

BRIEF SIX

6. Tracking the next syndemic

**The relationship
between HIV and non-
communicable diseases**

Research briefs on non-communicable diseases in South Africa

Percept has developed a series of briefs aiming to explain, explore and quantify the burden of non-communicable diseases (NCDs) in South Africa. Throughout the briefs, both existing quantitative data as well as emerging qualitative data are drawn together. The primary qualitative data – presented in the form of vignettes – was collected by Dr. Beth Vale through in-depth ethnographic research, which was gathered in a community in the Karoo. Given the rising global burden of NCDs, particularly in low- and middle-income countries (LMICs) these briefs are incredibly relevant. They also present important insights as Covid-19 continues to attack those with pre-existing conditions more fatally.

Given South Africa's high prevalence of HIV, there's also recently been a focus on the link between HIV and NCDs, especially since the population living with HIV grows increasingly older with the successful uptake of ART. As we'll explain in the briefs, an ageing population is more at risk for NCDs. Moving towards universal health coverage (UHC), it's imperative to understand the current needs of our population – and how these may change going forward.

Percept is grateful for the generous funding provided by the following three partners. The views presented are however the authors' own.

- + Actuarial Society of South Africa (ASSA): ASSA has an interest in being part of the development of high-quality evidence to support resource allocation and decision-making, and the interplay between the supply and demand sides of the health system.
- + RGA Reinsurance Company of South Africa Ltd (RGA): RGA has an interest in the ways in which life insurance can be responsive to the changing burden of disease, and the ways in which we can use data to drive decision-making.
- + Board of Healthcare Funders (BHF): BHF is a regional representative body of health funders, administrators, and managed-care organisations. It is committed to universal health coverage, value-based healthcare, and accountability for health. Addressing the NCD burden is an important element to achieve some of its objectives.

Take-home messages

- + Due to the lifesaving effects of antiretroviral therapy (ART), the human immunodeficiency virus (HIV) infection has gone from being a death sentence to a manageable chronic illness. The life-prolonging effects of ART mean that people living with HIV (PLWHIV) are living longer and therefore developing non-communicable diseases of old age.
- + Although ART allows PLWHIV to live longer, it doesn't completely restore their health. Prolonged exposure to ART is also associated with the development of NCDs and NCD risk factors such as hypertension, obesity, insulin resistance, diabetes, and high cholesterol.
- + The HI virus itself is also associated with the development of NCDs by causing premature ageing and making one more susceptible to cancer-causing viruses due to a weakened immune system. Despite the side effects of ART, PLWHIV who are adherent to ART are less likely to develop these "AIDS-defining cancers" compared to those who are not adherent. Therefore, ART adherence is still a crucial part of managing multimorbidity in PLWHIV.
- + Although there are biological factors that cause multimorbidity in PLWHIV, there are also social factors that impact treatment adherence. Therefore, the HIV and NCD epidemics are considered a "synergistic epidemic" or "syndemic," because biological and social factors associated with these diseases reinforce each other causing them to co-occur.
- + The social factors which impact treatment adherence include poverty, rurality, gender, stigma, and mental health. Since these factors impact treatment adherence, they also influence the likelihood of PLWHIV developing NCDs. Therefore, policies that aim to reduce the multimorbidity of HIV and NCDs should not only address the biological determinants of these diseases, but also their social determinants.

Introduction

The early story of HIV infection was that it was a death sentence. An HIV-infected person would eventually develop acquired immune-deficiency syndrome (AIDS) and their life would be cut short. Combination antiretroviral therapy (ART) has managed to improve the health of people living with HIV (PLWHIV), extend their lives, and substantially reduce the risk of transmission. This has increased the life expectancy of PLWHIV, and those that enroll and adhere to treatment have a life expectancy not much shorter than people without HIV.¹ Furthermore, early initiation and adherence to treatment can suppress the viral load to an undetectable level so that an HIV-infected person will not be able to transmit the virus, thereby reducing the incidence (new infections) of HIV.² It's called "treatment as prevention" (TasP), because PLWHIV remaining in care and on treatment prevents new cases.³

South Africa has one of the highest rates of adult HIV prevalence in the world (20.4%), and the highest number of PLWHIV in the world (7.7 million people).⁴ The country follows the test-and-treat policy of the World Health Organization (WHO),⁵ which means that as soon as someone tests positive for HIV, they are initiated on treatment. This further improves life expectancy, decreases HIV-related morbidity, and reduces the incidence of HIV in the general population.

Despite these policies, HIV is still one pillar of South Africa's quadruple burden of disease. This refers to the burden of HIV; NCDs; maternal, new-born and child-health-related incidents; and a high prevalence of injuries from accidents and interpersonal violence⁶. It should be noted though that these four disease burdens are not mutually exclusive. From an infectious disease perspective, the epidemiology and comorbidity of HIV and TB are well documented and widely understood, and South Africa is considered the epicentre of the HIV-TB co-epidemic.⁷ However, concurrent to this co-epidemic, another has emerged – that of HIV and NCDs. The drivers of the multimorbidity of HIV and NCDs are multifaceted, and this brief aims to estimate the prevalence of the comorbidity of HIV and NCDs, unpack how this multimorbidity has come to be, examine how it manifests itself in the South African context, and understand what the implications are for the South African (SA) healthcare system.

Data and methods

Two broad quantitative data sets were used: household survey data and medical scheme data. Survey data includes General Household Survey (GHS) data, Demographic and Health Surveys (DHS) data and National Income Dynamics Study (NiDS) data. When analysing the quantitative datasets for comparison against one another, we standardised them based on age and sex, given the relationship between age and NCDs (see brief 2), and sex and NCDs (see brief 3). This standardisation was done against the 2018 Statistics South Africa (Stats SA) mid-year population estimates for all datasets to achieve fair comparison.

