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Access to Tuberculosis testing among adolescents living with Human Immunodeficiency Virus in the Eastern Cape, South Africa: social factors and theoretical considerations

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DEFINITION AND ABBREVIATIONS:

HIV: Human Immunodeficiency Virus

PLHIV: People living with HIV

ALHIV: Adolescents living with HIV

TB: Tuberculosis

XDR-TB: Extensively drug-resistant TB

MDR TB: Multidrug-resistant TB

WHO: World Health Organisation

UNAIDS: The Joint United Nations Programme on HIV/AIDS

AIDS: Acquired immunodeficiency syndrome

ART: Antiretroviral treatment

TST: Tuberculin skin test

GeneXpert sputum test: The use of polymerase chain reaction to detect the presence of TB bacteria in sputum

Adolescents: 10–19-year-olds

UCT: University of Cape Town

Mzanzi Wakho: Research collaboration about youth health in South Africa. The study is based in the Amathole district in the Eastern Cape.

STATSA: Statistics South Africa

ABSTRACT / SUMMARY

Background: Addressing adolescent tuberculosis (TB) is a critical step towards eliminating TB in high burden countries, especially in HIV endemic communities. South Africa has the highest rates of TB/HIV co-infection and the largest population of adolescents living with HIV (ALHIV) in the world – contributing substantial risk to TB-related morbidity and mortality in this already vulnerable cohort. Previous research on TB has largely overlooked adolescents and ALHIV which has left knowledge – and potential service provision – gaps, but also opportunities for important research. TB among ALHIV is a complex public health challenge, needing to be understood in the context of the unique socio-emotional life stage of adolescence. This dissertation aims to provide insights into the critical first step in the ALHIV TB care cascade: access to TB testing. Through quantitative analysis, I explore the social factors that promote or prevent ALHIV from accessing TB testing in South Africa.

Methods: In this longitudinal study, I analysed the Mzantsi Wakho cohort data from n=1046 ALHIV (10-19 years old) from 53 health facilities across the Amathole district of the Eastern Cape. N= 933 (89%) ALHIV – those who participated in the second and third cohort waves – were included in this analysis. Data were collected through self-reported questionnaires, assisted by trained and experienced researchers three times between 2014/2015 to 2017/2018. The selection of social factors that influence access to the outcome of TB testing was informed by an extensive scoping literature review. These factors were initially categorised using WHO's social determinants of health framework, which applies the Ecological Model. Thereafter, factors were filtered through the People Centred Model of TB care – to draw focus to the factors pertaining to the individual (both inter- and intra-personal) rather than factors imbedded in health systems and services. Analysis was conducted in four steps: First descriptive analyses was used to summarise socio-demographic characteristics, relevant TB clinical data and HIV related factors at each interview (T2 and T3). Secondly, cross tabulation and frequencies of factors were done, comparing ALHIV who tested for TB to those that did not. Thirdly, univariate analysis was performed to identify factors with statistically significant associations with having a TB test or not. Lastly, multivariate regression models of these significant factors were run, both for each time point and over time (across both time points) using a stepwise approach by Hosmer-Lemeshow. The "why" or "how" these specific factors affected the probability of TB testing were then explored through the application of sociological theories and concepts, including the life course approach, social action theory and habitus.

Findings: Consistently experiencing the following factors over time were linked to greater odds of TB testing: being 15 years and older (OR 1.43, CI 1.06-1.92, p 0.019), female ALHIV (OR 1.34, CI 1.02-1.75, p 0.033), in a relationship at both time points (OR 1.79, CI 1.23-2.62, p 0.002) and having had a viral load test each year (OR 1.50, CI 1.11-2.02, p 0.008). Having TB symptoms at either wave 2 or 3 was associated with TB testing (OR 1.46, CI 1.08-1.96, p 0.013). At Wave 2, no sim card phone (OR 0.64, CI 0.47-0.85, p 0.002) and having to pay R10 or more to get to the clinic (OR 0.68, CI 0.51-0.92, p 0.011) were associated with lower odds of TB testing, while viral load testing in the past year (OR 1.74, CI 1.26-2.40, p 0.001), living in a rural setting (0R 1.54, CI 1.10-2.16, p 0.012), being 15 years and older (OR 1.60, CI 1.19-2.15, p 0.002) and reporting any TB symptoms (OR 1.72, CI 1.29-2.30, p <0.001) were

associated with higher odds of TB testing. At Wave 3, when most of the participants were in late adolescence being 15 years and older (OR 1.61, CI 1.19-2.19, p 0.002), living in informal housing (OR 1.58, CI 1.07-2.37, p 0.023), being in a relationship (OR 1.58, CI 1.15-2.18, p.005), experienced community violence (OR 1.43, CI 1.05-1.96, p 0.023), food security (OR 1.53, CI 1.11-2.11, p 0.010) and experienced any TB symptoms (OR 1.65, CI 1.25-2.20, p 0.001) had higher odds of reporting TB testing.

Discussion and Conclusion: In this Eastern Cape cohort of ALHIV, factors linked to where ALHIV live (living rurally, cost to get the clinic more than R10, living in informal housing and having experienced community violence) as a reflection of the deep structural issues that shape health symptoms and healthcare access, who they are (age, sex) and their close emotional and nutritional support (being in a relationship, food security) have shown to strongly influence TB testing. Some of these factors are directly linked to increasing risk of TB exposure or vulnerability to TB: rural residence, informal housing and unsafe communities. To delve into why these factors shaped TB testing in ALHIV, sociological theories and concepts were applied to these findings.

This dissertation took a holistic approach to bridge a critical knowledge gap in ALHIV's entry into TB care, extending our biomedical understanding with applied sociological frameworks. The work of this dissertation could enhance the current HIV services package offered to ALHIV by creating an awareness and identifying adolescents that may not be reached by current TB testing services. With this insight, TB services in South Africa, and perhaps broader afield, can introduce targeted interventions and social protection measures tailored to address adolescent TB testing, particularly in terms of integrating TB testing into HIV services.

INTRODUCTION AND STUDY RATIONALE

Despite Tuberculosis (TB) being a curable disease, it has disrupted the lives and development of millions of adolescents. Worryingly, the World Health Organization (WHO) estimates that almost two fifths of all TB patients are "missing" – this refers to people with TB disease that are not diagnosed and treated appropriately.[1] Finding and treating TB cases, particularly in children and adolescents is an "urgent operational priority, particularly in high-burden countries"[2] to prevent individual morbidity and mortality and stop the ongoing spread of TB.[1] A recent study from western Kenya documented TB prevalence in adolescents to be six-fold higher than that reported by case notifications.[3] A knowledge gap exists in understanding the extent of TB in adolescents as there is a scarcity of age specific data collection and reporting in this age-group, in part due to poor case detection and linkages to TB testing.[2]

Addressing TB among adolescents living with HIV (ALHIV) is a critical step towards eliminating TB in South Africa. The early diagnosis of TB is critical; delays in case detection increases mortality, morbidity, resistance and allows for the continued transmission to others. A single person with active TB can infect up to 15 people over a course of a year.[4] This poor continuum of TB care is a significant contributor to South Africa having the highest TB incidence among people living with HIV (PLHIV) in the world.[1] However, adolescent TB is a complex public health challenge that needs to be understood in the context of adolescence, as a unique socio-emotional, neurocognitive and physical life stage. Understanding adolescent TB not only medically, but also socially and psychologically is critical to designing individual, facility and system-wide solutions. The widespread gap in adolescent TB case detection and treatment is primarily due to a poor service delivery and a lack of evidence-informed interventions to prevent, diagnose and treat TB in adolescents.[2] There is limited evidence on adolescents with TB and their specific needs, highlighting a significant gap in our response to the TB epidemic.[5] It is recognised that TB is a condition that has disproportionately affected those populations burdened by poverty,[6] and has been described as the "biological expression of social inequalities".[7] The key structural and social determinants of TB epidemiology, globally, are evident throughout the socio-economic landscape of South Africa and this reflects the distribution of TB in the country.[7–9] Rapid urbanisation and population growth has significantly contributed to the rise in social conditions that have accelerated South Africa's TB epidemic.[9] An ecological, spatial study of TB prevalence in the Eastern Cape province of South Africa echoes the findings across the world – that the prevalence of poverty, population density and average household size are strongly related to TB disease and outcome.[7,9,10]

HIV and TB in South Africa

The social, economic and environmental conditions enforced by Apartheid allowed the HIV and TB epidemics, separately and in parallel, to ferment in South Africa.[11] The historical conditions of overcrowded informal (squatter) settlements, 'oscillatory migration' (cyclical migration linked to limited employment opportunities) and limited health services, entrenched in the South African landscape, continue to define the nature of HIV and TB in our country.[12,13] South Africa has the largest HIV epidemic in the world[14] as well as the

highest rate of TB per capita, and the highest HIV positive – TB incidence in the world, accounting for 25% of the global burden of HIV associated TB.[1,15]

South Africa's response to HIV/AIDS, and since 2020 to COVID-19,[16] has been marred by denialism and an initial slow and ineffective response that significantly contributed to South Africa becoming the epicentre of both HIV and TB.[17] HIV and TB epidemics are closely linked medically, socially and structurally. It is impossible to view the TB and HIV epidemics in isolation, as HIV has driven the TB epidemic in South Africa.[18] The incidence of new TB cases has increased 4 fold over the last twenty years in South Africa, largely due to HIV epidemic.[19,20] HIV acquisition is the most significant risk factor in progressing from TB infection to TB disease which makes the 7.7 million people living with HIV in South Africa[14] very vulnerable to TB disease and likely vectors for TB transmission. This vulnerability is evidenced by the fact that 60% of South Africans living with HIV are co-infected with TB.[1]

South Africa has made significant strides in HIV treatment/management and implemented the largest ART (antiretroviral treatment) program in the world. Over the past 15 years, South Africa has achieved the 1st 90 of the 90-90-90 goals, now the 95-95-95 goals, set out by UNAIDS and is on track the achieve the 2nd and 3rd .[21] However, this success has not translated to adolescents, as only 14% of adolescents and young adults are accessing ART.[22] This is in part due to their underutilisation of available services due to perceived and actual barriers,[23–25] as well as the challenges of navigating living with chronic and acute illnesses in adolescence, a life-stage characterized by considerable changes and socio-emotional transition. The poor treatment coverage of ART places adolescents at even greatest risk for TB as unsuppressed HIV viral loads is an independent risk factor for developing TB disease.[26]

TB is not as easy to diagnose as HIV and often requires repeated health care facility visits and testing before a decision to start treatment can be made. These repeated encounters to access healthcare are barriers to TB care. Patients have to overcome their social and economic obstacles every time they make contact with healthcare facilities.[18] In a large linkage to care study amongst PLHIV in South Africa and Uganda, only 34% of people with symptomatic TB underwent diagnostic testing and more than half of those with confirmed TB disease were not started on treatment. In contrast, there was a 92% success of HIV linkage to care.[27] Understanding and promoting access to TB testing and initiating treatment is even more important in an HIV endemic setting like South Africa, given the risk of long-term illness and mortality.

ALHIV and TB

Globally, there were 727 000 adolescents that developed TB in 2012 which accounts for 17% of all new TB cases.[2,28–30] Sub-Saharan Africa is home to 84% of the world's ALHIV[2] and although there is an estimated 60% TB/HIV co-infection in South Africa,[1] there is little research on the co-infection of HIV/TB in adolescents, underlining the importance of this research dissertation. A single study quantified HIV/TB co-infection in a cohort of adolescents in South Africa where the prevalence was found to be 18.5% in younger adolescents (10-14) and 12.9% in older adolescents (15-19).[18]

South Africa has the largest number of HIV positive adolescents in the world and in 2018 recorded 33 000 adolescent girls and 4200 adolescent boys as newly diagnosed HIV positive.[14] Whether vertically or horizontally acquired, ALHIV will be living with HIV for the longest span of their lives, including their reproductive and social contribution (employment, active & legal citizenship) years.[31] As people are living longer with the use of ART, the 10% annual risk of developing TB increases adolescents' likelihood of developing TB in their lifetime.[32] TB is the leading cause of mortality in children and ALHIV [33] and without proper treatment almost all people living with TB/HIV co-infection will demise.[4] This is important as it validates the use of TB testing in adolescents and in this dissertation.

Studies from India, South Africa and Uganda found that adolescents are as vulnerable to TB infection in a household with a TB contact than older age groups.[34–36] In overcrowded households, common in the high burden TB settings, adolescents often have to share a poorly ventilated room which is primed for TB transmission. STATSA documented that 42.3% of South African-born adolescents live in households of six persons or more.[37,38] Moreover, schools have been identified as a setting for significant TB transmission among adolescents. A Cape Town based study found that half of TB transmission in adolescents occurred at schools.[39,40] In the same study, it was found that TB exposure on public transport, among the most common modes of transport among school going adolescents,[41] had a similar importance to schools in TB transmission to adolescents.[39,40] This transmission of undiagnosed TB can create a pool of undiagnosed TB in the community. Furthermore, the risk of TB disease dramatically increases during adolescence until early adulthood[29] and can, in most cases, be proven bacteriologically[42] using tests such as a GeneXpert. This underscores the exposure risk of ALHIV to TB and the TB transmission risk that adolescents pose to their communities and families.[2,15,42,43]

HIV/TB co-infection in adolescents and young people is a risk factor for increased loss to follow up.[18] In a recent study of ALHIV in South Africa, only about 56% reported retention in care (both adhering to their medication and attending all their clinic appointments).[44] Notably, adolescents are known to have poor adherence to both HIV and TB treatment,[18,45] becoming part of the cycle of re-infection and secondary transmission. There are many reasons people are lost in the TB continuum of care.[46] Understanding the experiences of TB testing among ALHIV is an urgent research gap. Moreover, exploring factors affecting adolescent's barriers to enter TB care through TB testing needs to be disentangled.

South Africa is failing this dual epidemic in adolescents. Young people (ages 13-24) are the only age group in which AIDS related mortality has risen.[47] Latent TB infection in South African adolescents is disproportionately high and remained at a constant 48.5% average prevalence, and an even higher prevalence of 53% in a lower socio-economic cohort, over the past 10 years.[48] This demonstrates a failure of health services to safeguard adolescents and that the current TB control measures have had little impact on reducing TB infection in this age group. With the high prevalence of latent TB in an adolescent population with the highest number of HIV positive cases in the world, South Africa finds itself in a defining and critical moment to do more for this age-group.

It is well worth investigating the reasons for lost to follow from TB care among ALHIV, as these reasons may be the same social factors that are associated with not accessing TB

testing. There is a single study that examined risk factors for loss to follow up while receiving TB treatment in adolescents with HIV/TB coinfection. This study demonstrated that having previously received TB treatment, being male, and being an older adolescent were risk factors for being lost from TB care.[18] Importantly, there was no association found between receiving antiretroviral therapy (ART) and loss to follow up.[18] While this study provides valuable information, it examines loss to follow up once on TB treatment. There are no studies pertaining to TB/HIV co-infected adolescents that investigates the social determinants and barriers affecting their ability to enter TB care by being tested for TB and initiating treatment.

ART has improved the survival rates and life expectancy of PLHIV.[49] As a result, HIV vertically acquired children are surviving into adolescents – there is an expected epidemic of these survivors in Southern Africa.[50] ALHIV have many years of life ahead of them. The focus must shift from the mortality of TB to protecting adolescents from the detrimental long-term effects of TB on their physical, psychological and social wellbeing. This underlines the importance of constant surveillance for TB in ALHIV at each contact with the healthcare system and the early investigation of adolescents with TB symptoms.

On a review of the methods used in studies pertaining to adolescents and TB: studies determining the sensitivity and specificity of TB screening in this age group frequently made use of retrospective longitudinal cohort analysis – using relevant databases[51] and statistical modelling was commonly used to quantify the burden of TB in adolescents, and specifically in ALHIV. Loss to follow up and TB outcome in South African adolescents was likewise assessed using a retrospective cohort study. There are a number of qualitative studies that took place in South Africa that focused on the experience of adolescents on MDR-TB medication and the impact of this treatment on an individual, family and social level.[52–54] Furthermore, qualitative studies have also offered a different perspective by reviewing healthcare worker's challenges in providing TB and HIV care to adolescents and the recommendations and needs of adolescents in the South African healthcare system.[53–55] Perhaps the study closest in structure, but not in content, to this dissertation is a prospect cohort study by *Maskew. et.al.* The research sought to identify factors, that included social determinants of health, that are potential barriers to accessing ARTs among ALHIV through the use of quantitative and qualitative questionnaire data. [56]

Despite calls for action to shift TB management goals to social aspects of the disease, in the past two decades there has been an emphasis on TB related medical technologies research.[9] Social interventions to control TB has been have been primarily aimed at influencing behaviour change. Recently, this has begun to change with many researchers and clinicians expanding their vison of TB management and control to include social determinants of TB. *Wingefield et al.* re-examined the importance of social aspects of TB and re-affirmed the success of social support in preventing TB and the consequences of not addressing it.[57] In spite of growing attention, the social determinants of health have not yet been applied to adolescents and their ability to access TB testing. As the social reasons shaping access to TB testing have not yet been studied in this age group, there has been no such research into why certain factors come to the fore and have the impact they do on ALHIV ability to test for TB. This research endeavours to contribute to filling of that void.

The importance of Social Protection

UNAIDS defines social protection as "economic support, social health insurance, employment assistance and social care to reduce poverty, inequality, exclusions and barriers to accessing social and medical services".[58] South African data has shown that an alarming 12% of adolescents, between the ages of 15-17 have experienced sexual abuse. An increased risk was introduced in rural dwellings, where parental substance misuse and poor caregiver-child relationship contributed to abuse.[59]

Govindasamy et al., in a mixed-methods systematic review found that the majority of young PLHIV in Sub-Saharan Africa have experienced familial death and form part of non-nuclear families, thereby leading to financial insecurity and diminished social protection. The review went on to describe that social networks were central to the wellbeing of young PLHIV. Correlates and themes with ties to social protection, such as social support, acceptance, belonging and education were noted as part of young PLHIV's experience of wellbeing.[60]

The impact of the social determinants of disease on adolescent health is underlined by the marked improvement in a wide range of health outcomes when social protection is used to mitigate these circumstances.[61–63] While studies on the effects of various forms of social protection in a young South African population has been focused on HIV risk behaviour, this can be extrapolated to ALHIV at risk of TB.[64–66] Varying combinations of different baskets of social protection in the form of cash, care and 'cash plus care' have shown to reduce structural deprivation, psychosocial problems and HIV risk behaviour amongst adolescents.[67] Social protection in the form of food security, social support and monitoring have shown to dramatically improve ARV adherence,[68] which protects adolescents from developing opportunistic infections such as TB.

The identification of social factors pertaining to the individual, in a representative ALHIV South African cohort, that have a negative impact on adolescents' ability to access TB testing has the potential to guide social protection initiatives. The same principles can be used in the early detection of "at-risk" individuals and direct measures to be put in place to strengthen access to TB testing and TB treatment for ALHIV. This dissertation looks not only at the individual and their behaviour but how they are influenced by their community and other structures that influence TB testing, laying the foundation for targeted interventions at all levels of the ecological model.

