.

11.9 Chapter 11 References

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