We also use qualitative data in this brief, based on primary data collection in one pocket of South Africa, to marry the quantitative findings to the reality on the ground.

What drives the multimorbidity of HIV and NCDs?

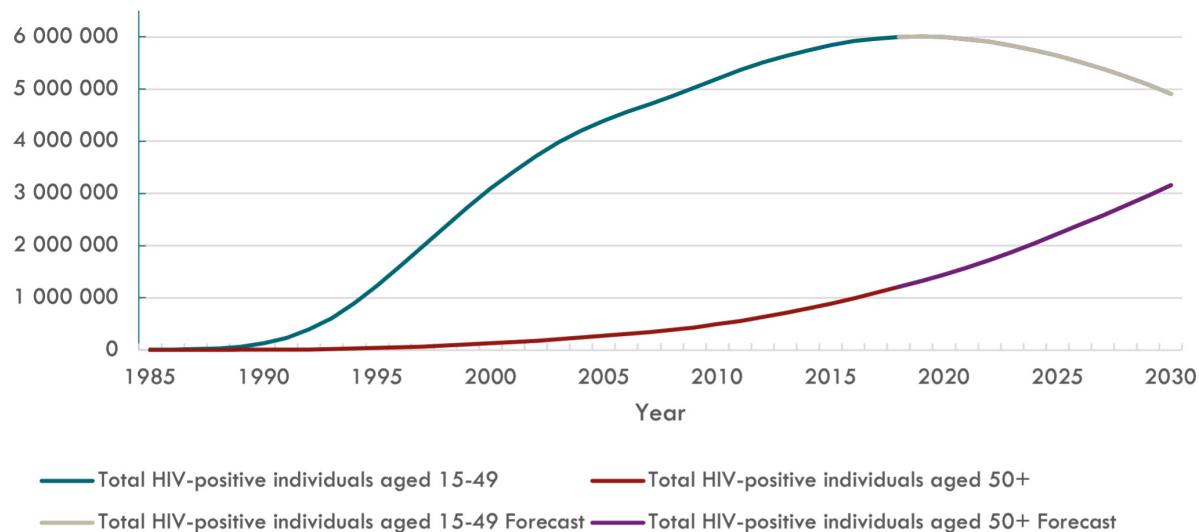
Multimorbidity refers to the presence of one or more diseases at the same time. Due to the life-extending effects of ART and the side-effects of its prolonged use, ART users often end up with multiple illnesses that require treatment in addition to HIV itself in the long term.¹ This may affect the healthy ageing of PLWHIV. We discuss four channels through which NCDs develop in PLWHIV. The first two are linked to ART, through the life-prolonging effects of ART and the side-effects and cumulative toxicity caused by prolonged ART use. The third and fourth relate to HIV infection itself. HIV infection has been linked to premature ageing and increases the likelihood of developing certain types of cancer.

The effects of ART: ART extends life

The public roll-out of ART in South Africa began in earnest in 2004. Since then, all AIDS-related deaths have been a quarter of what they were at their peak in 2006⁸, and the life expectancy of PLWHIV who adhere to treatment has increased to a level comparable to those without HIV.¹ But those ageing with HIV are often neglected: the life-extending effects of ART mean that the number of stable and adherent people over 50 with HIV is increasing.⁹ Although the vast majority of PLWHIV are in the 15 to 49 age group, this number is predicted to have peaked in the South African population and in future years, the fastest-growing population with HIV will be those over 50 (Figure 1). The life-prolonging effects of ART also have an impact on South Africa's population pyramid, moving the country away from the bottom-heavy pyramid it has previously had. It's therefore important to analyse and forecast the implications of this for population health and resource allocation, particularly as the country contemplates universal health coverage (UHC).

ART enables PLWHIV to live for longer. This means that, like people without HIV, they become prone to developing the diseases of old age, and are therefore likely candidates for multimorbidity.

Figure 1: HIV prevalence by age group in South Africa (Johnson 2017)¹⁰



NCDs are considered the most important health issue for those older than 60, and the ageing population with HIV are not protected from this NCD “pandemic^a”.⁹ NCDs cause 55% of premature mortality (deaths occurring before the age of 70) in South Africa.^{11,12}