Past and current efforts to address adolescent health in South Africa

Adolescents in lower-income countries encounter multiple disease burdens and colliding epidemics. These health concerns, in the setting of poverty and a lack of adolescent responsive health services, have grim implications for adolescent health and wellbeing.[69]

Only recently has the health of adolescents and young people been prioritised in global health and social policy.[69,70] The Sustainable Development Goals and the Global Strategy for Women's, Children's, and Adolescent Health (GS 2016 – 2030) has brought attention to adolescent health and set out targets for countries to work towards.[71] In response, the South African Department of Health has developed strategies, such as the Adolescent and

Youth Policy,[72,73] and initiatives to achieve these grand goals for adolescent health and to meet the WHO's Adolescent-Friendly Health Service standards of care. One of South Africa's first steps to promote adolescent health was the National Adolescent-Friendly Clinic Initiative that was implemented from 1999 to 2006.[24] This has since been followed by a number of programmes and campaigns that include: Adolescent Sexual and Reproductive Health and Rights Framework, Integrated School Health Programme, Ideal clinics, B-Wise, She Conquers Campaign and the South African Adolescent and Youth Friendly Services initiative (AYFS).[74]

There is no evidence that clinics applying Youth Friendly Services in South Africa are more adolescent-responsive than clinics not implementing these services. South African adolescents have expressed their dissatisfaction with Youth Friendly Services that are indeed available.[24,70,75] Furthermore, a review of 30 health facilities across Gauteng and the North-West province found that none of the facilities met the minimum standards of the South African AYFS.[76]

TB care for ALHIV during the COVID-19 pandemic

The first COVID-19 case in South Africa was confirmed on 5 March 2020, after which South Africa entered a "state of disaster" with varying degrees of lockdown and COVID-19-related restrictions implemented since the 17th of March of the same year.[77]

South Africa faces unprecedented challenges in managing the COVID-19 pandemic as well as the TB epidemic, while providing healthcare to 7.7 million PLHIV.[14,77] Furthermore, research identifies HIV and TB as risk factors for COVID-19 associated mortality.[78] As global and national guidelines reallocate resources to COVID-19, there has been a deprioritisation of TB.[77] This is demonstrated by a weekly average decrease of almost 50% in the volume of GeneXpert TB diagnostic tests being performed in South Africa during the pandemic.[79] Modelling suggests that COVID-19 has led to a 25% world-wide reduction in TB detection leading to a 13% increases in TB mortality and 1.4 million TB deaths could be registered between 2020 and 2025 as a result of COVID 19.[80]

Amongst the most vulnerable cohorts during this pandemic are ALHIV.[81] It is reported that there has been a near 50% drop off in the collection of HIV and TB medication in some parts of South Africa.[82] While being at low risk for the virus, mortality rates in children and adolescents may be among the most affected from disrupted health care service provision.[83] Moreover, as adolescents demonstrated poor adherence to ART before COVID-19, the COVID-19 related disruptions to HIV services[84] could lead to more adolescents developing active TB. Modelling suggests that a 6-month disruption of ART therapy, due to COVID-19, could cause 500 000 additional AIDS-related deaths in Sub-Saharan between 2020 and 2021.[85]

Now, there has never been a time more critical in South Africa to ensure TB care not only continues but escalates. Understanding factors shaping access to TB testing among ALHIV is a key step to responding to this pandemic.

Study Aims:

The WHO's END TB Strategy and the STOP TB Partnership strategy have set ambitious targets for the reach and success of TB care, including TB testing. There has also been acknowledgement that healthcare attention has long overlooked TB in adolescents and called for a need to gain momentum to address this.[2,86–88] The work of this dissertation fills this knowledge void and can significantly contribute to attaining these goals. Specifically, this dissertation can help to achieve one of the 3 main END TB Strategy targets of cutting new cases by 90% (by reducing ongoing adolescent TB transmission) and the STOP TB Partnership Global Plan's target of reaching 90% of people with TB, particularly the most vulnerable populations, through early detection and thereafter prompt treatment.[2,86–88]

The finding and treatment of adolescent TB cases should be a priority in South Africa. A new initiative by the WHO, "Find. Treat. All." has combined the efforts of WHO, the Stop TB Partnership and the Global Fund to Fight AIDS, Tuberculosis and Malaria to address these "missing cases".[89,90] This dissertation is tailored to this initiative, laying the knowledge foundation and the sociological reasoning to improve the "finding" of ALHIV with TB. This dissertation is well aligned to South Africa's National adolescent and Youth policy where testing for TB is specified as part of objective three of the six key objectives to improve the health and well-being of adolescents and youth in the country.[91]

This dissertation aims to identify key social factors that can be targeted by interventions to help achieve these targets. Specifically, it aims to explore the factors that promote or prevent ALHIV from accessing TB testing. A framework to answer this research question is uncoiled and explored through a conceptual framework, informed by theory. A stepwise quantitative analysis was performed to identify significant factors, informed by theory and the conceptual framework. These factors and the "why" of their significance were then interpreted by applying sociological theories and concepts.

RESEARCH QUESTIONS

1. What social factors experienced by the adolescents at home, school, and communities promote or prevent TB testing in ALHIV?
2. Why and how do the identified factors influence TB testing among ALHIV and how are they linked to existing theoretical and conceptual models?

MY STORY: INTERNAL STUDY RATIONALE

This section is taken from my reflections, both pre-written and contemplative, as well as from a series of informal retrospective interviews I conducted with health care workers, who were colleagues at the time. By this process I reviewed what lead me to undertake this Master's and to provide the reader with context, as to why this dissertation is important to me.

As a medical student I saw medicine through a finite biomedical lens – incorporating clinical presentation, asking pertinent questions, test, diagnose and treat. As much as there was exposure to multidisciplinary teams and an awareness of "seeing someone as more than just a patient" this approach to healthcare was certainly not front and centre. The study material and clinical exposure was tailored to medical management and focused on these elements. This is by no means incorrect as it is the essential when practicing, but is it enough?

When I entered my internship, I was exposed to the unthinkable magnitude of PLHIV and TB and the far reaching, devastating effects of these conditions. As an undergraduate you are predominately based in a tertiary hospital. This skews your perspective as the vast majority of TB cases are at primary and secondary levels of care. In my time in a secondary hospital, I found my passion in HIV/TB and decided to enrol in UCT's Post Graduate Diploma in HIV/TB management. Through operational research I investigated the aspects missing from the TB care offered and critically examined TB care management given to PLHIV.

The medical aspects of TB care can be fine-tuned and adapted and in-hospital TB care largely functions very well. Over time it became apparent to me that the same patients were continuously returning to hospital. On inquiry, they told me that they just did not have the means nor the resources to support themselves – they could not remain on their treatment. I started to gain an appreciation for the social aspects of HIV/TB and its importance.

One of the lecturers in the Diploma was an author of the *Road Map of Childhood Tuberculosis*. She instilled in me an awareness of adolescent TB and its "missing middle status". Now that I was aware, I had not seen a single adolescent with TB over the course of two years. I decided to do my Community Service year in of South Africa's largest HIV/TB hospitals. I became overwhelmed at how well patients did when they were socially supported. Unlike the demands of an acute hospital, patients at this facility are able to remain in hospital until they complete their course of treatment. Patients are given three meals a day, access to exercise equipment, training sessions, occupational therapy, social worker support and psychological assistance. Almost all patients successfully completed their treatment and went home physically and mentally different people from the person they were when they arrived. Many also found the support from other patients, going through the same thing, as comforting and inspiring.

Although these experiences lead me to conduct this research, these same lessons and expectations may influence my interpretations and justifications. To conduct meaningful

research, it is important to work against introducing your own bias. I found the meetings with my supervisors and colleagues in the Sociology department to be very helpful in this regard. Having my thinking and my methods challenged pushed me to produce more objectively sound research, consider alternative explanations and develop a sound evidence basis for the findings of this analysis.

Of all the patients I admitted, I only came across a handful of adolescents. *Where were they? What prevents adolescents from accessing TB care?* I started researching this and, serendipitously, I was introduced to my supervisor who was a central part of a large study of ALHIV. I embarked on this research to find out what social determinants influenced TB testing in adolescents, as an entry point into TB care. I decided not to focus on the healthcare system, but rather place the individual at the forefront of this dissertation.

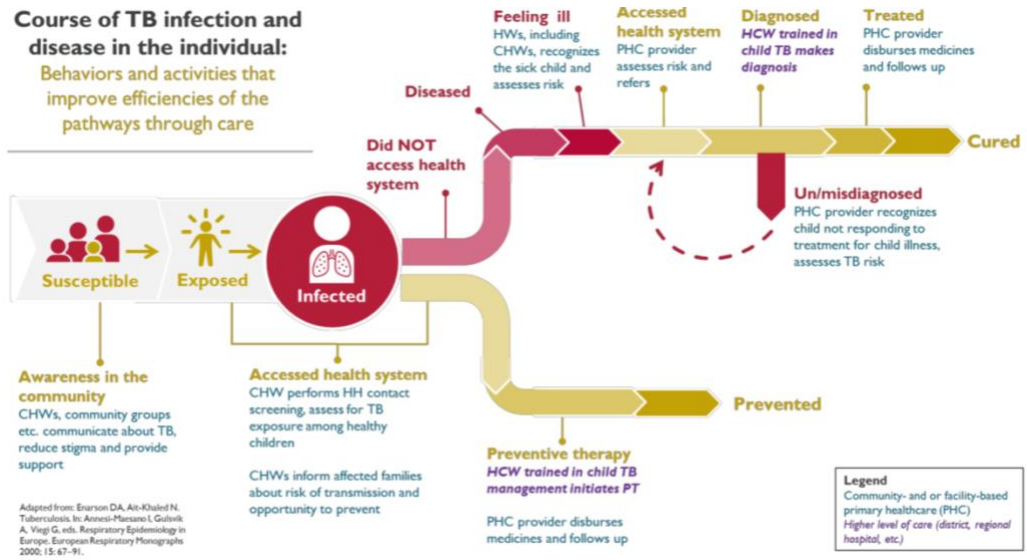
LITERATURE REVIEW

To inform the methodology of this dissertation, I conducted a literature review on factors associated with TB testing among ALHIV in sub-Saharan Africa – expanding the scope beyond South Africa to ensure that I had a rich and broad understanding of this topic. This literature review included reviewing articles from peer reviewed journals and published reports from reputable organizations such as UNAIDS and the WHO. The UCT online library as well as research databases CINAHL, Medline, Embase, PubMed and PsychInfo were used. Literature relating to the topic both from sub-Sharan Africa and specifically to South Africa was sought. Although published works note a loss of adolescents (10-19 years[92]) in the continuity of TB care as a critical failure,[93,94] available studies only explore factors shaping access to TB testing and treatment amongst adults.[2,95,96] This literature review found that the social determinants of HIV care in adolescents is well studied in comparison to TB,[97–99] where TB is seen as only as part of HIV care.[100] As research on this specific topic is limited, a slightly less specific, but still contextually relevant, investigation of available research contributed to a meaningful literature review.

TB continuum of care: it all starts with screening and testing

The TB care cascade includes TB screening, testing for TB and then starting treatment or preventative therapy.[46,101]

Figure 1 - The continuation of care and in the management of TB at a primary care level



Source:http://leadernet.org/wpcontent/uploads/2016/09/Summary_of_Childhood_TB_seminar_on_LeaderNet_Septemer_79_2016.pdf

Little attention is given to the loss of ALHIV in the steps from having TB symptoms to being tested for TB and thereafter initiating TB treatment. This area of study, addressed in the dissertation, is under researched as it magnifies a step in the cascade which is often grouped in the broader categories of linkage to care, loss to follow up and starting TB treatment. A single study was found that used a broad literature review to create a framework with risk factors and upstream determinants of TB exposure, infection, disease,

TB care and outcome that was nonspecific to an age group nor HIV infection.[102] The social factors pertaining to accessing TB care and influencing TB outcome are informative, but their ability to translate to TB testing in ALHIV will need to studied. This dissertation examines these possible social factors in the specific context of access to TB testing in ALHIV. Research in TB often assumes the translation of findings to adolescents, and this research was undertaken to find adolescent specific factors.

Research shows that while TB screening is performed in almost all PLHIV[103] up to 92% of PLHV who have TB symptoms do not undergo further testing.[104] These findings concur with a large South African study where almost 80% of TB symptomatic people were screened for TB and only 1/5th submitted a sputum sample for testing. No available study quantifies this loss in TB testing in a TB symptomatic ALHIV population. Of those adolescents that are tested for TB, a high proportion are initiated on TB treatment[93] with ALHIV less likely to start TB treatment than adolescents without HIV.[93] Understanding factors that shape access to TB testing among adolescents living with HIV is central to a successfully entering the TB cascade both for themselves and their close family/relations.

The failure of entry into the TB care, through TB testing, in one part of South Africa has ramifications for TB control in the country as a whole. There is a strong migration pattern that exists between municipalities in the Eastern Cape and the City of Cape Town region. From 2001 to 2011, 162 380 people from the Eastern Cape migrated to Cape Town.[105] It was found that half of all XDR-TB cases detected in the Western Cape were from strains originating in the Eastern Cape, showing how the failure of a healthcare service in one setting can add to burden of disease country wide.[106] 48% of migration from the Eastern Cape was to other provinces in South Africa and those aged 15-24 years were the predominate inter-provincial movers.[107] The drug-resistant TB epidemic in South Africa is caused primarily by the transmission of MDR-TB strains and the spread of resistance due to poor use of inappropriate empirical drug regimens.

The frequent mobility of people in Southern Africa not only affects the individual, but also leaves and creates a social instability. The resulting fluid nature of households introduces disruptions to interpersonal relationships, support structures and a sense of belonging – a home.[108] This mobility presents challenges to PLHIV and increases their risk of developing TB as they are more likely to lose engagement with HIV care.[109,110] Young people are a key group experiencing this mobility as they routinely leave or complete school to take up work.[111]

Overlooked - TB in adolescents

Research on adolescents with TB has largely overlooked TB testing and its value in connecting ALHIV into TB care. Previous studies on adolescents with TB have been directed towards the prevalence of latent TB,[112–114] the incidence of active TB[18,29,115] in South Africa, adherence to TB treatment, TB prevention treatment[116] and treatment outcomes.[18,29] Most of these studies pertaining to adolescents with TB included only limited results specific to ALHIV.[18,93,113,117] Overlooking the social factors shaping access to TB testing.

Age-disaggregated data on adolescent TB is not routinely collected and reported on.[118] TB statistics, drug regimens, monitoring and prevention programs are specific to certain age groups but ignores adolescents and young adults as a distinct group.[15] While the social barriers to TB testing and treatment are researched in adults living with HIV; there is limited research investigating these factors in ALHIV.[27,119–121] This considerable "gap" provides an opportunity for essential research specific to ALHIV.

"Currently, there is little data available, insufficient awareness and limited evidence generation on the increased risk for TB, treatment outcomes among adolescents, and their specific needs, creating a considerable gap in strategies and action in the response to TB" (Global Fund to Fight AIDS, TB, Malaria, 2016). In response to this dilemma, The Roadmap to ending TB in children and adolescents require the following key actions: Scale-up of child and adolescent TB case-finding and treatment, encourage child and adolescent TB research and to improve data collection and reporting.[15,118]

Difficulties in entering TB care

Early diagnosis of TB and initiating treatment is essential as delays increases mortality, morbidity and allows for ongoing TB transmission.[122] Analysing delays in access to TB care provides insight into the voluntary and involuntary social determinants to accessing testing and treatment.

Research on delays in accessing TB testing and initiating treatment is typically divided into patient related factors and healthcare related factors.[93,120,123–125] Of the limited research available, no relationship was identified between living with HIV, in high TB and HIV burdened countries, and patient or healthcare delays.[125] A systematic review of barriers to TB treatment initiation in sub-Saharan Africa found that the experiences of children and youth were not well described and no studies exploring loss to follow up as a function of age were found.[126]

A systematic review of sub-Saharan African countries with high HIV and TB burdens found that patient factors for delays in TB testing and starting treatment were: a lack of TB knowledge, seeing a traditional healer or self-medicating, being a rural resident, cost of care and fear of a positive HIV test and stigma.[125] Health care related factors for delays included multiple clinic visits before a TB diagnosis,[121] misdiagnosis, travel distance and transport, rural health clinics and lack of coordination between public health facility referrals.[127–129] In a recent study in Ghana, there was typically a median time of a 104 day delay from first contact with a healthcare facility to reaching a TB diagnosis.[120] In Brazil, patients co-infected with HIV with TB symptoms had a median delay of 82 days to starting TB treatment. It was found that illiteracy was associated with longer delays and inversely, high HIV viral loads and severe weight loss were associated with reduced delays.[124] TB in adolescents is often diagnosed late in the disease progression and because of this, adolescent TB is a significant transmission risk to the community.[29]

Theoretical Framework – Literature Review and Application

This dissertation brings together the WHO's application of the ecological model to social determinants of adolescents' health and the People-Centred Model of TB care to shed light on the social dynamics shaping access to TB testing among ALHIV in the Eastern Cape province of South Africa.

Unpacking the social determinants of health

Structural determinants of health can be defined as the conditions that create or reinforce social stratification.[130] This in turn leads to unequal distribution of social determinants of health, including "material living conditions and psychosocial circumstances as well as behavioural and biological risk factors." [130] Bronfenbrenner's ecological model can be used to unpack the health of adolescents and demonstrates that health is not solely determined by the individual, but shaped by interrelating social and community factors that affects and influences the individual.[131] These factors constrain the adolescent's choices and ability to live a healthy, disease-free life.[131] Adolescents are moving through a transitional stage of their development, from being dependent to more independent, and at the same time learning to live with a lifelong transmissible disease.[132]

Adolescents in South Africa living with HIV are a vulnerable population facing developmental and psychosocial issues along with the dangers of opportunistic infections.[22,133,134] ALHIV commonly have not only a physical delay in their growth and puberty,[132] but it has been shown that HIV related psychosocial factors negatively impact the cognitive functioning of these children and adolescents.[135] As these adolescents are often delayed in the development of executive congitive functions and abstract thinking, ALHIV are particularly vulnerable to high risk behaviour with reward consequences.[126,136,137]

Living in poverty has a negative impact on adolescents' health habits, as adolescents are exposed to structural issues – including violence – that impedes their free access to health resources and impairs their ability to remain adherent to treatment.[126] ALHIV have to navigate through feelings and experiences defined by externalized stigma as well as internalized stigma.[138] Young people with HIV faced a higher risk of discrimination and victimization as well as more internalized stigma than any older age group.[139] Vulnerable groups such as adolescents have a higher prevalence of TB disease, increased mortality and less seldom seek out TB care.[140]

While there is a large body of research that focuses on the biomedical aspect of TB; there is less research evaluating the cultural and socioeconomic aspects affecting the individual and their communities.[141,142] The South African National TB program has focused on treatment success as a measure of the country's TB response; where 4 out 5 people in South Africa, who have been newly diagnosed with TB, are successfully treated and defined as cured of TB.[143] This measure, however, overlooks patients with TB who are not diagnosed, notified and started on treatment which is estimated to be 30% of all TB cases in South Africa.[46] There is currently no data on the estimated adolescents with TB that are "missed". The burden of TB remains so significant because of delays in diagnosis, inadequate treatment and case detection as well as poor treatment seeking behaviour.[144]

TB statistics, drug regimens, monitoring and prevention programs are specific to certain age groups but ignores adolescents and young adults as a distinct group.[15] The adopted TB screening questions from the National guidelines is divided between children and adults, where "children" and "adults" have no given age definition. No provision is made for adolescents and it is up to the clinical opinion of the health care provider under which grouping adolescents fall. A recent large study describing TB screening in adolescents has called for a more accurate screening tool to optimize screening in ALHIV. The current adopted TB screening in adults was applied to ALHIV and children with HIV, the screening was found to have high specificity and a low sensitivity.[51]

Understanding the socioeconomic factors associated with accessing TB care will continue to be essential to controlling TB disease.[9] Barriers preventing access to TB care and clinical outcome include stigma, weak healthcare systems, lack of social protection, malnutrition, cultural/geographical/economic barriers and HIV.[2,95,96] To improve adolescents health outcomes we must better understand the exclusion points and vulnerabilities with their contact with the South African health system.[145]

Conceptual models are well poistioned to explain social determinants of health being responsible for health inequalities. Previous conceptual models of social determinants of health categorised factors into classic factors, fixed-demographics factors and proxy factors. Of note, is that most of the existing conceptual models are applied to health concerns in the developed world. Leaving a space for this application in a resource scarce setting such as this research.[146]

Expanding on the social determinants of health in adolescents – review of applied theories

"Medicine is a social science" – Rudolf Virchow. Health is multidimensional and predominately affected by the social determinants of health.[146] Despite the acknowledgment that social factors largely determine adolescent health practices and risk taking; public health interventions have focused on changing individual behaviour rather than community level health intervention.[147,148] This approach has yielded limited success and has drawn from psychological theories or social-psychosocial theories with a behavioural approach[149] such as social cognitive theory[150] and attachment theory.[151] Sociological theories provide an alternative approach but are seldom used to inform interventions at a community level in public health. Reasons for this include government predilection for behavioural approaches, which are more accessible and easier to operationalise in comparison to sociological theories.[152] Sociological theories are both difficult to understand and apply. The sociology of medicine has been described as producing overly complex sociological theories and concepts that are difficult to implement and incapable of being reduced into precise and usable elements.[153]

The biological and psychological changes brought on by puberty and brain development modify health behaviours and capacities in adolescents and alter childhood health trajectories.[154] These modifiable trajectories are strongly affected by social factors experienced in adolescence and create inequalities of health and wellbeing of the adult

population. Examining and understanding the link between social determinants and health requires a robust approach. A systemic review of sociological theories identified theories that help to explain how social determinants of health affect adolescence. These theories are the *life course theory*, the theory of *fundamental cause* and the theories of *habitus, health belief model, social cognitive theory, social constructionist theory, situated rationality and social action, resistance* and *response to social constraints.*[130,155,156]

The Life Course Theory, groups social determinants of health into latent effects, pathway effects and cumulative effects. Structural determinants of health, which are the strongest determinants of adolescent health, such as national wealth, income inequality and access to education can be cumulative from childhood and creates a pathway effect in adolescents. The social stratification caused by structural factors establish 'intermediate' determinates that shape an adolescent's exposure and vulnerability to compromising health factors, leading to health or ill-health.[130,155,156] The Life Course model identifies education and supportive structures as an important mechanism to prevent health inequalities in adolescents that will go on to improve population health.[154] The life Course model is further suited to this dissertation as it allows for the examination of time. The importance of time and the duration of exposure to certain factors is commonly applied to diseases such as cancers, where there is a lag time between exposure, disease initiation and clinical recognition. TB follows a similar clinical sequelae with similar dire consequences.[157] Distinctly, there is definitive cure for TB. A review of conceptual models applied to social determinants of health found the need for indicators to be grounded in a life course approach.[146] This is particularly relevant to adolescents, and adolescence as a life stage, using a multidisciplinary paradigm to expose the connection between the context of adolescent's lives and TB testing.