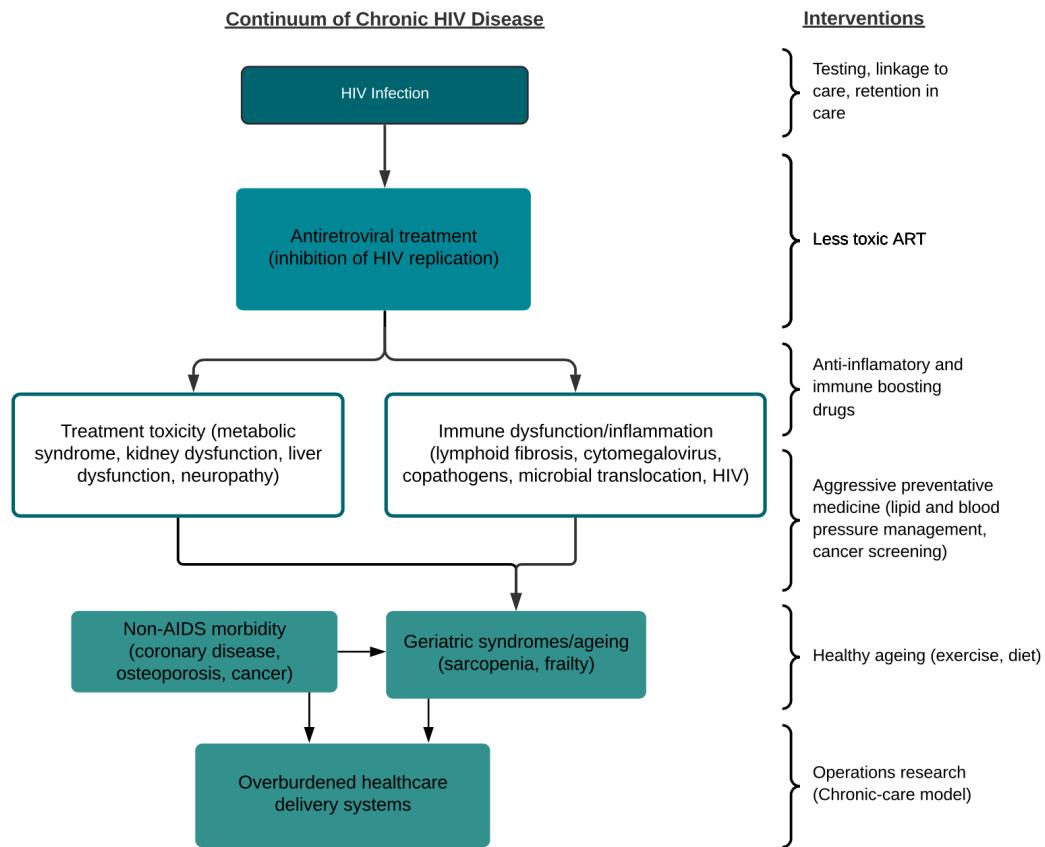
As is the case for those without HIV, older people with HIV tend to have a higher prevalence of NCDs like diabetes, hypertension, chronic lung disease, and cancer.¹³ Therefore, as ART extends people’s lifespan, it also exposes them to diseases of old age, making PLWHIV likely candidates for multimorbidity.

The effects of ART: ART associated with development of NCDs and NCD-risk factors

When PLWHIV are adherent to ART, their viral loads are suppressed and they’re healthier and more resilient to secondary infections. However, ART doesn’t completely restore their health. Long-term exposure to ART can lead to cumulative drug toxicity, which can cause disorders of the metabolic system, and end-organ damage.^{1,14} In recent years, it’s become clear that the prolonged use of ART is associated with diseases that have no direct relationship with HIV infection (known as non-AIDS morbidities^b).¹⁵ These diseases include cardiovascular disease, liver disease and non-AIDS-defining cancers.¹⁵ Systematic reviews also confirmed that PLWHIV who were on ART had higher blood pressures and had an increased risk of developing hypertension compared to those who have never been on ART.¹⁶ Figure 2 below shows the continuum of how chronic disease may develop in PLWHIV and the interventions that may be implemented at each stage to treat or prevent the development of these illnesses. The last intervention suggested by Deeks et al. (2013) is operations research, which would help to inform the health system on how to treat and manage the ageing and multimorbid population living with HIV.¹

^a Whether or not NCDs meet the criteria for classification as pandemic is debated, since they are by definition noncommunicable. However, we choose to refer to them as pandemic here because in some cases, such as cervical cancer and NHL, they are transmitted via viral vector, but they are also transmitted through “societal vectors” such as social and economic conditions (see NCD and HIV as Syndemic section) and genetic predispositions.⁶¹ In addition to this, in line with the definition of a pandemic, NCDs are also increasing in prevalence worldwide, crossing international boundaries (some argue in part due to the socioeconomic effects of globalisation), and affect a large number of people.⁶²

Figure 2: HIV Infection and chronic disease (Deeks 2013)¹



A side-effect of long-term ART is HIV-associated fat redistribution syndrome or lipodystrophy syndrome.^{17,18} This is when PLWHIV develop abnormal or excessive amounts of fat, including visceral fat, in the trunk, upper back and neck. Fat redistribution syndromes resulting from long-term ART exposure are associated with many of the same NCD risks as metabolic syndrome, such as obesity (particularly fat accumulation around the waist), insulin resistance and diabetes, high blood pressure and high cholesterol.^{1,17,19} Vignette 1 describes the story of Sonette, who battles with HIV and hypertension.

Vignette 1: HIV and hypertension

In June 2019, I spent a day observing consultations at a small-town primary healthcare clinic in the Eastern Cape Karoo. One of our patients was a petite woman in her 50s, who'd come to enquire about a disability grant:

"What's wrong with you," the doctor asked. "There needs to be something wrong."

"I'm very sick," she answered.

^b AIDS-defining morbidities or illnesses are diseases which are more prevalent among HIV-positive people and may be an indication that they are in the more advanced stage of HIV infection called AIDS. Non-AIDS-defining morbidities are those that fall outside of this category.

The patient, who I'll call Sonette, was HIV-positive and on ARVs, but appeared otherwise healthy.

"But you're controlling your HIV well," the doctor said.

The patient was silent for a moment, while the doctor took her blood pressure. As the blood pressure monitor depressed, the doctor's expression switched from bemusement to one of deep concern:

"Do you get blood pressure pills?" she asked.

"No," the woman answered, matter-of-factly.

"This blood pressure is very high."

The diastolic reading was 130, far above the normal range (which would be below 80). The doctor grew agitated:

'I think you must go to hospital. I'm worried you're going to have a stroke.'

By this point, I'd seen many patients with co-morbid hypertension and HIV – one of the ways in which NCDs and infectious diseases collude. If unmanaged, the consequences of this collusion could be severe. In fact, in one municipal hospital ward, I'd even met a 44-year-old woman on antiretroviral treatment (ART) who'd suffered four debilitating strokes.

However, Sonette was in her 50s – a testament to the victories of South Africa's ART roll-out. One primary healthcare nurse suggested to me that when HIV-positive patients had multiple conditions, HIV was prioritised:

"When there is both HIV and hypertension, say, you focus on HIV. You almost forget about those other things."