A siloed approach is inadequate to understand and respond to the complexity of adolescents' and their relationship with and social determinants of health. It has been proposed that a hybrid model that integrates the Ecological model and the Life Course approach will be best suited to capture the risks and find the links between social determinants of health in adolescents and risk factors over time. This synergy will allow for the investigation of social determinants of health within the circles of influence of the Ecological Model, within an adolescent's immediate and extended environment. Adolescents' potential can be realised through enabling across the life course.[158]

Theory of Fundamental Cause plays an important role in defining health behaviour in adolescents, specifically based on their socio-economic status. The theory of fundamental cause, chiefly developed by Link and Phelan and first officially published in 1995, suggests that members of a higher socio-economic status are able to prevent disease and improve mortality in a wide range of health circumstances due to the resources available to them.[159] The theory goes on to propose that people belonging to a high socio-economic status – have available to them a set of "flexible resources", that people of a lower socio-economic status do not have at their disposal. These are resources that can be adapted and used in different ways and in different circumstances to promote and protect health and wellbeing in adolescents.

While adolescence is a period of increased risk-taking behaviours such as sexual risk taking and substance use. This time is considered the most significant in initiating health related practices that are associated with the greatest health burdens in later life.[160,161] These health risk behaviours are associated with ill health, increased morbidity and premature mortality. While there is a recognition within public health of the importance of the health inequalities brought on by structural, environmental and cultural barriers, health practices amongst adolescents are also influenced by cultural, economic and legal contexts.[162] In the context of this sociology research, culture is defined as the ways of life of a group of people – encompassing language, beliefs, values and norms.[163] Culture is not static, but continually changes to reflect society.[164]

The following 3 theories relate to health behaviour and risk taking in adolescence as a function of their experienced social factors. *Habitus*: The routine of health related behaviour is formed in the context of a social location and position, that instils their world view.[165,166] *Situated rationality and social action theories:* "A person's risk-taking can be seen as rational when set in the context of the other risks they face".[167] *Response to social constraints:* "Social and institutional constraints may result in risk-taking[168] particularly in the context of low social status".[169]

These theories can be applied to both HIV and TB in adolescence. While the concept of sexual risk taking in adolescents can easily be understood as a risk for HIV transmission, which is an independent risk factor for TB; co-morbidities introduced as a result of these behaviours, that are relevant to TB, emerge or are exasperated in adolescence.[29,170] Risk taking in adolescence includes disease specific non-adherence and suboptimal engagement with healthcare facilities.[171] The routines of healthy behaviour such as attending clinics, following up on results and remaining adherent on HIV and TB treatment are difficult for adolescents to adopt in an environment where social and economic constraints present barriers to care.[172] As the theory on situated rationality suggests, the response of adolescents experiencing TB symptoms, getting tested and taking treatment may be a product of social constraints or an autonomous decision - deemed less essential to their health in the context of living with HIV. Another risk that prevents health seeking behaviour amongst ALHIV or/and with TB is stigmatization. Stigma is known to disrupt social unity and causes isolation as people hide their illness for fear of discrimination.[77]

Another consideration to expand on the results of this dissertation is to make use of the health belief model. The health belief model provides a firm framework to structure an understanding of age of ALHIV and the association with TB testing. This model has four basic dimensions: perceived vulnerability, perceived severity, perceived benefits, perceived barriers.[173]

While these sociological theories offer reasoning for the entanglement of adolescent health and their experienced social factors; it also underlines why adolescent health and well-being is important on each level of the ecological model. The concepts of the sociological theories described will be applied to this dissertation's analysis and provide a lens to delve past the figures and seek an explanation as to what the results represent and inform. They set a framework for the interpretation of findings and discussion to help explain why certain factors have a particular significance on access to TB testing.

Applying these models to adolescents' access to TB testing

Adolescents face unique challenges as they transition from child to adult health services.[174] In order to better understand the factors that shape the determinants of adolescents' health and in particular TB, one can apply the Bronfenbrenner's ecological model to adolescents social determinants of health, that was developed by the WHO.[131,175,176] The benefits of using the ecological model to understand adolescents' relationship with healthcare is that the model acknowledges the many dimensions that influence their health service utilization.[177]

There is value in reviewing research pertaining to the barriers that youth face in accessing healthcare in South Africa. Young people in South Africa have had a low uptake of health services[178] and tend to perceive health services as unresponsive to their health needs, a negative construction.[145] Youth Friendly services are not well implemented[24] and adolescent services are usually absent in endemic Tuberculosis settings.[179]

A recent qualitative study used a variant of the socio-economic model to explore the utilization of health services by young people in South Africa.[178] It was found that barriers to accessing care on an individual level were: negative attitudes of health workers and the perceived poor competency of staff.[178] At a social and community level: gossip and fear of stigma were found to be a barrier.[178] Structurally: a lack of transport, limited resources and staffing and inconvenient opening hours negatively affected adolescents' access and utilization of health care.[178]

There were no available studies that used the ecological model to specifically examine adolescents' access to TB testing. However, a recent review on adolescent TB applied a simplified ecological model to categorise barriers to TB care faced by marginalized adolescents and young adults. This model divided factors into "individual", "health systems" and "social and community factors". The placement of factors into respective groupings and the factors identified themselves served as reference point for this dissertation.[43]

The more detailed Bronfenbrenner's ecological model, applied by the WHO to adolescents' social determinants of health, was used as a framework for this dissertation to pool literature findings and identify barriers related to TB testing. This model encouraged a multi-level, engaging review into the lives of ALHIV – provoking considerations and investigations of factors shaping TB testing in these adolescents. On an individual level, the ability to exhibit personal health seeking behaviour depends on the legal age to give consent and the need for a guardian to accompany an adolescent.[180] An adolescents' perception and knowledge of TB and its consequences to self and others as well as the importance placed on diagnosis and treatment influence their use of health services.[181] Both stigmatization and mental health issues prevent adolescents from entering TB care.[182] Adolescents expressed a fear of paternalistic scolding and disapproval of their morals, lifestyles and choices by health care-providers as reasons to not attend HIV services.[145] While it is conceivable that similar reasons explain why TB testing is not sought amongst adolescents, there are no studies specific to ALHIV and TB. Communities are also likely to isolate people for fear of associating with someone with TB because it is believed that TB cannot exist without HIV.[144]

Interpersonal factors such as social networks where violence and drugs are rife has a negative effect on being able to seek out TB care.[183] A study in rural KZN reported that adolescents that lived too far to walk to clinics incurred expensive transportation costs, particularly as adolescents and youth frequently travelled outside their "catchment area" to maintain their privacy. Interestingly, adolescents and youth felt their confidentiality and privacy was breached with the use of mobile clinics.[145] The average time it takes a South African to attend a clinic by foot or by public transport is 90 minutes and the use of public transport is considered a hot spot for TB transmission which inadvertently contributes to community transmission.[184]

Adolescents receive sparse attention not only in TB care but in any healthcare, with their unique needs undeniably overlooked due to a combination of a lack of research, media attention and specific adolescent healthcare policies.[185]As this is a novel research question within a research limited pocket, similar but distinct existing literature was sought. This brought together related adult studies, HIV studies and adolescent studies that did not specifically investigate TB testing. Nevertheless, a thread of factors presented itself which, due to repetition and applicability, were used to guide factor testing for this dissertation. A wide, scoping review of research on social determinants affecting the outcome of respective research domains was summarized into categories: TB testing in adult populations, TB treatment in adult populations, TB treatment in youth and children, general utilisation of healthcare in adolescents and youth, HIV care and retention in ALHIV, TB utilisation in adolescents and TB care follow up in ALHIV.

The extensive literature review identified these factors in contextually relevant populations which are summarized in table 1 and Figure 2. These social factors, where then placed into the Bronfenbrenner's ecological and the WHO's application to adolescents' social determinants of health and set into the most appropriate bracket. This step was followed by applying the "People Centred TB Model'.

Integrating the People-Centred Model of TB care

The 1st strategic pillar of the WHO's END TB strategy is "Integrated, patient centred TB care and prevention".[186] Patient centred TB care allowed for a more holistic approach and included an importance in understanding the physical, emotional and psychological aspects of each patient. Patient-centred TB care has over time evolved into person-centred TB care, incorporating the individuals social, economic and cultural environment as well as families and communities. This concept has now formed the basis of global TB policies and frameworks such as the "Health 2020" and the WHO's "People Centred Model of TB care".[87]

The WHO's "People Centred Model of TB care" document provides a blueprint and a framework tailored to better supporting persons with TB. In this way, social protection for ALHIV is invariably linked to this model. The People Centred Model of TB care refocuses our attention to the individual, exposing the aspects of ALHIV lives that shapes their ability to test for TB. This adjustment of importance will provide evidence to guide and inform social protection interventions. The approach of this model can be summarized by its definition, "People-centred care is focused on and organized around the health needs and expectations

of people and communities rather than on patients or disease". "People Centred Model of TB care" approach delineates action on health service delivery into People, Services and Systems.[187]

This dissertation will apply the conceptual model of "People Centred model of TB care" to review factors, already categorised from the ecological model, guided by the definition of "People Centred TB Care". The application of this model serves as an magnifier or filter of the social factors identified in the Social Determinants of Health Model. This allows for the zooming in and focus of the factors to pertain specifically to the individual and not factors more related to healthcare systems and healthcare services that influence TB testing. It must be remembered that interrelating social and community factors also affects and influences the individual, and will be included. Furthermore, this model is a tailored fit for this research, offering a clear lens and a refined outlook – specific to TB. Importantly, this model, in line with this dissertation, aims to puts people at its centre. This will allow for a deeper exploration of the factors and the application of sociological theories pertaining to the social determinants shaping the individual's access to TB testing. This step is the final filter to inform which variables from the Mzanzi Wakho database will be tested – if they indeed shape TB testing and treatment in ALHIV.

It must also be acknowledged that the distinction between the individual and health services and healthcare systems are not easily delineated. For example: the cost to get to a clinic is a product of a host of factors that includes where the individual lives, their access to and mode of transport as well as the position and availability of healthcare services, but the cost incurred, is the crux determinant affecting the individual. Likewise, it can be argued that Viral Load and CD4 count should not be included after applying the People Centred Model. This viewpoint does have merit and the health service and system plays a critical role in performing this test and providing a result. However, the Viral Load and CD4 count variable were set out in the questionnaire, asking ALHIV if they had these tests in the past year, to which they responded yes or no. The manner in which this information was retrieved, speaks to the knowledge of the individual, knowing not only that a test was performed, but also which specific test. Another consideration is that having the test relies as much on the individual than the health service. The adolescent needs to engage with the health system for long enough to identify a need test and the to follow through with having a test. The variable for experiencing any TB symptom was included after applying the model as whether symptomatic adolescents were tested or not is linked to individual level factors.

Table 1 - Literature supported factors to guide selection of variables influencing TB care in ALHIV

TB testing in adult population	**TB treatment in adult population**	**TB treatment in Youth and children**	**General utilization of healthcare in adolescents and youth**	**HIV care and retention in ALHIV**	**TB care utilization in adolescents**	**TB care follow up in ALHIV**
Travel distance Road conditions Cost of travel TB awareness Trained staff Testing Resources Available HCWs Traditional Healer Multiple contacts with Health care service No medical insurance Stigma Drug and alcohol use *HIV positive adults* Male More than 1 TB symptom AIDS Unable to receive results (not contactable) Alternate diagnosis Travel time Traditional healers Multiple return visits	TB regimen Stigma Regular visits *HIV positive adults* Not returning to start treatment	Females HIV status Older adolescents Limited TB knowledge Beliefs about TB Health system delays Distance to clinic Rural areas Stigma Multiple visits	Negative attitude of health providers Perceived poor staff competencies Stigma Distance to clinics Limited resources Limited staffing Opening times not convenient for schools Drug/alcohol use Mental health Violence Caregivers Confidentiality	Stocked clinics Money for transport Accompanied to clinic Staff with time Kind staff Costs Financial grant Stigma School attendance Peer support Groups Regular appointments Friendly environment Clinic Opening times Peer influence Family Support Perceived benefits of care	Mental health Stigma Importance placed on diagnosis	Previous TB treatment Male Older adolescents

The below graphic of the ecological model depicts the bibliography referenced factors on the left and the hypothesized factors that can be explored from the Mzansi Wakho data set on the right.

Figure 2 - Factors Transcribed into the Ecological Framework

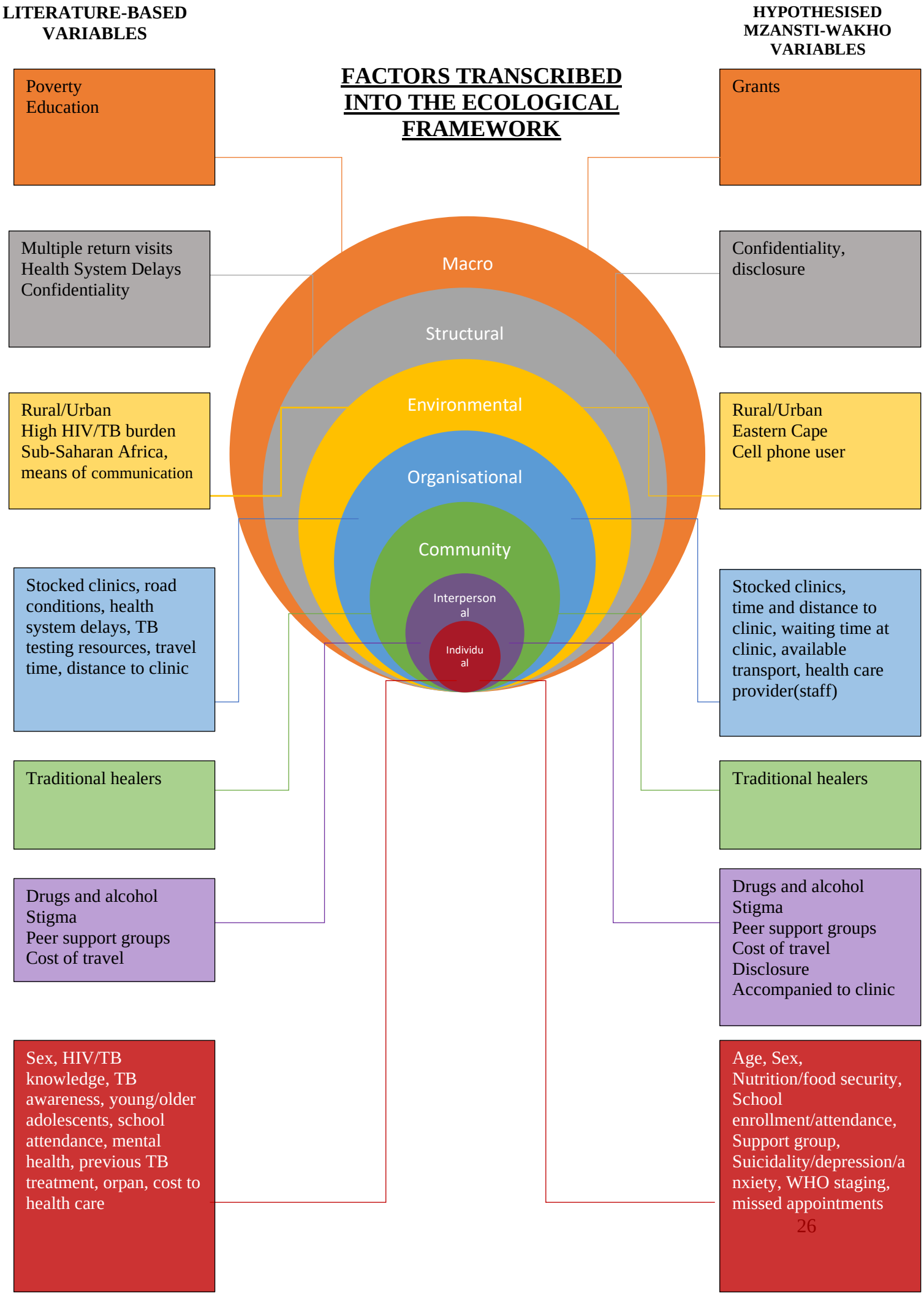
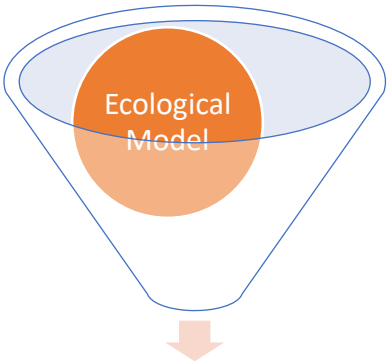
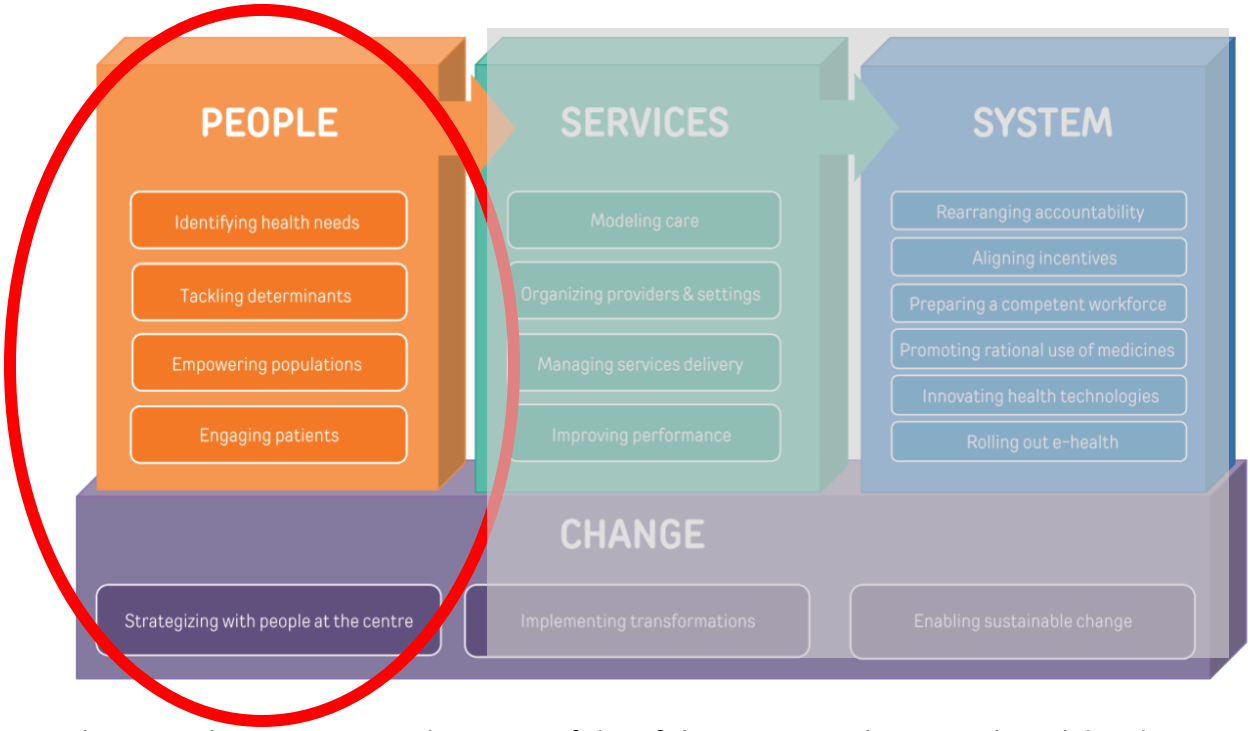


Figure 3 - Graphical representation of the filtering of factors



Factors from the ecological model were filtered through the TB Centred Model of Care. Factors relating to health services and health systems were excluded.



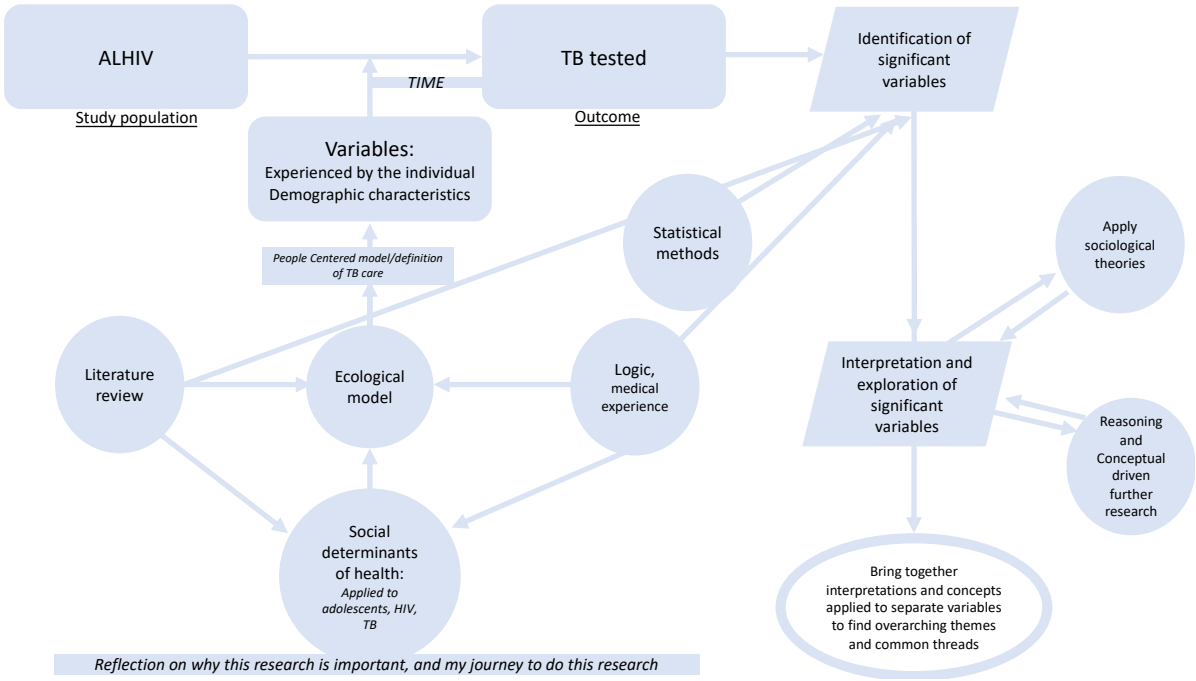
These graphics summaries the intent of the of the WHO People Centred Model in drawing a distinction between people, services and systems. This graphic also brings attention to "tackling determinants" and "engaging patients"– tying in well with this research and creates a refined criterion, along with reviewed literature support, in selecting variables. This graphic was adapted from the: WHO, People Centred TB Model – WHO.[187]

Conceptual Framework – Literature Review and Application

A conceptual framework is a structure with which a researcher explores the research problem. It is formulated using a combination of concepts, empirical research and important theories in systematizing knowledge relevant to the study. This research approach allows for study in an integrated way, offering several advantages over a Theoretical Framework and is for this reason, will be applied to this dissertation.[188–190] A single existing theory will be insufficient to create a firm structure for this research and, because of the lack of pre-existing information and research, it is essential to allow for linking and applying multiple theories and concepts. This approach also allows for a deeper engagement with the literature and applying my own experience to the findings at each step of analysis.

The following conceptual framework will guide the analyses for this research. It allows for exploratory analysis and the understanding of overarching themes, as well relationships between individual factors and TB testing. The reasoning for the connections between factors is in existing literature and sociological theories while allowing for concept-driven review of the findings exposed.

Figure 4 - A graphic representation of the Conceptual Framework of this dissertation



Conceptual frameworks are frequently used to guide and improve elements of TB care and management. They are considered critical in developing targeted strategies and deciding on research priorities and policy transitions.[191] It is acknowledged that in the review and analysis of TB control programs and challenges in TB care that a conceptual framework can be used to facilitate understanding in a comprehensive way.[192]As conceptual approaches have already proven their worth in existing literature related to TB, it can be regarded as an appropriate approach to this research. In addition, as this research examines a number of

factors at cross sections and over a duration of time, there is potential for the introduction of bias – to fit explanations into a fixed lens, rather than allow the findings to guide the introduction of concepts and theories.

METHODS

Research Questions
1. What social factors experienced by the adolescents at home, school, and communities promote or prevent TB testing in ALHIV?
2. Using a conceptual framework to explore why the identified factors influence TB testing among ALHIV

The aim of this dissertation is to explore the factors that promote or prevent ALHIV from accessing TB testing, in the context of adolescence as a unique life stage.

Context/Study Area

This study was conducted among ALHIV (10-19 years) in the Amathole subdistrict of the Eastern Cape. The Amathole District Municipality in the Eastern Cape is made up of 7 local municipalities consisting of peri-urban, rural settlements and smaller towns[193]. The Amathole District Municipality has a population of 880 791 which is made up of almost exclusively African South Africans with the vast majority being Xhosa speaking.[194]

The subdistrict is burdened by pervasive unemployment and strained health infrastructure and health resources throughout its urban, peri-urban and rural settlements.[193,195] The Eastern Cape is the province in South Africa with the highest proportion of adolescents, where the vast majority rely on the public health system for their health needs.[196] These clinics are under the jurisdiction of the Eastern Cape and National Health Department and are directly influenced by their budgets, policies, staff hiring and staff competencies. The high HIV and TB co-infection rate in the Eastern Cape coupled with the low number of people screened for TB has been identified as a "gap and a challenge" by the Eastern Cape Provincial AIDS Council. As part of the province's improvement plan the Eastern Cape AIDS Council has placed an emphasis on TB case finding, screening and using the GeneXpert testing algorithm.[197] Along with KZN, the Eastern Cape has the greatest burden of TB in South Africa,[198] which is driven by the high HIV-TB co-infection in the province.[199] The area has an estimated HIV prevalence of 13.6%.[200] Tuberculosis and HIV are the leading causes of mortality amongst adolescents in South Africa and TB is the leading cause of death in the Eastern Cape.[37,38,194]

Before the Apartheid era, colonial conquest in the early 1900's lead to the local deposition and the formation of "Native Reserves". These reserves were predominately inhabited by wives and children as men migrated to urban areas and mining towns for work. This initiated a cycle of poverty, poor health and a subordinate economic position, both for migrants – poorly paid and living in densely populated urban areas and in those who remained in more rural regions where work was scarce and infrastructure was lacking –- contributing to rural poverty, malnutrition and poor health. The idea of these reserves was reinforced during Apartheid when the Ciskei region, of the Eastern Cape (in which the Amathole district is found), among ten others, was a designated as a "homeland". The South African government enforced policies of racial discrimination, resulting in poor health circumstances and healthcare services for non-white South Africans living in these areas.[201–204] Health challenges in these areas were compounded by state neglect.[205] In the 1960s –

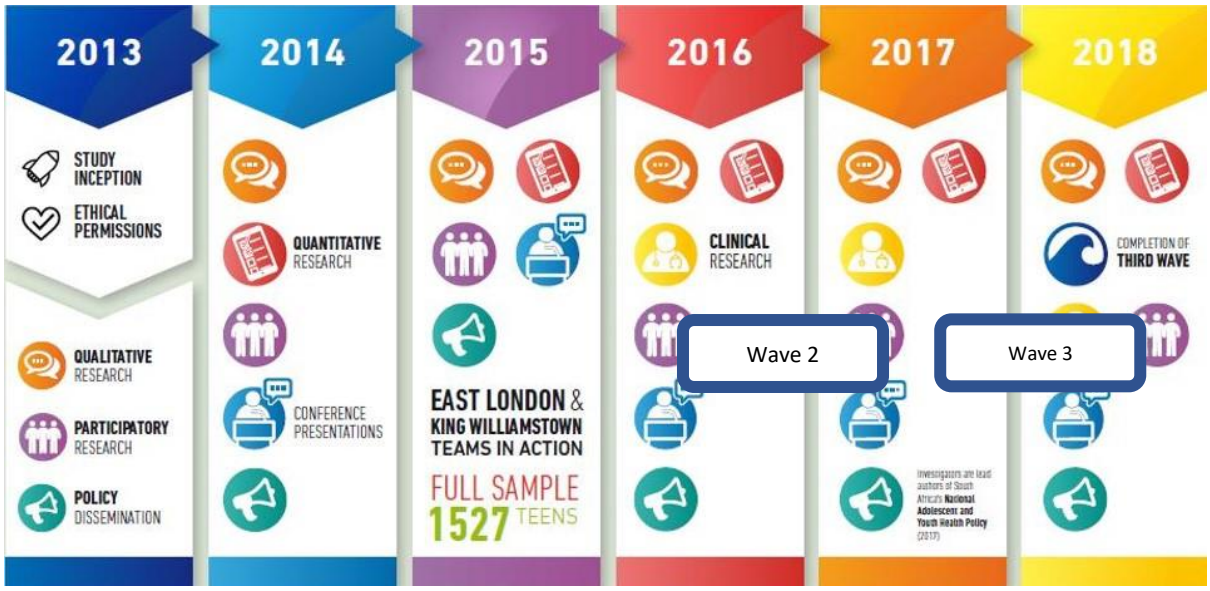
1980s the Ciskei region had a doctor to patient ratio of 1 to 87070. Furthermore, the majority of healthcare facilities had no electricity, slow ambulances and relied largely on the management of nurses.[206]

The problems faced in many South African healthcare facilities and the constrained capacity of available healthcare services, as in the Amathole subdistrict, can be traced to these systematic practices of discrimination. Healthcare resources and infrastructure in these areas where never developed and what was built, often did have the financial support to prevent deterioration. [207]

Dataset

This longitudinal quantitative study made use of three data sources: (1) Self-reported interviews from social science questionnaires, (2) health records and (3) facility profiles. There were 3 "waves" of data collection, taken from 3 rounds of interviews. The baseline interviews took place in 2014-15, the first follow up (wave 2) up was conducted in 2016-17 and the second follow up (wave 3) in 2017-18.

Figure 5 – Mzantsi Wakho Data Collection



Procedures for data collection

53 health facilities were included, which met the benchmark of providing ART to a minimum of 5 adolescents. In each of these health facilities, electronic and hardcopy clinical files were used to identify participants. To ensure a representative sample of ALHIV, both adolescents engaged in care and lost to follow up were recruited, this was also done to reduce recruitment bias. Participants were traced to 180 communities and schools where they completed the self-reported questionnaire on android tablets using the OpenDataKit platform. The questionnaire remained, for the most part, unchanged for each wave of data

collection and for each wave, adolescents were supported by trained researchers, experienced in working with vulnerable adolescents and children. The questionnaires were translated and back translated into Xhosa, which is the local language and participants completed the questionnaire in the language of their choice. The questionnaire used in the study can be found as hyperlink in this dissertation. The self-reported answers have been matched with administrative data such as clinic records and health facility level information.

An additional n=467 cohabiting adolescents, without HIV were interviewed. They answered questionnaires which were HIV non-specific and were excluded from analysis.

Study Sample

Eligible participants (10 -19 years old and living with HIV, identified as ever initiated ART – irrespective of current or previous health service attendance) were identified across the 53 health facilities. 90% of those eligible entered the study at baseline (n=1046). At the wave 2 follow up period n=979 were re-interviewed (93.6% retention, 1.5%mortality, 1.4% refusal, 3.1% untrace-ability). At Wave 3, n=933 were interviewed (95.3% retention, 2.0 % mortality, 1.83% refusal, 0.7% untrace-ability).

The 933 participants that were interviewed across each wave were used as the population cohort for this dissertation research. As these participants took part in the study at each time point, it is noteworthy that these participants were also allowed the opportunity to become more familiar with the questionnaire, supporting more reliable recall of pertinent factors, TB symptoms and TB testing over the time period in question. Another reason is that this dissertation's data is taken from a very rich and diverse data source, enabling future researchers to compare the results of this cohort to their own hypothesis at any time point, or across any time duration in the larger study.

The use of 933 participants was primarily to allow for the reviewing of how different social factors shape TB testing in the same cohort of ALHIV and how these factors change at cross sections (wave 2 and wave 3 separately) and across time (across wave 2 and wave 3).

Why the first wave was not used in this research

In conjunction with my primary supervisor, who is one of the principal investigators of the Mzanzi Wakho study, we decided to not include the first wave in this dissertation. After the first wave, the timeline of previously experienced TB symptoms changed from 6 months to 12 – affecting all TB symptom variables. This would distort the uniformity of the timeline for wave 2 and wave 3. In addition, the breakdown of specific TB tests used by ALHIV were only added in T2, along with a few key variables such as access to (own/share) a sim card phone.

Outcomes/explanatory variables

The variables in the data set were taken from the extensive range of questions in the questionnaire. Questions pertain to various aspects of the participants life, ranging from mental, physical, cognitive and sexual and reproductive health to their economic and social circumstances.

Answers to questions from the questionnaire and information/date gathered from clinic records and facility level information were abbreviated accordingly and coded into Microsoft Excel©, along with the original question to participants – if clarity was needed. This ensured the correct variable was used for the appropriate question. This document is saved as "Codebook" and is only accessible on request. Responses to questions were coded numerically, deepening on the nature of the question. Yes/no questions were coded yes (1) and no (0) and questions with options were coded with a number representing each possible answer, including a "I don't know" response.

TB-related variables

The nationally adopted South African TB screening guideline categorizes TB symptom screening into "adults" and "children" with no defined age groups. There are no specific TB screening questions tailored to adolescents. The current TB screening questions used in South Africa are found below. The presence of any TB symptoms requires workup and investigation.[208,209]

Figure 6 - Standard TB screening question for adults and children

TB SYMPTOM SCREEN

1. ADULTS

Symptoms (Tick √)	Yes	No
Cough of 2 weeks or more OR of any duration if HIV positive		
Persistent fever of more than two weeks		
Unexplained weight loss >1.5kg in a month		
Drenching night sweats		

2. CHILDREN

Symptoms (Tick √)	Yes	No
Cough of 2 weeks or more which is not improving on treatment		
Persistent fever of more than two weeks		
Documented weight loss/ failure to thrive (check Road to Health Card)		
Fatigue (less playful/ always tired)		

If "Yes" to one or more of these questions, consider TB.
If the patient is coughing, collect sputum specimen and send it for Xpert testing.
If the patient is not coughing but has the other symptoms, clinically assess the patient or refer for further investigation.

NDOH. 2014. *National Management Guidelines, 2014*

As adolescents are not accounted for in the standard TB screening tool, any single self-reported TB symptom that falls into the "children" and "adult" categories will be considered a reason to consider a TB diagnosis; this is especially relevant in an HIV positive cohort.

The study had two sources of data on TB testing and whether or not participants started TB treatment. Data was extracted from patient files from the 53 health facilities where ALHIV received care, as well as the questionnaire at each wave of the study.

The self-reported TB symptoms that will be used include:

1. A cough where you spit up green or yellow stuff

2. A cough with spit
3. A cough with blood
4. A bad cough lasting three weeks or longer
5. Night sweats
6. Tired easily, little energy
7. Lost a lot of weight, or could not put on weight
8. Fever(often)

The self-reported answers to TB testing that will be used include:

1. Have you ever received any of these tests for TB in the last year?
    a. They pricked my skin with a needle to see a reaction
    b. I coughed sputum into a little bottle or container
    c. I had a chest X-ray

Participants were asked these questions as part of the questionnaire at each wave of interviews.

Social factors shaping access to TB testing

The literature supported factors were used to hypothesize factors, from the existing data, that would shape ALHIV access to TB testing. Anonymized information from the Mzantsi Wahko data set was used to identify factors shaping access to TB testing and initiating TB treatment. The information was sorted into categories that impacts access to TB testing as informed by the social determinants of health framework and WHO People Centred Model of TB care.

Figure 7 - Filtered social factors

These below set of factors were the final factors taken from the Mzantsi Wakho data set: after applying the WHO People Centred Model of TB care to the completed Ecological Model. Factors were coded as binary variables. While the layout of factors was kept as demonstrated below, factors imbedded and relating to service delivery and health systems functioning and management were excluded. Only factors pertaining more directly to the individual were analysed.

Individual factors	**Interpersonal factors**	**Organizational level factors pertaining to the individual**	
Age ≥ 15 years	Experienced Stigma External	>1Hour Travel Time to Clinic	
Male	No support group	Cost to get to clinic above R10	**Macro level Factors pertaining To the individual**
Not Food secure past week	No Treatment Buddy	**Environmental level factors pertaining to the individual**	Family **did Not** receive a Grant
Not enrolled in school	Unaccompanied to clinic	No sim card phone	
Missed school >= 1 week	Female Care giver	Household type informal	
Experienced Stigma Internal	High Social Support	Lives Rural	
Mental health issues	In a relationship boyfriend/girl friend	Cell Health information	
Missed clinic appointments	**Structural level factors pertaining to the individual**		
WHO Stage 3/4	Not confident in confidentiality at clinic		
Any TB symptoms	**Community level Factors pertaining to the individual**		
Alcohol + Drug use ever	Used Traditional medicine in Past Year		
Retention in HIV Care	Experienced Community violence		
Last CD4 count in past year	Unsafe at clinic		
HIV viral load in the past year			
Have not disclosed HIV Status			
Orphan any			
Necessities ALL			
Missed school to attend clinic			
Pregnant last year			
Missed ARV dose in the last week			

Data Analysis

This Master's dissertation was a quantitative analysis of a longitudinal cohort study. R statistical software© was used to perform the analysis. Please, see a detailed data analysis and accompanying reasons in the addenda section of this dissertation. The addenda section also includes the cross sectional, cross tabulations for Wave2/T2 and Wave 3/T3.