Without thinking about the ways in which HIV might render patients more vulnerable to NCDs, patients like Sonette might fall through the cracks.

ART enables PLWHIV to live for longer. This means that, like people without HIV, they become prone to developing the diseases of old age, and are therefore likely candidates for multimorbidity.

As new generations of drugs are released, these toxic side effects of prolonged exposure to ARTs are becoming fewer.¹⁴ However, given that these drugs are taken for decades, even small levels of toxicity add up over time. Therefore, the treatment guidelines need to account for this, and the NCD risks of the drugs prescribed.¹ PLWHIV should be regularly screened for common NCDs. Their risk factors need to be managed and they should be counselled during interactions with healthcare providers.

Not all of the risks of developing non-AIDS morbidity can be fully attributed to ART toxicity.¹ Studies show that PLWHIV on ART have higher levels of several different types of inflammatory markers^c compared to individuals of a similar age who don't have HIV.¹ These inflammatory markers are associated with all-cause mortality, coronary artery inflammation and atherosclerosis.^{1,20}

It should however be noted that changes in highly active antiretroviral therapy (HAART) over the last decades have resulted in improvements in some of the side-effects of treatment.²¹ Results from a recent randomised trial of two new HIV drugs, dolutegravir and tenofovir alafenamide fumarate (TAF), have shown promising results compared to the standard of care.²² ART regimens that included dolutegravir were found to be as good as the standard of care, and regimens that included both TAF and dolutegravir combination were found to have less of an impact on bone density and renal function compared to the standard of care.²² However, regimens that included dolutegravir (with or without TAF) resulted in significantly more weight gain among women compared to the standard of care.²²

The effects of HIV infection: premature ageing

Given that many of the comorbidities associated with HIV infection are considered diseases of ageing, there is a debate about whether HIV infection causes premature ageing or simply makes the occurrences of these diseases more likely at any age.¹

Increased immune activation and long-term chronic inflammation are important contributors to the progression of ageing. Among patients with HIV, these processes are more prevalent and as a result, they're more prone to developing age-related illnesses, even when the infection is adequately controlled.²⁰

Another way in which premature ageing is understood is by measuring the "frailty" of PLWHIV.¹ There is no universal definition for frailty, but it's generally understood to be a vulnerability in ageing that makes one unable to perform the normal functions of daily living when faced with physical, social or emotional stress.^{15,23} Studies show that older PLWHIV are frailer than those who don't have HIV, due to the high prevalence of HIV-related co-morbidity, and this frailty is a predictor of morbidity and premature mortality among PLWHIV.^{15,23}

The effects of HIV infection: cancer

In high-income countries, cancer is a leading cause of death among people with HIV.²⁴ Cancers that affect PLWHIV are divided into AIDS-defining (ADC) and non-AIDS-defining cancers (NADC).²⁴ Kaposi sarcoma, non-Hodgkin's lymphoma (NHL) and cervical cancer are classified as ADC, while all other cancers that affect PLWHIV are classified as NADC^d

Although HIV doesn't directly cause cancer, it creates an immunosuppressed environment that enables malignancies caused by other viruses to develop.^{25,26} This is why ADCs are primarily caused by tumour viruses, such as the Epstein–Barr virus (EBV), which causes NHL, Kaposi's sarcoma herpesvirus (KSHV) that cause Kaposi sarcoma cancer (which was a very rare cancer before the HIV/AIDS pandemic, but its incidence has increased exponentially since), and the human papillomavirus (HPV), which causes

^c One explanation for the causal process of this increased immune activation and chronic inflammation is that macrophages are white blood cells that act as HIV reservoirs.²⁰ They exist in many of the tissues and organs associated with age-related comorbidities, such as fat, liver, bone, and brain tissue, as well as vascular walls.²⁰ If the infected macrophages (white blood cells) release cytokines that cause inflammation inside of these tissues, they may cause local inflammation and related comorbidities.²⁰

^d the prevalence of cancer in South Africa is explored in brief 7 of this series – titled "A deep dive into cancer".²⁴

cervical cancer.^{25,26} Despite the dichotomy between ADC and NADC, many NADC can be biologically and epidemiologically linked to HIV infection.²⁴ Silverberg et al. (2011) found that PLWHIV are at higher risk of developing melanoma, anal and liver cancer.²⁷ Both liver and anal cancer are known to be caused by viruses.²⁷

In line with the findings in more high-resource settings, PLWHIV in South Africa show an elevated risk of developing Kaposi sarcoma, NHL, and cervical cancer.²⁸ Of the NADCs, PLWHIV have an increased risk of developing conjunctival cancer and cancers associated with HPV infections such as penis and vulva cancer.²⁸ Adherence to ART and maintaining a high CD4 count has been shown to reduce the incidence of these AIDS- and non-AIDS-defining cancers, but the risk of developing them is still elevated among PLWHIV.^{24,27} This has implications for policy and resource-need forecasting.

Increased immune activation and long-term chronic inflammation, which are associated with premature ageing and increased frailty, are more prevalent among PLWHIV. HIV infection also creates an immunosuppressed environment which makes PLWHIV vulnerable to cancer-causing viruses. As a result, HIV infection itself can weaken the body in ways that make PLWHIV susceptible to developing NCDs.