Broadly, this data analysis included:

1. Descriptive analysis:
    - Factors describing the basic demographics of ALHIV (place of residence, sex, age) at each wave were sought, as well the WHO stage of HIV. The median was used to describe the age of ALHIV and frequencies of demographic factors were tallied. The total number of participants was N=933 and the

frequency of participants with each factor was represented by N; percentages (%) reflected proportions.

- Using factors that correspond to the selected WHO TB screening symptoms and using all ALHIV in the cohort (N=933), total frequency (N) and percentage (%), represented the proportion of ALHIV that reported experiencing a certain TB symptom, was described.
- This step was repeated for the type of TB test an ALHIV reported having (Total N=933).
- To calculate the frequency of ALHIV who had any TB symptom, but did not have a TB test: N=544 (Total ALHIV with any TB symptoms) and N= 351 (Total ALHIV who did not report any TB symptoms) was taken from the table describing TB symptoms in ALHIV. Percentages (%) were used to represent the proportions of ALHIV who had TB symptoms and did/did not have a TB test.
- The prevalence of the two modes of HIV infection in the cohort of this dissertation, either vertical (Vertical infection in this dissertation used the condition of starting ART in ALHIV less 10 years of age, this is in line with existing literature from a Sub-Saharhan cohort)[31] or behaviourally was described. The number (N) and proportion of ALHIV in each category was described using percentages (%) out of the total number of participants (N=933).
- Total frequency from each mode of HIV acquisition was calculated, HIV Vertically acquired (N=729) and behaviourally acquired (N= 204) was used to describe the number (N) and percentage (%) of these ALHIV in terms of age, sex and whether or not they had a TB test. Univariate analysis, using a chi squared test was done to elicit an association between factors and mode of HIV acquisition, $p \leq 0.1$ was considered significant.

2. Cross-tabulation of calculated frequencies (of literature review guided identification of social factors) with the outcome of TB testing or NOT TB testing. These cross-tabulation tables were created for both wave 2 and wave 3.

3. Univariate analysis and regression by way of Chi squared test was applied, using the frequencies of each factor in the cross-tabulation tables, to explore the relationship between the hypothesized social variables and the outcome of TB testing. A Chi squared test value of $p \leq 0.1$ was considered significant.

    a. Cross section of Wave 2/T2, found in addenda: *Factors identified from the literature review, that were then sorted into the ecological model and then filtered through the People Centred TB model were included in the table. These factors were used to create a cross tabulation with outcomes of TB testing and Not TB testing. Frequencies were recorded as well as proportions. The Chi squared test was used to determine if there is a statistically significant relationship between the factor and the outcome.*

    b. Cross section of Wave 3/T3, found in addenda: *Factors identified from the literature review, that were then sorted into the ecological model and then filtered through the People Centred TB model were included in the table. These factors were used to create a cross tabulation with outcomes of TB testing and no TB testing.*

Frequencies were recorded as well as proportions. The Chi squared test was used to determine if there is a statistically significant relationship between the factor and the outcome

4. Multivariate analysis and regression methods to explore the relationship between the hypothesized social variables and the outcome of TB testing factors: As the number of factors identified were too large to add directly into the model without the risk of overfitting – factors from the cross tabulation that had a significant relationship, ascertained from the chi squared test ($p \leq 0.1$), with the outcomes of TB testing/Not TB testing were added to the multivariate analysis model for wave 2 and wave 3. The models were further refined by making use of a stepwise logistic regression (Hosmer-Lemeshow)[210] with set significant level p values of ≤ 0.1 after step 1, $p \leq 0.05$ after step 2 and factors with a p value ≤ 0.05 after the step 3 model were considered significant.
    a. The significant factors from the cross sections of T2 and T3 were collated and entered into a combined model for T2 + T3 (across T2 and T3) – where factors identified were present across T2 and T3 (2 years). This model was further refined by making use of a stepwise logistic regression consisting of three steps. The models were further refined by making use of a stepwise logistic regression (Hosmer-Lemeshow)[210] with set significant level p values of ≤ 0.1 after step 1, $p \leq 0.05$ after step 2 and factors with a p value ≤ 0.05 after the step 3 model were considered significant. (It is important to mentioned that it was decided that the factor for "TB symptoms" for this multivariate logistic regression was coded as having TB symptoms at T2 or T3 and not like the other factors that were coded as T2 and T3)

5. Marginal effects models of factors derived from the T2 + T3 (across T2 and T3) multivariate analysis was constructed. The effects of this model were displayed graphically in two, line graphs. One graph for the cumulative effects of significant factors on males and another graph for females. Each line graph displayed trends for ALHIV 15 years and older and 14 years and younger.

Explanation and Justification of statistical models:

A step wise regression model was used after initial chi squared analysis. These methods were used to filter factors down to those that were the most significant. It was decided that models would run at wave 2, wave 3 and across wave 2 and wave 3. The same cohort of ALHIV was used to maintain consistency across each time point. The modelling method was likewise consistent for each time point and for every model run.

Logistical regression is the statistical technique used to predict the relationships between predictors (as independent variables) and predicted variables (dependent variables) where the dependant variable is binary. This suited our data very well as all factors and the primary outcome, TB testing, were binary. To fit a regression model that was unbiased, an automated, backward regression technique was used to refine the list of factors in order to find the most significant factors, while eliminating "noise". Backward multivariate regression is a well-established filtering method and allows for the significance of factors to be tested against less significant factors. It also allowed for the review of which factors were excluded at each level of significance. This was cross checked with existing literature to analyse each finding's direction and magnitude.

The use of a multivariate regression method was selected as there is evidence of its use in related studies, both in the context and in the population in question. Examples include the investigating of associations of social factors and unfavourable TB treatment outcomes among adolescents and youth [211], factors associated with delayed Tuberculosis Test seeking behaviour[212] and the impact of socio-economics on TB treatment related outcomes[213]. All of these studies settings were in countries deemed to be resource constrained.

Backward multivariate stepwise regression has the distinct advantage that each step of significance can be investigated for confounders or outlier findings. It is acknowledged that there are some opposing views to the use of backward multivariate regression. It has been stated that a problem with a stepwise regression is that some real explanatory variables, that have causal effects may happen not to be statistically significant, while less important variables may be considered significant.[214] Through repeating the model at different time points and across time, the results were compared and served as an internal control.

ETHICAL CONSIDERATIONS

While I was not involved in collecting the Mzantsi Wakho data analysed for this dissertation, the combination of my medical experience with the decade-long experience of the research team, driven by the following steps and considerations were critical to ensuring that this dissertation engaged with the topic in an ethical way.

Ethical approval and use of Mzantsi Wakho data

"Mzantsi Wakho" has a strong developmental and social responsive agenda, investigating and documenting the factors that promote and obstruct good health outcomes for young people. The project's principal aim thus far has been to gather, publish and disseminate high-quality data according to the highest standards of ethical rigour.

Ethical approval for the "Mzantsi Wakho" study was granted by Research Ethics Committees at the Universities of Oxford (SSD/CUREC2/12–21) and Cape Town (CSSR 2013/4 & 2019/11), the Eastern Cape Departments of Health and Basic Education, and ethical review boards of the health facilities involved. Voluntary informed written consent was obtained from adolescents who were older than 18 years, or their primary caregivers when participants were less than 18 years old. Consent procedures were also read out loud in case of low literacy, in a language of their choice. There were no financial incentives to take part in the study. Irrespective of whether adolescents took part in the study, they received a snack, a small gift pack and a certificate.

Confidentiality was maintained unless the participant was at of risk of harm. This includes, amongst others, suicidality, rape and severe untreated illness such as TB. Participants who were found to have active TB (N=27) were escorted to a health care site, if they so wished and consent was given, to have a TB test. This assistance is referred to as a "referral", and the research team followed this up to ensure the participant was indeed helped.

Mzantsi Wakho Data Access and Sharing Policy V.1.0 And for associated studies like HEY BABY! and From STOP to GO! Was read, understood and agreed to. In particular "The procedures for data access reflect the general principles of:

1. *4.1. Ensuring high quality research is fostered that will advance knowledge and help strengthen research capacity.*
2. *4.2. Ensuring compliance with UK and South Africa legal and regulatory requirements (e.g., the UK Data Protection Act, 1998; The South Africa Protection of Personal Information Act 2013).*
3. *4.3. Protecting the confidentiality of participants and acting within the scope of their signed consent"*

Ethical considerations and representation

The synthesis of research questions, the analysis of the information and the presentation of these findings honoured the ethical pillars of autonomy, beneficence, nonmaleficence and justice. The ALHIVs' autonomy was respected by appreciating the free will of all ALHIV, and their caregivers, to participate in the study as well as to leave the study at any point. Furthermore, this study relied on ALHIV having complete autonomy of the self-reported answers to the questionnaires. The research team strived to produce work that would benefit all ALHIV throughout South Africa, and the greater world, through quality, evidence supported research. This research was initiated to improve access to TB testing by providing the grounding for social protection, targeted interventions and to learn what shapes ALHIV access to TB testing. This research and the subsequent writing of the dissertation was conducted in this spirit and this consciousness was held in front of mind throughout. Specialised training, suited personal, language and an environment free of discrimination and stigma contributed to nonmaleficence. Adolescents living without HIV were also included. The dissertation honoured the principle of justice as not only the cohort, but all ALHIV would benefit from this work.

This research study was conducted in a manner that was mindful of the sensitive nature of the subject matter and was acutely aware of its role in shaping the narrative in further research, practice, policy and public perception on the topic. This research endeavours to be presented within a framework that will provide protection to participants and respects their culture norms, age and gender roles within families and communities. Limitations imposed by socio-economic circumstances were respected and every effort given to ensure fair and contextual interpretation of results.

My thoughts on analysing social science data

In comparison to research in medicine, social science data and the subsequent analysis felt to have more depth, being complex and intertwined. Even though I was guided by my supervisors and the available literature, for two years I consistently reviewed, adjusted and questioned my approach to understanding what I was observing and how I was analysing and interpreting these observations. I still feel an overwhelming sense of duty – not only to be a fair, representative storyteller for these ALHIV, but also to ensure I ask the right questions and set up analysis that has meaning and value.

Data access

Access to the Mzantsi Wakho data followed the study's data access procedures (see addendum – Table 17) and was approved by the study PIs (Cluver, Toska). One of the study's co-PIs was the lead supervisor for this analysis, supporting with contextual and study-specific background information, dataset history and results interpretation.

Data collection tools

Adolescents in the study answered the questionnaire on tablet devices or used printed pdf copies of the questionnaires during load shedding. The questionnaires consisted of twelve

sections. Section 3 was titled “Health and Wellbeing” and was the source for the majority of data related to TB symptoms and TB testing. The questionnaire

With the help of adolescents and a pilot run with ALHIV in the Eastern Cape, the questionnaire was crafted to be engaging and non-stigmatizing. The questionnaire was colourful, user friendly and made extensive use of stockholder input and specialist expertise to ensure the questionnaire was age appropriate. Questions were completed in the language of the adolescent’s choice. Participants were supported by research personal that were trained and had experience in working with vulnerable adolescents.

1. Final questionnaires used for data collection, can be found in the following links: First follow up (T2), 2016-2017
2. Second Follow-Up (T3).2017-2018

RESULTS

First, I explored participant characteristics through descriptive analyses. The median age was 15 at wave 2 and 16 at wave 3. At both time points, just under a quarter of all participants lived in rural areas. WHO stage – a marker of HIV/ AIDS progression[215] – at wave 2 indicated that adolescents were in good health with only 11% in Stage 3 or 4.

Table 2 - Basic demographics and characteristics of participants at Wave 2 and Wave 3

	Wave 2 (N=933) All ALHIV		**Wave 3 (N=933) All ALHIV**
Characteristic	**N (%) or otherwise described***		**N (%) or otherwise described***
Age (*median)	15		16
Rural	230(24.65)		223(24.97)
WHO Stage	Stage 1	502(53.80)	Not available
	Stage 2	326(34.94)	
	Stage 3	86(9.22)	
	Stage 4	19(2.04)	
Female	514(55.10)		514(55.10)

A substantial portion of ALHIV reported having TB symptoms. 58% of ALHIV experienced TB symptoms at Wave 2 and 37.6% at Wave 3. Both waves had near identical ranking order of symptoms, based on proportions. In descending order: Tire easily, Cough with Sputum (2nd in Wave 2, 4th in Wave 3), Night Sweats, Weight loss (4th in Wave 2, 2nd in Wave 3), Any cough for a prolonged period >21 days, Fever Often, Cough with Blood.

To improve early detection of TB, the WHO recommendation is that TB screening form a central part of intensified case finding in children and adolescents living with HIV who present to health facilitates.[51] It is therefore important that the best screening tool is used, specific to adolescents. In a cohort of adults living with HIV – cough, followed by fever and then weight loss were the most common TB presenting symptoms.[216]

It is reasonable to question the inclusion of "tire easily, little energy" as part of an adolescent TB screening tool and its ranking as the most common identified TB symptom. As adolescents do not currently have age-specific TB screening tool there is a level of uncertainty of which TB symptoms to include. This symptom is presently grouped in the children TB screening tool as "fatigue (less playful/always tired) as per *National Management Guidelines, 2014*. As non-specific as this symptom may be, it is not much less specific than any of the other, adult TB symptoms and may have a place in a unique to adolescent screening tool. In lieu of this, it must be noted that the similar order of presenting TB symptoms across time points – suggesting a pattern. This consideration will require further research. In a study reviewing TB screening in high school adolescents in South Africa, an unexplained cough was the most common TB symptom and the only symptom associated with diagnosed TB cases. This study did not include, fatigue linked symptoms.[112]

There is literature that describes TB clinical presentations in adolescents as “peculiar”, although likely to have cavitating disease, similar to that of adults.[217,218] The findings presented in the above table support the notion that adolescents are able to cough and eliminate TB bacilli, similar to adults. This draws a distinction between children and adolescents – where cough expectoration is not always possible. Furthermore, any cough of any duration is a positive TB screen in people living with HIV. The high percentage of different types of cough indicates a prevalence of possible pulmonary TB in this age group – requiring TB testing.

Concerningly, a long-term cough was noted in 14.3% of ALHIV at Wave 2 and 7.4% at Wave 3. In this high-risk population, it is plausible that this represents a delay in accessing TB screening and as a consequence, delayed TB testing.

Table 3 - TB symptoms in all ALHIV at Wave 2 and 3

	Wave 2 (N=933) All ALHIV	**Wave 3 (N=933) All ALHIV**
TB Symptoms	**N (%)**	**N (%)**
Cough Blood	12 (1.2%)	7(0.8%)
Any cough for a prolonged period >21 days	132 (14.13%)	69(7.4%)
Fever Often	27 (2.89%)	23(2.5%)
Cough with Sputum	216 (23.15%)	75(8.0%)
Night Sweats	199 (21.32%)	105(11.3%)
Tire easily, little energy	302(32.37%)	175(18.8%)
Any weight loss	164(21.36%)	119(12.8%)
Any TB Symptom	544 (58.3%)	351(37.6%)

The TB test used by the highest proportion of ALHIV in Wave 2 and Wave 3 was a sputum test. In Wave 2 and Wave 3 this was statistically significant, in comparing proportions to the other TB tests used at each wave. In Wave 2, using a chi-square test, the significance was p-value < 2.2e-16 and in Wave 3, a p-value < 2.2e-16.

The distribution of the proportions of TB tests is not surprising. The standard TB testing algorithm in South Africa makes use of the GeneXpert sputum test as the first line TB test.[219] Furthermore, the question posed to ALHIV does not specify which sputum test was performed. The sputum variable contains all sputum tests, namely sputum smear and TB culture along with GeneXpert. These tests are among the most definitive tests in diagnosing pulmonary TB. TB testing represents an entry point into TB care.

Tuberculin Skin Test (TST) measures a delayed hypersensitivity response and is an indication of TB infection. A positive test result cannot distinguish between TB infection and TB disease. This test is often used in children, as part of the diagnostic work up of TB.[220].

Both the TST and sputum TB test, often rely on the Chest X ray (CXR) to aide in the diagnosis of pulmonary TB. This is most notably true in people living with HIV and in children. Both children and ALHIV, who are able to expectorate, commonly have paucibacillary TB (fewer

microorganism), making a TB diagnosis challenging. As part of the adopted GeneXpert sputum testing algorithm, all ages who are living with HIV and have a negative GeneXpert sputum test with TB symptoms should have a CXR. This allows for the review of diagnostic signs such as hilar lymphadenopathy in the later stages of HIV progression. In addition, people living with HIV are frequently TB smear negative – this lowers the sensitivity of the GeneXpert sputum test. While this research reviews testing related to pulmonary TB, it must be acknowledged that extrapulmonary is significantly more common in people living with HIV. [208,209,221–225]

There is a drop off in the number ALHIV with TB symptoms from wave 2 to wave 3. This may be related to participant fatigue, but there are a number of medical and social reasons. Since the same cohort of adolescents is used in wave 2 and wave 3, but one year apart, it is conceivable that the ALHIV who screened positive in wave 2, went on to have TB testing, which lead to a diagnosis of TB disease and thereafter treatment. These ALHIV, or at least a significant portion of them started treatment and entered TB care. This would result in symptom resolution at the time of TB screening in wave 3; hence the drop off in number.

On reviewing the number of ALHIV who answered that they had a certain TB test: the total number of ALHIV who reported having "any TB test" and the total sum of each respective TB test is expected to be the same, but it is not. In Wave 2, 28 more ALHIV reported having any of the mentioned TB test than the sum of each test and 86 in wave 3. The most likely reason for this Is that an adolescent remembers doing a diagnostic TB test, but are unable to recall which specific test.

Table 4 - TB tests used in all ALHIV at Wave 2 and 3

	Wave 2 (N=933) ALL ALHIV	**Wave 3 (N=933) ALL ALHIV**
TB Test	**N (%)**	**N (%)**
TST (Tuberculin Skin Test)	32(3.4)	29(3.1)
Sputum	474(50.8)	358(38.4)
CXR (Chest X ray)	60(6.4)	29(3.1)
Any Test	594(63.7)	502(53.8)

When comparing the total number of ALHIV with TB symptoms in table 3 and the number of ALHIV who had a TB test in table 4: More adolescents had a TB test at each wave than the number of adolescents that had any TB symptom at each wave. Possible explanations include: TB testing of close contacts, part of a work up of extrapulmonary TB and the exclusion of active TB to safely start TB prevention treatment. Perhaps a simpler reason would be that ALHIV recall having a TB test with more clarity than having a TB symptom.

Table 5 - ALHIV with any TB symptom and whether they were tested for TB or not		
	Wave 2 (N=544)	**Wave 3 (N=351)**
Any TB Symptoms	**N (%)**	**N (%)**
Any TB Symptom + Any `TB test	365(67.1%)	221(63.0%)
Any Symptom + No Test	179(32.9%)	130(36.3%)

Vertically acquired HIV is defined as the transmission of HIV from mother to child during gestation, delivery or breastfeeding. [226]

A fifth of ALHIV acquired HIV through horizontal infection, presumably through sexual exposure. This mode and timing of new HIV infection, along with the difficulties of linking to HIV care may also explain why TB testing rates were higher among ALHIV recently infected.