The resultant multimorbidity in PLWHIV

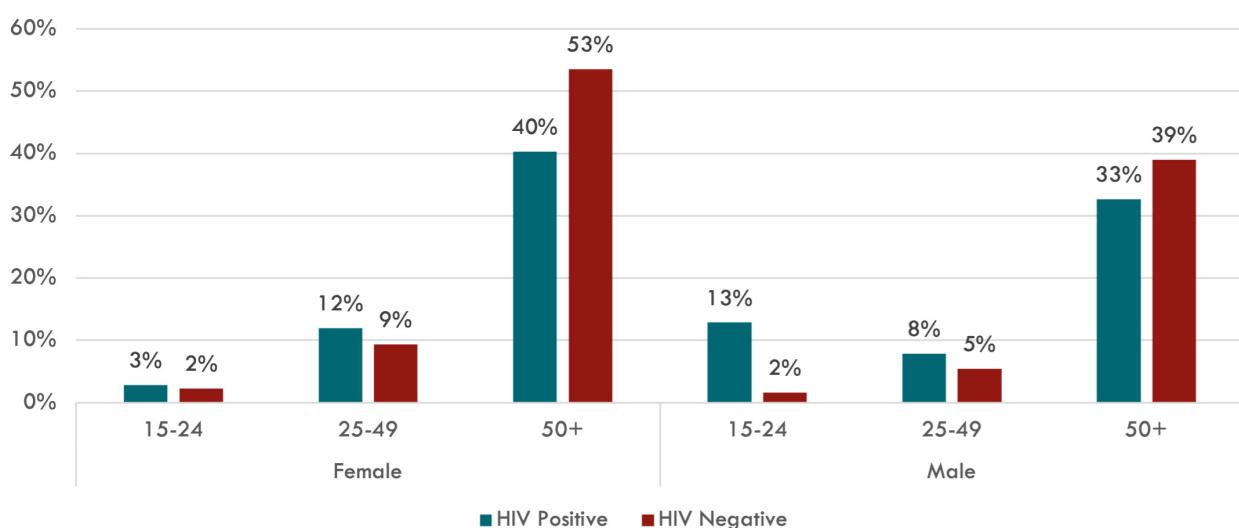
Studies indicate that the prevalence of the comorbidity of NCDs and HIV in South Africa is high, particularly in older age groups. Negin et al. (2012) estimate that 30% of PLWHIV that are 50 years and older have two or more chronic conditions. This finding is based on a nationally representative study.⁹ In a study of the prevalence of multimorbidity using data from a primary healthcare facility in the Western Cape, South Africa, Oni et al. (2015) found that 26% of PLWHIV aged 18 to 35 and 30% of PLWHIV aged 36 to 46 who were on ART reported having multimorbidity.^{3,29} Van Heerden et al. (2017) found that 80% of PLWHIV in their study had comorbid obesity, hyperglycaemia, hyperlipidemia or hypertension.³⁰

Using the South African Demographic Health Survey (SADHS) 2016 and the GHS 2018 – which are national representative datasets – we attempted to estimate the prevalence of the comorbidity of HIV with hypertension and diabetes, respectively. We used both objective and self-reported measures of disease, so each of these measures are likely to be underestimated, as not all participants would have consented to reveal their HIV status or being tested for the objective measurements of NCDs. As always with self-reported data, respondents could also inadvertently give false information because they may be unaware of their health status, or they might refuse to reveal this information. Where we discuss self-reported results, we also look at the likely biases and contexts influencing the results.

The graphs below use GHS and SADHS datasets to compare the self-reported prevalence of NCDs among PLWHIV with those who don't have HIV. These NCDs include hypertension, heart attack or heart problems, cancer, stroke, diabetes and asthma. In addition, the GHS also includes arthritis and mental illness. In Figure 3, the GHS data shows that NCDs are more prevalent among PLWHIV who are under the age of 50, compared to those who don't have HIV. For those over the age of 50, the

prevalence of NCDs is much higher in the non-HIV-positive population, although prevalence rates are very high for both groups compared to the younger population. This may be because PLWHIV who are older than 50 are on average younger than those in the same age cohort who don't have HIV. The prevalence of NCDs also appears to differ by gender. Among those 25 years of age and older, NCDs are more prevalent in women compared to men in both the HIV-negative and -positive populations. Given what we know about health-seeking behaviour in men^e, these differences by sex aren't necessarily a true reflection of the prevalence of NCDs among men (for example, NCDs may be less frequently diagnosed in men than in women).

Figure 3: Self-reported prevalence of any NCD in HIV-positive vs HIV-negative population (Statistics South Africa 2019)³¹

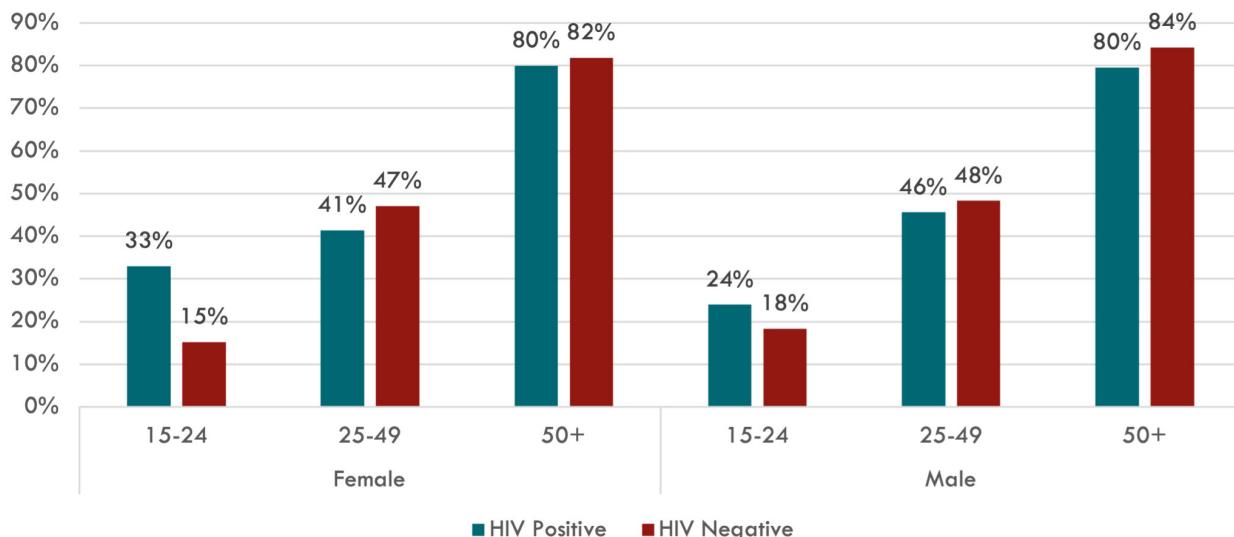


Hypertension, diabetes and HIV

The SADHS' objective measures of hypertension (Figure 4) show that PLWHIV between the ages of 15 and 24 have a higher prevalence of hypertension compared to their peers who don't have HIV, and this result is statistically significant. For all other age groups, PLWHIV have lower rates of hypertension compared to people without HIV.

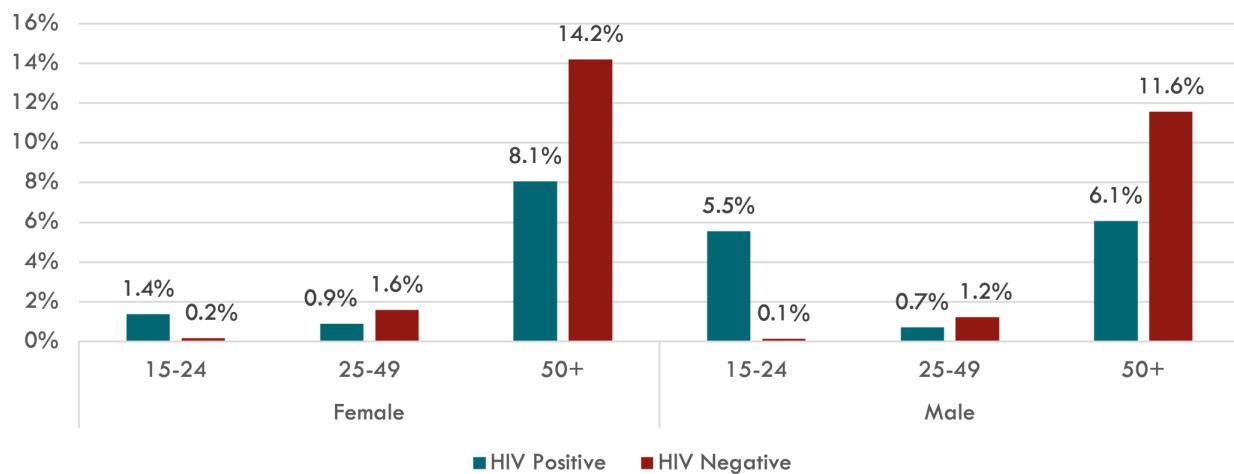
^e See brief 3 of this series – *Sex, gender and NCDs* – for more on the impact of gender on health-seeking behaviour.

Figure 4: Hypertension prevalence in HIV-positive vs HIV-negative population (SADHS 2016)³²



Self-reported estimates of diabetes from the GHS survey in Figure 5 show that the prevalence among PLWHIV under the age of 25 is much higher than that of HIV-negative people of the same age group – matching the findings from the objective measure in the graph above. Again, these prevalence rates are lower than those of HIV-negative people in older age groups, despite increasing with age.

Figure 5: Self-reported diabetes prevalence in HIV-positive vs HIV-negative population (GHS 2018)³³



The survey data appears, to an extent, to echo some of the findings of much of the literature. Much like people who don't have HIV, PLWHIV are developing more NCDs as they age. PLWHIV also seem to be developing these NCDs, such as hypertension and diabetes, at a younger age compared to HIV-negative people of the same age. However, if PLWHIV are developing NCDs sooner, this would translate into a higher prevalence of NCDs among older PLWHIV, (unless PLWHIV who develop NCDs early on are less likely to live to older ages than their counterparts who do not develop NCDs early on) which the survey data findings don't seem to show. These findings were tested using regression

analysis and no statistically significant relationship was identified between HIV and the likelihood of having hypertension, diabetes, or both.^f

This result may be explained by self-reporting bias, as survey respondents may not want to disclose, or may be unaware of, their health status. This would result in these prevalence estimates being underestimated. Furthermore, young PLWHIV may be in contact with the health system more often, and more likely to know about their comorbidities compared to those without HIV who have relatively little contact with the health system. This may also explain why the prevalence of NCDs among women is reportedly higher than that of men, as illustrated in Figure 3. Women, particularly those in their reproductive years, are more likely to have more contact with the health system and are therefore more likely to be aware of their health status compared to men. This is likely to hold for women living with HIV (WLHIV) as well.

NCDs and HIV as syndemic

Perhaps the most useful conceptual framework for considering how the NCD and HIV epidemics are related is to understand them as synergistic epidemics – or syndemic. The term was coined by Merrill Singer, a medical anthropologist, to describe “a closely interrelated complex of health and social crises”.³⁴ It speaks to the comorbidity of two or more diseases that mutually reinforce each other to negatively impact morbidity and the progression of each respective disease, but are also deleteriously affected by socio-economic inequalities.^{35,36} Syndemics specifically refer to both the biological interaction of these diseases in addition to how they are affected by the social, cultural, economic and physical environments in which people live.³⁵

In the previous sections, we described the biological mechanisms through which the HI virus itself, the treatment for HIV, and the lack of treatment adherence can cause or be associated with the development of NCDs. In this section, using the syndemic framework, we aim to describe the socio-economic factors which create these clusters of chronic illness and NCDs among PLWHIV.