There are few studies available examining the risk of TB disease in adolescents who acquired HIV horizontally, creating space for theoretical explanations for this result; there is a need for further research on this niche aspect. One possible theoretical explanation is that adolescents with horizontally acquired HIV may only became aware of their HIV status when presenting with TB symptoms and needing a TB test. Adolescents that are not aware of their status are likely to have unsuppressed viral loads and more at risk of developing TB disease. Adolescents with undiagnosed HIV may first present with TB symptoms. It is often at this stage that healthcare workers may perform a first HIV test, as part of their diagnostic work up. HIV and TB are inextricably linked and the social circumstances that are associated with high risk behaviour for HIV transmission among adolescents[227] are evident in the social conditions associated with TB. Ongoing HIV transmission among undiagnosed adolescents remains a serious concern. HIV disease progression is also affected by HIV re-infection and places these ALHIV at further risk of TB disease.

Interestingly, horizontally acquired HIV infection was associated with having a TB test at both wave 2 (77.94%, p <0.001) and wave 3 (63.3%, p <0.003). This suggests that TB re-infection, poor TB treatment adherence, or at least reinvestigating for TB occurs more frequently in this cohort. This again alludes to social factors that are associated with defaulting TB treatment and being at risk of re-infection of TB.

A large proportion of ALHIV who acquired HIV vertically reporting having a TB test at each wave (59.67% at Wave 2 and 51.17% at wave 3). This correlates with existing literature explaining the cumulative risk of developing TB while living with HIV. HIV is the single most significant factor in the progression from latent TB to TB disease. PLHIV are 20-30 times more likely to develop TB than people who are HIV negative and the 10% lifetime risk of reactivation of latent TB in HIV negative individual compares to 10% yearly risk in HIV positive individual. The long duration of living with HIV predisposes these adolescents to developing TB disease.[228–233] Another consideration in vertically infected ALHIV is the experience of ART fatigue and adherence challenges.[234] In a cohort of perinatally HIV infected adolescents in Cape Town, it was shown that these adolescents are at a fourfold increased risk of developing TB in comparison to adolescents not living with HIV.[235]

A greater proportion, and statistically significant, of female ALHIV were behaviourally acquired/horizontally HIV infected. This reflects the current crisis present among women of child bearing age in South Africa, that are disproportionately affected by new, behaviourally acquired, HIV infections.[236,237] In sub-Saharan Africa, adolescents and young women are up to six times more likely to acquire HIV than men and account for 20% of new HIV infections while only representing 10% of the population. Comparing to study of ALHIV from Mozambique describing the mode of HIV infection, 35% of females were vertically infected were 65% from horizontal infection; 83% of males acquired HIV from vertical transmission and 17% from behaviour.[230] Please, see addenda for Cross tabulation tables and univariate analysis for T2 and T3.

Table 6 – Mode of HIV acquisition across T2, T3 and T2 and T3 – all ALHIV (N =933)

	Yes – at all waves	**No – at all waves** (Behaviourally acquired)
	N (%)	**N (%)**
Vertically infected	729(78.13)	204(21.86)

Table 7 - Vertically Infected ALHIV across T2, T3 and T2 and T3 – Age, Sex, TB Testing

	Wave 2				**Wave 3**				**Across Wave 2 and 3**		
Factors	**Vertically infected at Wave 2 (N=729)**	**Behaviourally acquired at Wave 2 (N=204)**	**Chi squared Wave 2**		**Vertically infected at Wave 3 N=729**	**Behaviourally acquired Wave 3 (N=204)**	**Chi squared Wave 3**		**Vertically infected at Wave 3 (N=729)**	**Behaviourally acquired at Wave 3 (N=204)**	**Chi squared Wave 2 + 3**
	N (%)	**N (%)**	**N (%)**		**N (%)**	**N (%)**	**N (%)**		**N (%)**	**N (%)**	**N (%)**
Age >15 years	335(45.95)	180(88.24)	<0.001		429(58.85)	194(95.09)	<0.001		333(45.68)	180(88.24)	<0.001
Girls	369(50.62)	145(71.08)	<0.001		369(50.62)	145(71.08)	<0.001		369(50.62)	145(71.08)	<0.001
TB test	435(59.67)	159(77.94)	<0.001		373(51.17)	129(63.3)	<0.003		274(37.59)	109(53.43)	<0.001

Factors associated with TB testing in univariate analyses

Being an older ALHIV (15 years and older) and being a female was associated with TB testing at both time points. Attending school proved to be associated with not testing at both time points., this was supported by the findings of missing school for more than week – that was associated with TB testing at T3. At T3 cross tubulation, having a mental health issues was associated with TB testing, likely due to more encounters with healthcare services.[238] Having been pregnant in the last year at T2 was associated with TB testing, understandably so as the ALHIV would enter maternal care health services. Being an orphaned ALHIV was also associated with TB testing at T2 while having a female care giver was associated with testing at T3. Orphanhood is often used an indicator of poor social circumstances,[239] predisposing an ALHIV to developing TB, and having a female caregiver is related to having a level of social support, enabling TB testing. Proxies of HIV retention in care: viral load testing was associated with TB testing at T2 and CD4 count was associated with TB testing at both T2 and T3. Of the TB symptoms, having a cough with sputum was associated with testing at

both cross sections. Interestingly, the TB symptom included specifically in the children's' TB screening questions was associated with TB testing at T3. Paradoxically, having a HIV treatment buddy was associated with not testing at T2, while being in relationship was associated with TB testing at both time points – speaking to the importance of the nature of relationships and their role on influencing TB testing in ALHIV. Please, see addenda for written results for section Cross tabulation tables and univariate analysis for T2 and T3.

Factors associated with TB testing – using Multivariate logistic regression Analyses

After the initial cross tabulation and analysis, the strength of statistically significant association (using a chi squared test) with TB testing ($p < 0.1$) was further determined through logistic regressions.

Table 8 - T2 Regressions

Multivariate regression models tested associations between factors experienced at T2 and TB testing reported in T2. Factors with a chi squared p ≤ 0.1 were selected from cross tabulation of T2 and added to the regression model. Interestingly, when controlling for these variables many individual, interpersonal, environmental factors that were significantly associated with TB testing were not found to be significant in the multivariate analysis. These factors include male, not enrolled in school, being an orphan, having no treatment buddy and being in a relationship. After a 3-step regression process, being 15 years and older (OR 1.60, p 0.002) having had a viral load test in the last year (OR=1.74, p 0.001), living rurally (OR 1.54, p 0.012) and having any TB symptoms was strongly associated with TB testing (OR=1.72, p < 0.001). Having a cost of more than R10 to get the clinic (OR 0.68, p 0.011) and having no sim card phone (OR= 0.64, p 0.002) was associated with not testing.

STEP 1

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	0.91	0.39 – 2.13	0.827
15 years and older	1.40	0.99 – 1.96	0.154
Female	1.28	0.96 – 1.71	**0.097**
Enrolled in School	0.88	0.50 – 1.51	0.655
Has a treatment buddy	0.85	0.64 – 1.13	0.255
No sim card phone	0.66	0.49 – 0.88	**0.005**
Lives rural	1.51	1.08 – 2.13	**0.016**
CD4 count in the past	0.86	0.56 – 1.32	0.476
Viral load taken in the past year	1.88	1.21 – 2.94	**0.005**
Has boyfriend or girlfriend	1.24	0.85 – 1.81	0.268
Pregnant in the past year	1.04	0.49 – 2.40	0.916
Orphan, any	1.13	0.84 – 1.50	0.422
More than R10 to get to clinic	0.70	0.52 – 0.94	**0.018**
Any TB symptoms	1.69	1.27 – 2.26	**<0.001**
Observations	933		
R^2 Tjur	0.078		

Set significance level p = ≤ 0.1

STEP 2:

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	0.79	0.46 – 1.37	0.404
15 years old or older	1.57	1.17 – 2.12	**0.003**
Female	1.26	0.95 – 1.66	0.109
No sim card phone	0.65	0.48 – 0.86	**0.003**
More than R10 to get to clinic	0.68	0.51 – 0.92	**0.011**
Viral load taken in the past year	1.71	1.24 – 2.36	**0.001**
Lives rural	1.53	1.09 – 2.15	**0.014**
Any TB symptoms	1.71	1.28 – 2.29	**<0.001**
Observations	933		
R^2 Tjur	0.074		

Set significance level p ≤ 0.05

STEP 3:

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	1.11	0.78 – 1.60	0.552
15 years old or older	1.60	1.19 – 2.15	**0.002**
No sim card phone	0.64	0.47 – 0.85	**0.002**
More than R10 to get to clinic	0.68	0.51 – 0.92	**0.011**
Viral load taken in the past year	1.74	1.26 – 2.40	**0.001**
Lives rural	1.54	1.10 – 2.16	**0.012**
Any TB symptoms	1.72	1.29 – 2.30	**<0.001**
Observations	933		
R^2 Tjur	0.072		

Set significance level p ≤ 0.05

Table 9 - T3 Regressions

Multivariate regression models tested associations between factors experienced at T3 and TB testing reported in T3. Factors with a chi squared p ≤ 0.1 were selected from cross tabulation of T3**,** added to the regression model and controlled for. After controlling for these, the following factors were no longer statistically significantly associated with TB testing or not TB testing: Being enrolled in school, missed school for more than 1 week, having a support group, having a female caregiver and using a cell phone for health information. Having a boyfriend/girlfriend (OR=1.58, p 0.005), being female (OR=1.41, p 0.014), being 15 years and older (OR 1.61, p 0.002), being food secure (OR 1.53, p 0.010) and having TB symptoms was strongly associated with having a TB test (OR = 1.65, p 0.001). Curiously, experiencing community violence (OR=1.43, p 0.024) and living in informal housing was associated with TB testing (OR =1.58, p 0.035).

STEP 1

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	0.31	0.13 – 0.74	**0.008**
15 years and older	1.42	1.03 – 1.96	**0.034**
Female	1.37	1.04 – 1.82	**0.026**
Food secure	1.68	1.21 – 2.36	0.003
Enrolled in school	0.90	0.59 – 1.36	0.613
Mental Health Issues	1.14	0.76 – 1.73	0.529
Missed school for more than 1 week	1.64	0.98 – 2.81	**0.067**
Any support group	1.28	0.76 – 2.20	0.362
Female primary caregiver	0.69	0.42 – 1.11	0.130
Lives in Informal housing	1.54	1.03 – 2.30	**0.035**
CD4 count in the past year	1.28	0.96 – 1.71	0.160
Has boyfriend or girlfriend	1.49	1.07 – 2.07	**0.018**
Use Cell phone for Health information	1.09	0.68 – 1.76	0.719
Experienced community violence	1.44	1.05 – 1.98	**0.024**
Any TB symptoms	1.57	1.17 – 2.10	**0.002**
Observations	933		
R^2 Tjur	0.086		

Set significance level p ≤ 0.1

STEP 2

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	0.21	0.12 – 0.37	**<0.001**
15 years or older	1.60	1.18 – 2.18	**0.002**
Female	1.40	1.07 – 1.84	**0.015**
Food secure	1.60	1.16 – 2.23	**0.005**
Missed school for more than 1 week	1.65	1.00 – 2.81	0.056
Lives in Informal housing	1.56	1.06 – 2.34	**0.027**
Has boyfriend or girlfriend	1.57	1.14 – 2.17	**0.005**
Experienced community violence	1.43	1.05 – 1.96	**0.023**
Any TB symptoms	1.60	1.20 – 2.13	**0.001**
Observations	933		
R^2 Tjur	0.079		

Set significance level p ≤ 0.05

STEP 3

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	0.22	0.13 – 0.39	**<0.001**
15 years and older	1.61	1.19 – 2.19	**0.002**
Female	1.41	1.07 – 1.85	**0.014**
Food secure	1.53	1.11 – 2.11	**0.010**
Lives in Informal housing	1.58	1.07 – 2.37	**0.023**
Has boyfriend or girlfriend	1.58	1.15 – 2.18	**0.005**
Experienced community violence	1.43	1.05 – 1.96	**0.023**
Any TB symptoms	1.65	1.25 – 2.20	**0.001**
Observations	933		
R^2 Tjur	0.076		

Set significance level p ≤ 0.05

Table 10 - Regressions for Factors across T2 and T3, TB Testing at T3

Multivariate regression models tested associations between factors experienced consistently at both time points and testing reported in T3. Experiencing the following factors over time were linked to greater odds of TB testing: being 15 years and older than (OR 1.43, CI 1.06-1.92, p 0.019), female ALHIV (OR 1.34, CI 1.02-1.75, p 0.033), in a relationship at both time points (OR 1.79, CI 1.23-2.62, p 0.002), and having had a viral load test each year (OR 1.50, CI 1.11-2.02, p 0.008). Having TB symptoms at either wave 2 or 3 was associated with TB testing (OR 1.46, CL 1.08-1.96, p 0.013).

STEP 1

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	0.37	0.24 – 0.57	**<0.001**
15 years and older	1.44	1.06 – 1.96	**0.019**
Female	1.37	1.04 – 1.79	**0.024**
More than R10 to get to clinic	1.11	0.77 – 1.60	0.576
Lives rural	1.07	0.78 – 1.46	0.693
Lives in Informal housing	1.45	0.97 – 2.19	0.071
Any TB symptoms	1.40	1.04 – 1.90	**0.029**
Viral load taken in the past year	1.51	1.12 – 2.05	**0.007**
Food secure	1.31	0.99 – 1.73	0.060
Has boyfriend or girlfriend	1.76	1.20 – 2.59	**0.004**
Experienced community violence	1.39	0.94 – 2.06	0.098
No sim card phone	0.98	0.73 – 1.33	0.896
Observations	933		
R^2 Tjur	0.067		

Set significance level p ≤ 0.1

STEP 2

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	0.38	0.26 – 0.56	**<0.001**
15 years and older	1.45	1.08 – 1.96	**0.015**
Female	1.37	1.05 – 1.80	**0.022**
Food secure	1.30	0.99 – 1.72	0.057
Experienced community violence	1.38	0.94 – 2.05	0.100
Lives in Informal housing	1.46	0.98 – 2.20	0.064
Any TB symptoms	1.39	1.03 – 1.88	**0.031**
Viral load taken in the past year	1.52	1.13 – 2.06	**0.006**
Has boyfriend or girlfriend	1.73	1.19 – 2.54	**0.005**
Observations	933		
R^2 Tjur	0.067		

Set significance level p ≤ 0.05

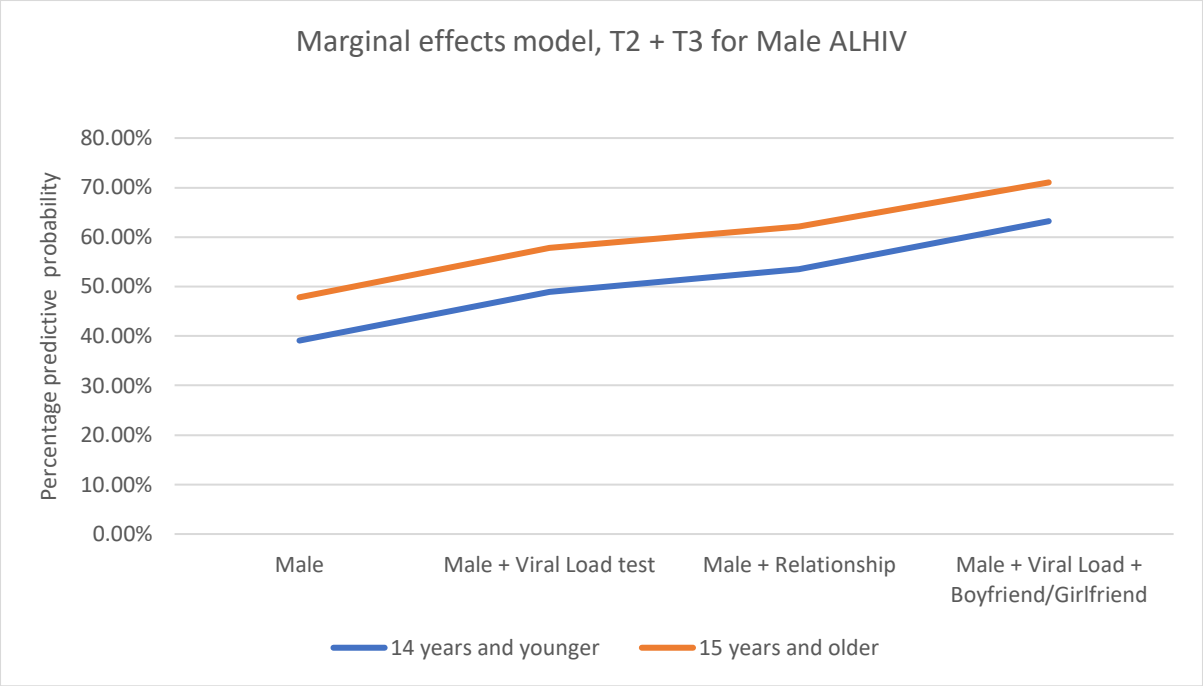
STEP 3

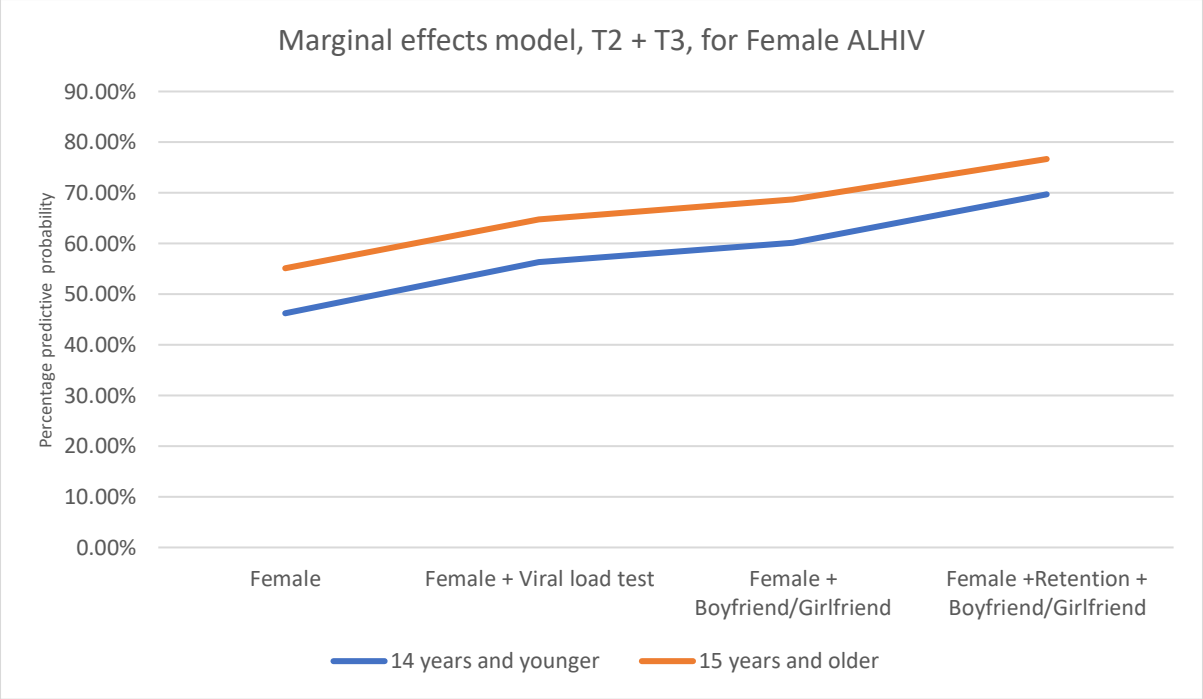
Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	0.49	0.35 – 0.68	**<0.001**
15 years and older	1.43	1.06 – 1.92	**0.019**
Female	1.34	1.02 – 1.75	**0.033**
Any TB symptoms	1.46	1.08 – 1.96	**0.013**
Viral load taken in the past year	1.50	1.11 – 2.02	**0.008**
Has boyfriend or girlfriend	1.79	1.23 – 2.62	**0.002**
Observations	933		
R^2 Tjur	0.057		

Set significance level p ≤ 0.05

Figure 8 - Marginal Effects Model T2 + T3

Probabilities of reporting being tested for TB with different combinations of significant individual and interpersonal factors were mapped using marginal effects modelling.





Among only male adolescents younger than 15, while all other factors were kept constant, the predicted probability of testing was 39.1%. This increased to 49.0% (+ 10.0%) for having a viral load test each year for two years, a marker of retention in HIV care, and 53.5% if younger males had a girlfriend. A male ALHIV, with all factors present, would have a predictive probability of 63.2% of having a TB test. Males that were older than 15 years without any other factors had a predictive probability of 47.8% with a similar 10% increase in probability when having had viral load testing. Again, being in a relationship was a stronger positive predictor of TB testing than viral load testing (53.5%). A difference was noted with all factors present in the older age group (71.0%) – being significantly higher than the younger cohort of ALHIV with all factors present.

Older ALHIV females with all factors present had a 76.7% positive predictive probability compared to younger adolescents that 69.7%. Being in a relationship had slightly less of an effect on females' predictive probability of TB testing than males in both the older and younger age groups (+ 13.7% in younger females and 13.6% in older females)

Male ALHIV 15 years and older had a 0.48 predicted probability of testing. Probability increased in this group for those who were retained in care – 0.56, and those with a boyfriend and girlfriend 0.63. The probability of ALHIV older than 15, in a relationship and retained in care is 0.69. Viral load testing had less of an effect than being in a relationship with predictive probability values of 56,3% in younger females and 64.8% in older adolescents.

Model checking and fit

The modelling was performed in conjunction with a statistician, doing his PhD at the University of Cape Town, and my supervisor ,Dr Elona Toska, who has extensive experience in quantitative analysis. Each factor was carefully fitted and the factor reduction was robust, using chi squared analysis and stepwise multivariate regression in a large population size. The direction of findings was debated, reviewed, rerun and checked using different methods to the same endpoint if there was any doubt. All models underwent a goodness of fit test. A likelihood ratio test was conducted on the final model, after the stepwise regression, at each time point and across T2 and T3. The results were: T2 $p<0.001$, T3 $p<0.001$ and T2+T3 $p<0.001$. Since the p value is less than p 0.05, the null hypothesis, in favour of the full model, can be rejected for each model run. The models were a good fit.

DISCUSSION

My analysis suggests that a series of factors shape TB testing among ALHIV at different stages of adolescence and over time. In this section, I interpret these results by applying different sociological theories and concepts.

Overview of Multivariate analysis findings

There were five factors from a single cross section that were significantly associated with TB testing at both a cross section multivariate analysis and across time: Being 15 years and older, being female, having a boyfriend or girlfriend, having a viral load test and unsurprisingly, having TB symptoms. Factors rooted in demographic features such as living rurally was associated with having a TB test at T2, while factors related to financial means such as not having the ability to pay more than R10 to travel to the clinic and being food secure were found to be associated with not testing at T2 and testing at T3, respectively. Showcasing the value of access to information and communication to TB testing, not having a sim card phone lowered the odd ratio of an ALHIV having a TB test. Viral Load testing at T2 almost doubled the odds of having a TB test, more so than experiencing TB symptoms – giving support to the importance of retention in HIV care and closely monitoring ALHIV.

T3 multivariate analysis revealed how an ALHIV's environment affects TB testing, largely by association of community violence and living informally with greater TB burden and therefore requiring TB testing. This same multivariate model demonstrated that unmodifiable factors age and sex had a significant impact on ALHIV and TB testing.

The combined model of T2 and T3 produced a mix of factors that could be targeted by social protection (viral load – retention in care), but also draws attention to males and younger ALHIV and their lower odds having a TB test – generating a high-risk cohort where special attention is required and interventions can be targeted.

The benefit of being retained in HIV care, where viral load across T2 and T3 was used as a proxy, for both a longer duration of time (T2 and T3) and at a cross section (T3) was shown to be associated with TB testing. However, being in a relationship had higher odds ratio of TB testing than having TB symptoms or being retained in HIV care. In light of the findings of the value of being in a relationship for TB testing; in a recent article from census data investigating HIV testing in South Africans – age nonspecific findings reflected that being female and married was associated with HIV testing.[240]

It must be mentioned that the many factors that were statically significant for the same cohort at wave 2 were different in comparison to wave 3. Demonstrating how different factors test social support capacity and how barriers to TB testing change at different times in the life of ALHIV; or challenges with self-reported data.

Strengths and limitations of the data set

The data used for this dissertation had undergone cleaning and was categorised and coded with an easy-to-use index. In its formulation, the questionnaire had extensive expert input and was informed by evidence-based research. Thereafter the questionnaire was rigorously reviewed through a multidisciplinary, multi-centred team of academics, healthcare workers and other stakeholders. More than that, the data extracted from the questionnaires gave a holistic view of an adolescent's life. The adult TB screening questions as well as more general questions on health were included in the questionnaire, with the exception being a close TB contact. The database was large enough that all social factors identified through the literature review as well as child related TB screening questions were found due to the versatility of the large data set.

This was a secondary data analysis. The data was left in its raw form and collected and compiled into categories and themes. This study did not have to navigate data that was collected for a particular study - with its own aims and data interpretation. This allowed the data first to be put into a frequency tables to ensure adequate numbers and then to review the direction of chi squared tests of associations. This ensured that the direction and associations were reviewed by applying logical and, if needed, medical and sociological literature-based reasons for our findings.

The use of self-reported answers does introduce a level of bias. Participants may give answers to questions that they believe are more socially acceptable (social desirability bias), rather than truthful. Furthermore, this mode of data collection relies on adolescents to be self-reflective, introspective and to interpret the questions correctly. Importantly, a questionnaire of this length is at risk of response bias. Where previous responses given in the questionnaire influence later answers. In contrast to this, self-reported answers are often not filtered by caregivers and parents, offering an unfiltered truth.

As a clinician, it would be helpful to quantify certain factors such as weight loss, as this category of factor is heavily influenced by self-image, together with other confounding

factors. In addition, examining a patient to identify features of extrapulmonary TB would be beneficial.

The data is robust and multicentred, but it is sourced from only a single area in South Africa. Although in theory this study is translatable to other provinces and areas of the country, a multi provincial study in different settings may strengthen the generalisability and applicability of this work. This study has value to the rest of Southern Africa, but the social factors of significance in the Eastern Cape may differ from the Western Cape and so it might change in other countries. This is the complexity of social sciences work. From the level of government down to family structures, all levels influence adolescent TB testing and this may differ depending on where the study is conducted.

Justification of the use of TB testing as the outcome

TB testing was selected as an outcome as it is the entry point into the TB continuum of care. It is also a "stand-out" recognisable event, that could be more securely relied on in the self-reported recall. All ALHIV are a high-risk population for developing TB. Other than the baseline risk of LHIV, certain social and behavioural risk factors place cohorts of ALHIV at more risk of developing TB than others.

This dissertation showed that more ALHIV had TB testing than there were ALHIV who reported TB symptoms. This may either demonstrate recall bias, or that the screening tool used did not "catch" everyone. Furthermore, ALHIV may have had TB testing following atypical presentations or for other medical reasons. These reasons may include close contact tracing and testing or excluding active TB disease – so to start TB preventative therapy. In the same data source, it was found that even those who were screened negative can and do test positive for TB.[241] This shows that having TB symptoms is not the only reason ALHIV have a TB test. Additional reasons could include providers differential application of protocols, noticing symptoms that the self-reported surveys did not pick up (for example considerable weight fluctuations) or knowledge of additional co-morbidities and risk factors by the healthcare provider that we were not able to include in the analysis.

All ALHIV who took part in the study at both wave 2 and wave 3 were included in the study population. It was decided not to include only those ALHIV with TB symptoms. This decision significantly increased the population from 544 in wave 2 and 351 in wave 3 (this number would be further reduced if only those ALHIV who took part in both waves were included) to 933 in both wave 2 and 3. Moreover, it will be very unlikely that TB symptoms were experienced by the same ALHIV for two consecutive years. This unlikelihood would introduce the two different cohorts of adolescents at wave 2 and wave 3; preventing the use of comparison of social factors experienced by the same cohort at cross sections and across wave 2 and wave 3. The comparison of these cohorts using time as a variable is a particular strength of this dissertation – providing insight and knowledge of which factors influence TB testing and how they change at different time points and which remain constant.

This dissertation sought to focus on the associations with TB testing, at all levels of the ecological model. As part of these factors, TB symptoms were included as a factor. This allowed for engagement with existing literature and the application of my background as clinician to answer the "why" of these associations. The questioning of the direction and significance of the findings, with the use of sociological theories and previous literature, to understand if the associations were due to a challenge of access to TB testing, a social factor indicative of a greater TB burden or being at high risk of TB. A deeper level of explorative thinking and reason could thus be applied. This application exemplifies the uniqueness of this dissertation. This dissertation does not seek to answer why people had a TB test, it is to understand what factors may promote or prevent TB testing.

Age of ALHIV

Being an older ALHIV was statistically significantly associated with TB testing at T3 and across T2 + T3 using multivariate analysis, which is unsurprising as risk of TB increases in later adolescence. Older adolescents are known to have poor rates of TB care follow up[18] One can postulate that less engagement with health facilities, in turn, results in missed opportunities for TB testing. However, this dissertation found that being an older adolescent was associated with having a TB test. As the duration of review across T2 and T3 was two years, the oldest adolescent in the younger category was 13 at T2 and the youngest adolescent was 15 in the older category at the same time point. This brings into question how the difference between these ages, within the adolescent age group, impacts on TB testing and how we can support ALHIV of different ages to access TB testing.

Autonomy

Older adolescents are often more autonomous than younger adolescents and able to take responsibility for their own symptoms. Autonomy can be defined as the process of becoming an autonomous person, taking direction in one's own life and regulating their own action and behaviour. Adolescence is uniquely defined by the autonomous process.[242] [243,244]

Consent to access services

The Children's Act 38 of 2005 states that children older than twelve years of age can consent to their own medical treatment or that of their children. Very importantly, it continues that they may do so "provided they are of sufficient maturity and have the mental capacity to understand the risks, social and other implications of their treatment, according to Section 129(2)".[245,246] This law allows ALHIV twelve years and older to make their own decisions, but has strict provisors of maturity, competence, and comprehension. This offers a level of protection to adolescents, although at the same time restricts them. Bringing into question their autonomy, self-determination, competence and capacity, and how that is influenced by living with HIV – socially, physically and emotionally.

Buchannan and Brock, in their seminal work: *Deciding for Others, the ethics of surrogate decision making,* specifies "minors" as a unique case of assigning competence. Their work goes on to argue that competence is not universal and requires specifiers. Competency and capacity at one time point and situation does not translate to another. Three capacities for competency include: understanding and communication, reasoning and deliberation and a set of values of what is good. This presents a balancing act between parental and caregiver rights and the rights of minors.[247]

Literature review on the effects of HIV on an early adolescent's capacity to provide consent yielded no substantive evidence. However, using access to HIV testing, a case study shows a reduced uptake among adolescents for fear of negative caregiver/parental/healthcare worker reaction along with HIV stigma.[248] In a review of sub-Saharan African policies on HIV testing services, a 37% increase was noted in the number of clear age policies (12-16 years), regardless of HIV status as well as the introduction of mature minor exception which included being sexually active.[249] It is understood that before the ART era, HIV severely affected the neurocognitive and emotional development of children, particularly those children who were perinatally infected. HIV infection in children and adolescents resulted in delayed developmental milestones and cognitive ability. Fortunately, following the introduction of ART, these significant delays are much less common. Despite this progress, there is ongoing concern that these effects of HIV persist, although more subtle. Leading to impairments in language, thought processing speed, memory and attention[250–254] – all important components of capacity and ability to consent.

Literature supports that adolescents older than 14 years old have the capacity for informed consent, both in medical decision making and in the broader sense of capacity of consent. This empirical evidence is informed from studies investigating adolescents' understanding and comprehension of information more broadly – specifically adolescents with pregnancy decisions and adolescents with mental health difficulties and impairment.[255–257]

Younger adolescents are more reliant on caregivers to provide consent for medical testing. Bringing into question caregiver/guardian/parental capacity to give consent for adolescents. Issues with parental consent have been demonstrated in social science and health research. A South African study investigating parental consent found that parental consent response rate to be 94%, while only 65% of parents received the information letter and consent form. Of the 18 participants who denied consent on behalf of their children, 14 actually wanted their children enrolled.[258–260] Poor comprehension and misunderstanding of consent is of particular concern in South Africa, where barriers such as language and cultural differences negatively impact consent.[258]

Transitioning in Adolescence

The adolescent age group is divided into early (10-13), middle (14-16) and late (16 and older). The early stage is defined by independence and dependence struggles, occurring at the same time as the rapid physical changes of puberty.[250] The middle and late stages are characterized by developing a scope of feelings and emotions, along with placing greater emphasis on peer relationships. This later period is also associated with more risk-taking behaviours.[261] Adolescents undergo dramatic physical, emotional and mental change during

puberty. While there is no clear correlation between a single aspect of pubertal development and increased association of TB testing, when viewed in unison - these changes together may add insight and comprehension why older adolescents are associated TB testing.

The increase susceptibility to TB among adolescents, in comparison to children, is not well understood, but is likely due to sex hormonal changes, increased social contact and immunological changes.[29] It is proposed that ALHIV may have delayed emotional maturity due to a reduced expectation of survival and independent functioning. This places greater emphasis on dependency on caregivers and parents.[262] Early adolescents generally made use of concrete thinking and reasoning, in comparison to older adolescents who make use of formal operational thinking. Evidence of this is that adolescents older than 13 years have shown to have a better understanding of HIV, disease progression, and are more able to conceptualise future consequences of present actions.[263] It remains postulation and future will be required, but these emotional and mental changes may be used to explain the difference in TB testing within the adolescent age group.

Living with HIV affects normal physical development during puberty. In a large study of HIV infected 6-18 year old persons, many experienced delayed puberty and adrenarche[264]. Furthermore, in a low resource setting, ALHIV are slow growers and stunting, wasting and being underweight is commonly found.[265] Adolescents typically present with more cavitatory disease and effusions – unlike children who present with intra thoracic lymphadenopathy or milliary disease.[42,266] This makes TB testing and expectorate coughing for TB testing more convenient and possible, as adolescents present with adult type TB and similar Chest Xray changes. Extrapulmonary TB is more common in children, and much more common in people living with HIV. This complicates TB testing, making the TB diagnosis more difficult, the symptoms more nonspecific and the sensitivity tests lower.[267] It has not yet been researched, although it stands to reason, that delays in puberty and physical development may halt the progression of TB disease present in a more adult manner and/or despite their age may be present more frequently with extrapulmonary disease.

Transition in care

The transition from childhood to adolescent care is a global health and social issue. Adolescents are known to struggle to adjust to differences in culture after leaving child services. Ending a long standing relationship between health care workers, safe and familiar environments and a change in systems.[268] An established transition theory – guiding interventions for transition to adult services for young adults with life threatening conditions, highlights 8 keys points which include early start to transition process and orientation of young adults to adult services.[268]This transition is fraught with challenges for ALHIV and is associated with loss to follow up, poor retention in care and poor adherence to ART. In stark contrast to developed countries, the transition period is offered suboptimal appreciation in South Africa. Two large South African studies, that included 460 and 951 ALHIV respectively, found that 19% of ALHIV did not have at least one clinic visit after transition and almost 65% chose to remain in paediatric care. 10% of the participants of the larger study who transitioned were completely lost to follow up.[269–271]

Transition from paediatric to adult care typically takes place between 17 to 19 years of age.[268,272] In South Africa, this change in care is not given a transitional period and commonly takes place at ages as early as 12. In support of this, the widely adopted Practical Approach to Care Kit (PACK) Child guidelines only includes scope of 0 to 13 years old. This early transition frequently results in a precocial jump to adult care that does not meet the unique needs of adolescents.[273,274] This period is becoming more and more essential as an estimated 320 000 ALHIV will transfer divisions of care by 2028 in South Africa alone.

In a natural experiment of children living with HIV in South Africa, a cohort of children followed the national policy of transitioning to adult care at 12 years old and a cohort remained in paediatric care. The cohort who transition had a 49% retention in care and the cohort that remained in paediatric care had a 92% retention in care[274]. This transition offers at least part of a reason as to why, over the duration of two years (T2 and T3), being a younger ALHIV is not associated with TB testing. Even more so, age of ALHIV was not statistically significant after step wise multivariate regression. At a cross section, adolescents would either be in paediatric care or adult care and not have transitioned in care.

Age related to Education

Age determined "appropriate exposure" topics related to HIV and TB are important in educating adolescents about these conditions. A significant portion of ALHIV were enrolled in school. Schools provide an excellent opportunity to engage ALHIV with learning about HIV and TB. HIV education, as part of the National Department of Basic Education National Policy of HIV, Sexually Transmitted Infections and TB, was introduced by the National Government as part of the life orientation curriculum. This included the introduction of scripted HIV lessons from grade 8 (typically between 13 and 14 years) , through to Grade 12 (typically 18 years old).[275] School is the most common source of information on HIV/AIDS and the most useful source for the majority of learners.[276] High School children with healthy literacy are known to seek treatment and educate family members. Learners who are aware of TB symptoms and transmission prevention, can seek testing and treatment for themselves and adults. There is proven association between knowledge of TB symptoms, transmission, prevention and health seeking behaviour for themselves and their families. Learners in higher grades are more likely to seek TB care.[277–279] Literacy is also found to influence health-seeking behaviour. Other studies have shown improved literacy is associated with less diagnostic delays.[277,280,281]

Comparison to other studies

Two South African studies, conducted in Cape Town and Gauteng, found that loss to follow up in TB care, TB deaths and TB outcomes were better among younger adolescents.[126,266] This allows the assumption that older ALHIV are better at engaging TB testing and care and worse at remaining in care. Another explanation is that fewer younger ALHIV are engaging in TB care and figures pertaining to this age group are underrepresented.

Perceived susceptibility: A greater number of younger (10-14 years old) ALHIV are in paediatric care,[282] which is perceived to offer a very high standard of HIV care in comparison

to adult care, building trust and relationships over the course of their young lives.[274] With good, regular healthcare the perceived susceptibility among caregiver and younger adolescents to develop TB may be less. The alternative is that adolescents and caregivers therefore bestow greater trust in healthcare workers and health systems to order a TB test if needed. Younger ALHIV have not entered the age when formal education on HIV and TB will take place at schools, through the Life Orientation curriculum.[275] This may impact their own awareness and realization of their susceptibility to TB. Using the Life Course Approach theory, older adolescents have had more time living with the risk of developing TB and cumulatively, through experience, have had more opportunity to understand their own susceptibility to TB. Younger adolescents are typically more reliant on caregivers and less autonomous than older adolescents.[242] [243,244] Their vulnerability and cares are more often supported and protected by care givers. This is a reliance and belief that care givers will take on and share responsibility of their symptoms and look after them, lowering their perceived susceptibility. Younger ALHIV are often reliant on concrete thinking and have yet to develop functional rational thinking, lowering their perception of susceptibility.