Although ART is associated with certain NCD risk factors, adherence to ART and maintaining a healthy CD4 count is crucial for the prevention and management of the treatment of NCDs among PLWHIV. Therefore, when considering the socio-economic factors which give rise to the NCD-HIV syndemic, **it's necessary to understand which socio-economic factors affect access and adherence to HIV treatment.**

^f Logistic regressions were used to estimate the relationship between HIV and diabetes, hypertension, and the comorbidity of both diabetes and hypertension, using SADHS objective measures. Body mass index (BMI), gender, age, and socio-economic status (using a wealth index) were also controlled to more accurately estimate the association between HIV status and the likelihood of having hypertension, diabetes, or both. In addition to this, standard errors were adjusted to account for similarities between households.

Poverty and rurality

Studies analysing the barriers to ART adherence in South Africa identify that many of the primary impediments are related to poverty. Poverty is associated with food insecurity, which is one of the most important barriers to ART adherence.^{37,38} Food insecurity, which leads to poor nutrition, not only impacts adherence, but also treatment efficacy.³⁷ Young et al. (2014) describe three mechanisms through which food insecurity impacts treatment adherence. Firstly, the fear or the experience of increased or "intractable" hunger as a side effect of taking ART on an empty stomach.³⁹ Secondly, the fear of exacerbated ART side effects, such as nausea, vomiting and stomach pain, when ART is taken while inadequately nourished.³⁹ Lastly, in situations where resources are limited, PLWHIV often have to make the trade-off between getting their medication and getting food for themselves and their families, because of the time and costs required to visit a health facility.³⁹ The combination of undernutrition and the lack of adherence to treatment due to food insecurity leads to worse clinical outcomes for PLWHIV.^{38,39} This creates a vicious cycle as PLWHIV who are food insecure are unable to get healthy enough to look for or retain work, which makes them unable to earn a living in order to purchase food, creating a trap of both poverty and morbidity.^{38,39}

Poverty also forces people to make challenging trade-offs regarding their health to survive. In South Africa, PLWHIV can receive disability grants of R1,860 if their CD4 count falls below 200.^{40,41} This creates the potential for perverse incentives where some patients who are administered ART wilfully neglect to take their medication in order to suppress their CD4 count and continue receiving disability grants.^{37,41} In an analysis of data from the Africa Health Research Institute Demographic and Health Surveillance System (AHRI DSS) in rural KwaZulu-Natal, Haber et al. (2018) showed that the rules for qualifying for the state disability grant appear to unintentionally cause slower CD4 count recovery for patients who are close to the threshold of qualification for the grant. The study attributes slower CD4 count recovery to a change in adherence to ART when patient CD4 counts are low enough to qualify them for the disability grant.⁴¹ As described in the previous section, having a low CD4 count is strongly related to developing NCDs, particularly cancer, among PLWHIV.

Peltzer et al. (2010) found that those living in urban areas were almost three times more likely to adhere to treatment than those living in rural areas. Rurality is also associated with lower levels of adherence. This has been attributed to higher transport costs in rural areas, which make accessing treatment more costly.⁴²

Gender

Significant gains have been made in reducing the proportion of PLWHIV who have not been tested for HIV, and South Africa is well on its way to achieving the 90% HIV diagnosis target.⁴³ However, there are gender-specific factors that affect HIV testing, and treatment uptake and adherence in both men and women in South Africa. These factors relate to differences in health-seeking behaviour, poverty, patriarchal gender norms and other barriers to screening and testing.

Among women, poverty and gender interact to create conditions that put women at higher risk of contracting HIV and create barriers to treatment adherence.⁴⁴ Patriarchy and gender-related power dynamics can make it difficult for women to negotiate safe sex, force them to remain in abusive relationships, and lead many women to engage in transactional sex to fend for themselves

and their families.^{44,45} In South Africa, women aged 15 to 24 are two and a half times as likely to contract HIV as men in the same age group, and transactional sex is considered a major driver of this phenomenon.^{46,47} This puts WLHIV at risk of contracting STIs, such as HPV, which causes cervical cancer⁴⁸; the combination of immune suppression caused by HIV and compounded by a lack of treatment adherence, and exposure to STIs is what makes cervical cancer the most common cancer among WLHIV.

In a study of treatment adherence among HIV-positive pregnant women in rural KZN, issues related to domestic violence were cited as a reason for the lack of treatment adherence.⁴⁵ Some women reported that their partners threatened to beat or kill them if they found out they were HIV positive, others were discouraged from participating in the study by their partners, and one was threatened with violence for receiving calls from male nurses who were following up on whether they were adhering to treatment.⁴⁵

Men, on the other hand, fare worse every step of the HIV treatment pathway. A study that compared access to HIV care services and health outcomes among men and women in the Western Cape showed that, compared to women, men living with HIV (MLWHIV) were less likely to present for HIV treatment than women and when they did, they were more likely present at health facilities with more advanced HIV.⁴⁹ MLWHIV also were less likely to attend their annual health service visit, were less likely to be on ART, and had overall higher mortality even when receiving ART.⁴⁹ Part of this is driven by the fact that women have more contact with the health system due to reproductive health services, which means that they have more opportunities to get tested for HIV and receive treatment sooner.⁴⁹ However, men are more likely to be diagnosed with HIV compared to women, due to a concurrent TB infection. Therefore, they tend to present to the health system when their illness has progressed and are less likely to benefit from early detection and treatment.⁴⁹

Cornell et al. (2012) found that although there are gender differences in mortality among PLWHIV, these differences are not fully explained by baseline characteristics such as loss to follow-up on ART, poor adherence to ART, baseline differences in disease status, and differences in virological suppression.⁵⁰ They argue that when these factors are controlled for, the mortality differences between men and women living with HIV are not that different from those of men and women who are HIV negative.⁵⁰ Therefore, Cornell et al (2012) hypothesise that the remaining difference in mortality may be driven by poor access to and uptake of primary healthcare services for men in general.⁵⁰

Stigma

Stigma related to HIV status prevents people from being open about their status with their family, friends and employers.³⁷ These feelings of stigma and fear of discrimination are associated with lower levels of HIV treatment adherence.⁴² In an attempt to hide their status, some people choose to receive treatment in health facilities far from where they live, so that their community doesn't find out about their status, making adherence more difficult.³⁷ The timing of when ART is taken is also important for treatment efficacy, and when PLWHIV are unable to take their medication openly in front of friends, family and colleagues, it also compromises treatment adherence and efficacy.³⁷

Internalised stigma among PLWHIV is associated with lower CD4 counts and depression, whereas high levels of social support are associated with treatment adherence.^{42,51} Therefore, destigmatising HIV is not only important for ensuring adherence, but also reducing the comorbidities of HIV, since adherence is a crucial part of maintaining immune health.⁵¹

Mental health

There is a large body of literature, of both local and international studies, which show a strong relationship between mental health and HIV treatment adherence.⁵²⁻⁵⁴ A systemic review of studies that estimated the relationship between ART adherence and depression and alcohol use in sub-Saharan Africa showed that depression was associated with a 55% reduction in treatment adherence.⁵³ In a study of 101 PLWHIV who were on ART, Nel and Kagee (2013) found that 40% and 29% of participants showed moderate or severe symptoms of depression and anxiety respectively.⁵⁵ They also found that those who reported imperfect adherence to ART were almost three times as likely to have moderate to severe symptoms of depression, compared to those who reported perfect adherence.⁵⁵ There are several symptoms of depression and anxiety that may cause poor adherence to medication, such as low motivation, poor concentration, fatigue or loss of energy, and feelings of worthlessness.⁵⁵ These symptoms may cause PLWHIV to fail to attend clinic visits, forget to take medication, or even wilfully neglect taking medication due to feelings of hopelessness.⁵⁵

The factors mentioned in the sections above can also be considered to be social determinants of mental health, as people who live in poverty also face stigma and gender-based violence, and are likely to experience poor mental health too. Therefore, it is likely that all of these factors work together to reduce adherence to treatment. It follows that treating depression and anxiety alone, although important and necessary, may not be the whole solution and a more integrated approach is necessary.

Leveraging existing HIV treatment infrastructure to treat NCDs

The life-prolonging effects of ART have meant that HIV is now managed as a chronic illness and given that many of the comorbidities associated with HIV are chronic illnesses too, their management aligns. To this end, the National Department of Health (NDoH) developed and implemented the Integrated Chronic Disease Management (ICDM) model. This model of integrated managed care incorporates prevention, treatment and the care of patients with chronic communicable and non-communicable diseases at a primary healthcare (PHC) level within their communities.⁵⁶ This has meant leveraging existing PHC infrastructure, which was previously geared towards treatment and management of HIV, to treat other chronic illnesses.⁵⁷

The aspects of HIV care which can be leveraged for the control and treatment of other chronic illnesses are approaches such as defaulter tracing⁹ and peer-support programmes; tools used to register patients and capture their medical records; and systems such as monitoring and evaluation, drug procurement, referral and specimen-processing.⁵⁷ In addition to this existing infrastructure, new structures such as the Central Chronic Medicine Dispensing and Distribution (CCMDD) programme were created to enable patients to collect repeat prescriptions for chronic medications at alternative, more convenient pick-up points to assist in maintaining treatment adherence.⁵⁸

⁹ Although defaulter tracing for HIV is not that widespread, it is happening at a few clinics

There have been shortcomings reported by both patients and staff in the implementation of the ICDM model at PHC facilities which include, but are not limited to, long waiting times for patients, lack of or malfunctioning equipment, overburdened nurses due to increased workload created by integrated services, and sometimes even shortages of drugs. Despite this, the ICDM model has achieved small but significant improvement in the control of CD4 counts and blood pressure. However, strengthening these shortcomings is a necessary condition to further improve chronic-disease management outcomes.⁵⁷

Where to from here?

Using the syndemic framework to understand the comorbidity of HIV and NCDs forces one to consider not only the medical conditions which cause the conditions to co-occur, but also the social conditions. This approach allows for effective intervention at both the policy and clinical level to address the root causes of morbidity and the inequalities that give rise to them.^{35,59}

Despite beliefs around the perverse incentives created by them, disability grants provided to PLWHIV are one such attempt at bridging the gap between social and biological causes of these comorbidities. The CCMD-programme aims to address the inconvenience and cost of collecting chronic medication for patients, which also has the effect of increasing access to treatment and improving adherence.

As Goudge and Ngoma (2011) state, "multi-dimensional, intersectoral programs that tackle the social determinants of health, such as food insecurity, poverty, gendered inequities, and treatment adherence are more likely to be successful than single interventions to support adherence." Although South Africa's integrated chronic disease model has been successfully implanted,⁶⁰ more is needed to address the social determinants of the multimorbidity of these chronic diseases.

Conclusion

Some of the preliminary data presented shows that South Africa faces an immense NCD burden. This poses a very large and potentially destabilising burden to the health system and country's economy. There are high levels of still undiagnosed and untreated NCDs. This is driven by the very high prevalence of risk factors for NCDs in the South African population. Different groups are disproportionately affected depending on their socio-demographic characteristics – these characteristics can vary by sex or gender, age, or income, to mention just some.

This can have a very large negative impact on the everyday wellbeing of individuals, their family and society. It is therefore important that we understand and address the origins and risk factors (individual and systemic) of these diseases, be able to identify who is most affected, and continue to monitor and explore the interaction between different NCDs and other diseases.

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Acknowledgments

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