Elkind points out the characteristics of adolescent thinking: 'the imaginary audience'; that adolescents believe that they are always being evaluated and judged; the 'personable fable', the self-centeredness of the adolescent period; and 'apparent hypocrisy', which distinguishes between assumed bad motive and mental immaturity. Elkind's theory of adolescent egocentrism proposes the construct of the 'personal fable' to explain the perceived invulnerability and associated risk-taking behaviour of adolescence. The application of egocentrism to understand adolescent decision making was a landmark study in adolescent psychology. This theory has formed the framework for numerous qualitative and quantitative studies, that has taken theory into practice.[283] The modern relevance of this theory is demonstrated in a study of online risk taking among South African adolescents. The study found that higher levels of egocentrism (personal fable and imaginary audience) was a strong predictor of engaging in risk taking behaviour.[284] It must be mentioned that the critique of the theory is that it is not always generalisabile. It has been shown that only a few dimensions of personal fable followed the expected association with pubertal and cognitive development. [285]*Elkind's* theory of *Personal Fable* explains the lack of perceived susceptibility or invulnerability in younger adolescents peaking in grade 8 (14 years old). In support of this, Personal fables scores have shown to increase across grades 6,7,8. An offered explanation is the relevance of cognitive-social immaturity in addressing risk behaviours of younger adolescence. This effects not only perceived susceptibility, but also perceived severity.[283,286,287]

Perceived severity: It is known that all-cause mortality of TB increases with age[126] and higher levels of treatment failure occur in older adolescents. More specifically, adolescents and young adults with TB-HIV co-infection have poorer outcomes. Resulting in prolonged illness and disability for the patient as well as prolonged infectiousness of the patients causing continued TB transmission in the community.[15,126,288] As concepts of death and the severity of disease illness are being developed in younger adolescence, this may contribute to the perceived severity of disease. There are many other causes for TB symptoms, particularly in children and younger adolescents who frequently pick up respiratory infections. This may delay diagnosis and be seen as a perceived barrier, but also instil a false security that TB symptoms are attributable to another less severe infection.[289]

Perceived benefits: Older adolescents may greater perceive the benefit of having a diagnosis and an explanation for their symptoms. Also, being able to contain the disease and prevent ongoing transmission. Their most obvious benefit would be, by testing, that adolescents would enter TB continuum of care, start treatment, feel better and prevent long term complication allowing adolescents to live a normal life.

Perceived barriers: All the factors from the cross tabulation are applicable, but to highlight a few perceived barriers would include: living in a rural community and having to travel far to clinics or incur unaffordable costs, stigma associated with TB testing and being diagnosed, consent to testing and medico-legal hindrance, missing school, fear of health care workers, maintaining confidentiality and community violence.

Belief in a personal health threat: As older adolescents were much more likely to have exposure to HIV/TB education as well as being more likely to access basic sim card phones (chi squared $p<0.001$ across T2 and T3 on univariate analysis) to find important information. This aids in the understanding and perception of TB as a health threat. Older adolescents were also associated with being in a boyfriend/girlfriend relationship at separate time points ($p<0.001$ across T2 and T3 on univariate analysis). This speaks to how older adolescents tend to start thinking about how their decisions affect others around them – placing more emphasis on peer relationships in later adolescence. Along this train of thought, older adolescents also accept the responsibility of how not being tested for TB will affect their community and family. The abovementioned relationships may also be of a transactional nature – sexual intercourse in exchange for material goods, which have been linked to increased physical and sexual violence.[290]

Belief in the effectiveness of health behaviour: This can be explained by introducing the Theory of Reasoned Action. Martin Fishbein and Icek Ajzen developed the Theory of Reasoned Action in 1975 to determine the difference between attitude and behaviour. The theory can be used to explain and predict behaviour based on norms and attitudes. The construct of this theory begins with a behavioural belief, which forms the basis for evaluating behavioural outcomes which leads to attitudes that create subjective norms.[291] Having a motivation to complete a health behaviour is subjective to normative beliefs, motivation, and the expected outcomes. Older adolescents, and their widened social network, cumulative learnings, application of the life course approach as well access to information and education are generally more equipped to be motivated and have the intention to have a TB test.

Sex of ALHIV

Being a female was statistically significantly associated with TB testing at T3 and across T2 + T3 using multivariate analysis. Gender has been closely linked to HIV and is an important part of the fabric of the HIV epidemic in Southern Africa.[292] In turn, gender likewise plays a pivotal role in the TB epidemic. Female to male incidence ratio of TB in South Africa is among the highest in the world.[293,294]The feminization of the TB epidemic is related to the

HIV epidemic in Southern Africa. In a large South African study using National Health Laboratory Services (NHLS) – more female patients were tested for TB than males and accounted for an increasing proportion of all patients with presumed TB over the course of the study.[295]

While the overall male to female TB disease ratio in mid-to-lower income countries was 2.21 this ratio fell to 1.28 in the adolescent and youth age group. Furthermore, the male to female prevalence ratios were lower and demonstrated a female predominance in the setting of HIV.[296,297] There is a shifting demographic of TB to women. A previous study in South Africa found a female predominance under the age of 30, even more so in PLHIV. Active case finding of TB has shown to identify a greater number of young women with HIV associated TB[298]. Alarmingly, globally – HIV and TB co-infected women experience 20% higher mortality rate than their male counterparts.[297,299,300]

In terms of HIV care, women have multiple interactions with healthcare services, primarily due to child healthcare and free maternal care. There is also evidence that females are less impeded by stigma[301]. It is known that frequent contact with healthcare services, for any reason, may lead to improved identification and detection of TB,[302] offering an explanation for improved TB testing in females. Moreover, in a study comparing gender disparity among TB suspects in the Western Cape of South Africa, data suggests that there is a higher index of suspicion of TB among females that present to clinics than among males.[303] In South Africa, disparities in patient delay in accessing TB healthcare and provider delay (lack of index suspicion of detecting TB) between men and women are less responsible for the disparities in health seeking in comparison with Asian countries where women had longer delays in seeking TB care.[301,304] Studies have shown that women use more health services and go more regularly to seek healthcare than men, both in response to physical and mental health concerns.[305–308] In a large study of adults, women had significantly higher mean number of visits to primary care clinics and diagnostic services than men. This holds true for HIV services, among South African university students – it was found that women are more likely to attend HIV clinics than men.[309] Explanations include: reproductive biology, gender specific conditions, difference in health perceptions, reporting of symptoms and seeking help for the prevention and illness.[306]

The role of HIV as well as changes in behavioural, biological and structural risk factors offer an explanation of the rising TB burden in young women.[297] The age-sex trend of TB in South Africa correlates with other high HIV burdened areas, where more females than men are notified up until the age of 25.[143] More than 80% of patients with HIV associated TB are anaemic in South Africa, with 95% of cases linked to anaemia of chronic disease. In high HIV burdened settings, the prevalence of this type of anaemia is significantly higher among young women – supporting the hypothesis of an increased risk of TB among females in this age-group.[310] An important emerging biological risk factor is contraceptive use and related hormonal and immune related suppression. An example of this is the widespread use of Depo-Provera, an injectable contraceptive, in South Africa, which may contribute to the loss of oestrogen protection as well as an increased immune suppressive effect thereby increasing the risk of developing TB.[297,311,312] This is especially important in South Africa, where this injectable is the most common choice of contraception, especially in young

women, and half of all South African women of child bearing age are on contraception.[297,311,312]

Despite the paucity of research on TB in women, alcohol use and smoking have been identified as contributing factors to the rising prevalence of TB in young women. Both smoking and drinking are predisposing factors to developing TB. In comparison to much higher alcohol consumption rates in men worldwide, there is narrowing gap in alcohol consumption in South Africa. Similarly, there is an increasing prevalence of smoking in young women in South Africa and a narrowing of the sex-smoking gap. Smoking has been postulated to explain up to a third of sex differences in TB epidemiology.[313]

Peak TB prevalence in women occurs about 7 years earlier than men – which follows the peak incidence of HIV prevalence.[288,314,314] Part of the same large South African NHLS study – substantially more females were tested in the below 40 age group, including the less than 20 age group. It was found that more women were tested in the adolescent age group than males.[293] The changing patterns of TB testing between sexes and different ages are explained by the HIV epidemic and the rapid HIV disease progression associated with pregnancy and child bearing.[293,302]

With regards to gender differences in TB: Gender dynamics are key factors affecting the risk of becoming infected with TB and developing TB disease as well as access to health service, health seeking behaviour patterns and TB treatment outcomes.[315] A study from China found that women who experienced any TB symptom were significantly more likely to access health care than men.[316] A large study of South African adolescents found, relative to males a significant proportion of females desired to seek out general health services, counselling, and productive health services. Other African studies have confirmed that significantly more females access healthcare services than men.[317] Prior studies in South African have found that high rates of unintended pregnancies lead to women accessing healthcare to meet sexual and reproductive needs, abortions and antenatal care.[318–320] Other than these healthcare services, a reason to access medical care among adolescents was counselling for violence and physical abuse – where females are disproportionally affected. The most common reasons for South African adolescent girls to seek healthcare were to access general health services (a greater proportion than adolescent boys), counselling (considerably more than adolescent boys), reproductive health (a greater proportion than adolescent boys) and gynaecological health. In line with gender-based violence (GBV), the most common reason for hospitalization among adolescent girls was injury (sizably more than adolescent boys), TB(adolescent boys had a higher proportion – possibly explained by later presentation due to lack of TB testing) and obstetric causes.[321]

Complex social theory has been used to interpret the influence of sex on healthcare seeking practices across a number of health-related speciality fields. Perhaps the most prolific, and frequently applied to adolescents and youth, of these theories is Pierre Bourdieu's theory of habit. [322–324] Habitus as a concept exists in the subconscious and operates unconsciously. This represents a challenge when applying the concept empirically. To overcome this obstacle *Reey,2004* introduced a number of key elements: habitus as embodiment, habitus as agency, habitus as an individual and collective trajectories and habitus as past and present. These elements served as a framework to apply this theory to the dissertation's

findings. Pierre Bourdieu's concept of habitus and theory of habit states that habits are socially constructed and the embodiment of dispositions that generate actions and practices informed by deeply ingrained experiences of our surrounding culture and society. In turn, this orientates social practice and norms as well as lifestyles. Habitus is a compound of tendencies, gained through education and experiences. As an extension of the theory of habitus, Bourdieu introduced the important concept of a *practice sense*, allowing co-ordination of action in accordance with limits, constraints and available opportunities.[166,325–328] A gender-specific habitus is an identity that moulds individuals from the start of their lives; internalizing and externalizing the division and acceptance of responsibility of duties and labour between genders. According to Bourdieu, the social construction of masculinity and femininity shapes the body (and mind) and determines an individual's identity. Bourdieu goes on to theorise that masculine domination is the definitive mode of domination, using symbolic violence. Where symbolic violence is the outward display of a world view, informed by social order and anchored in the habitus of both sexes.[329–333] The concern of applying Bordieuan theories to these results is the reliance on broadly related literature to a unique population and setting. The quantitative analysis used in this dissertation is not tailored to understanding the interplay of the elements of habitus on its own. Qualitative analysis in conjunction with this dissertation's findings would provide stronger and more specific reasoning, largely removing the need for conjecture.

Masculinity

Masculinity is collective gender identity – not a natural attribute.[334] The gender relational axis is located in a much wider social, political, historical and economic context.[335,336]As much as there should be focus on why women more reliably seek healthcare services, it must be considered why men do not. Men typically have a longer delay in seeking healthcare, lower likelihood of remaining in HIV care and greater odds of deteriorating health after HIV diagnosis. It was found that stigma, fear and socially valued representations such has having strength, control, agency, earning capacity and being competitive, capable providers are threatened by testing for conditions such as HIV and are reasons for poor engagement with health services.[337–339340] These reasons are likely transferrable to TB testing.

In a qualitative study of Malawi men, care seeking determinants for chronic cough and TB symptoms were investigated as national surveys indicated a high number of undiagnosed men with TB, potentiating transmission of TB. It was found that the male gender contributes to poor TB control and outcomes. The paper applied two approaches to understanding this phenomenon. The first, a critical men's study approach – holding that gender is socially constructed and power relations are complex and fluid[336,338] and the effect of feminization and women's success in rebalancing power imbalance and shaping masculinity[338,341]. The study's findings were in line with recent literature that men's health has been influenced and often suffered direct consequences to assert control through competitiveness, aggression and physical strength.[336,342] A different and important perspective is the rising pressure placed on men and the failure to meet expectation is said to trigger a crisis response that drives risk taking and poor health behavior.[338,343–345] This same study found that men and women were in agreement that men should wait until symptoms were unbearable before seeking healthcare and that physical exercise will rid the body of illness.

Seeking help for "minor" health concerns was viewed as bad.[338] While studies hailing from Africa typically explore masculine control in the context of GBV, inequity, HIV/AIDS and sexual risk taking behaviours, there has been a more recent shift towards the vulnerability of African men and the psychosocial challenges related to HIV/AIDS and the pressures on the already poor and marginalized.[338]

South Africa is labelled as the country with highest statistics of GBV in the world. It is said to be the expression of toxic masculinity and gender inequality.[346] South Africa experienced a spike in GBV and femicide during the COVID-19 pandemic and ensuing lockdowns. The spate of GBV violence was described as the twin pandemic in South Africa[347]. Recent studies of school attending adolescents show that more than one in three adolescents experienced violence and a study reviewing women in South African data of over 12 years found that adolescent girls and young women were the most likely to report physical and sexual violence. One of the many consequences of GBV is long term physical and mental health problems.[68,348–351]

In an academic review of South Africa's unplanned pregnancies, South African men were found to display control over their female partners' contraceptive use and family planning. This opposition was attributed to male dominance, misunderstandings and physical abuse. In response, females either stopped using contraceptives or used it covertly. It has also been shown that adolescents girls were more likely to have older partners and typically unable to negotiate condom use. This is most evident in the "sugar daddy" phenomena.[290,352] There has been a normalization of adolescent motherhood in South Africa.[353]

Male adolescents are known to become disconnected from health services. Factors that have shown to reduce health seeking in male adolescents include: being an older adolescent, lacking knowledge and sources of information. Men are socialised to be tough, competitive and inexpressive. When this traditional masculine view was held in adolescent boys, they were less likely to use healthcare services.[354,355] In a related South African study, being male was associated with loss from TB care.[18]

Female role in African and South African culture

Women play an indisputably important role in African family life. To address the term "African" used here; the sociological demarcation is that race is a construct, but that the lives of the Xhosa adolescents engaged in the Mzansi Wakho study were shaped by apartheid structures of health and social living. Their "normative" roles are defined by a scope of duties that range from reproductive roles, raising children, looking after family members and caring for the sick. These roles have been entrenched by cultural and religious beliefs over generations in Africa's patriarchal society.[356,357] Because of these duties – the direct effects of HIV on women, having a disproportionate burden of HIV in South Africa and Africa and the indirect effects such as caregiving responsibility to young, old and sick, have diminished their skills and productivity.[358,359]There is an assertion that caregiving is feminized and women are socialized into nurturing roles. Around the world, females make up between 57% and 81% of informal caregivers. Importantly for this dissertation – these roles were taken on at a young age.[360–362] In a South African study, reviewing adolescent girls and female youth's participation in a combination HIV prevention programme (part of

the SA National Strategic Plan for HIV, STI and TB) among the significant barriers to participation were competing responsibilities, including family responsibility and childcare. As restricting as these responsibilities are, adolescents may be protected by these actions. Child caring, minding the elderly, as well as reproductive pressures bring adolescent girls to healthcare services – enabling and improving access to TB testing.

The prevailing social norms influencing reproductive decision making in South Africa is to encourage young motherhood in order to prove fertility. This belief is deeply rooted in traditional South African society, and stems from African culture, family and community.[305,363,364] Teenage pregnancy is common in South Africa and a serious health concern.[365] Among South African female youth across 4 provinces, 19.2% had an adolescent pregnancy while 5.8% of males indicated that they impregnated an adolescent girl, 16.2 % indicated that they had ever had an unwanted pregnancy and 6.7% had a termination of pregnancy.[366] Having children is an important part of the identity as an African woman and is expected as an essential part of a successful marriage. Married African women are said to experience excessive pressure to bear children, both from their husbands and extended family.[367] Furthermore, there is an understanding among African men and women whereby men work from outside the home and women are homemakers. This view was upheld in the context having a chronic cough and TB symptoms.[338] Reinforcing that their roles as women are to be at home. Discourse on "natural" mothering and a women's position as innate caregivers and men's duties by virtue of being providers and disciplinarians has exempted men from caring duties. This has contributed to the unequal gender construct passed down to children in South African homes.[368,369]

Applying the concept of habitus, social constructionist theory and impressionability to adolescence provides insight and offers an encompassing theoretic view into the explanation of why there is an association between TB testing and female ALHIV. Bourdieu stated that "habitus is understood as a system of lasting, transposable dispositions which, integrating all past experiences, functions at every moment as a matrix of perception, appreciations and actions.[333] Following Bourdieu's logic: adolescents' dispositions and outlooks are a function of their family, their surrounding inherited culture and place in society. The formation and embodiment of gender roles and expectations may be particularly impressionable on adolescents. As a uniquely vulnerable period, adolescents are easily reactive and sensitive to their external environments – shaping the formation of attitudes and behaviours.[370,371]

Friedrich Nietzsche said; "Facts do not exist, only interpretations." The social constructionist theory proposes that the social construction of gender and sexuality is based on power and control – with enduring discourse being an essential for gender inequality. It is this construction, rather than reality, that emphasises held beliefs and convention of health seeking behaviour among "strong" men.[372] As ALHIV are vulnerable to this influence in their own communities, it is natural that they too may adopt these social constructs as their own.

People learn from watching other people – this is the central principle of the social learning theory. The value of this theory has recently been shown by its applicability in exploring the effect of household violence among adolescents in South Africa. It was found that the influence of a parental figure is rooted in childhood, but imprinted in later development and

that violence was passed down and learnt from one generation to the next. [373]Social learning concept is most applicable to adolescents because of their impressionability. Psychologists have referred to impressionability as distinct to adolescence and young adults. The term impressionability refers to "changeability" and allows for an openness and susceptibility to public opinion, imitation and development of characteristics.[370,374,375]

My experience

The findings of this dissertation and the literature correlate well with what I have experienced in a clinical setting. In my experience, female adolescents seek out medical care sooner and are often in contact with healthcare facilities through accompanying family members, children and seeking treatment for gynaecological and reproductive concerns. If I am to generalise, female adolescents appear to be less resistant to having TB test and come across more candid about their symptoms. Females often ask about how having TB will affect the people they are caring for and concerned that they will spread TB or be too sick to function as a caregiver. Males, in comparison to females, tend to present later in TB disease progression and, are less open about their symptoms. Although it is conjecture, I am of the opinion that females are more likely to complete treatment, whereas males are more often lost to follow up during the course of TB treatment. These opinions are naturally biased by my experiences and where I have worked.

Being in a relationship

Being in a boyfriend/girlfriend relationship was associated with having a TB test. Interestingly, being in relationship over a two-year period or at a single cross section view had similar impacts on TB testing – shedding light on the value of adolescent relationships. Not only on "long term" relationships, but also their current relationship status.

Importance and value of social development in adolescence

Adolescence as a social period is defined by expanding peer networks, a greater emphasis placed on friendships and the beginning of romantic relationships. In this life period, close friends and romantic relationships overhaul parents as the primary source of social support and strongly contribute to an adolescent's identity and their well-being.[376–378] Adolescent relationships were once viewed as fleeting in nature, superficial and without substance and meaning – this has been unequivocally dispelled. Rather, these relationships are found to involve and provide meaningful support, intimacy and companionship.[378,379] Much of young people's time is spent being in romantic relationships or thinking and talking about them. As adolescents become more autonomous, they begin to rely more on romantic relationships.[380,381]

Much of the research on young adolescents has focused on intimate partner violence, psychosocial issues, sexual risk taking in the context of HIV/AIDS and unintended pregnancies.[382,383]. *Frizelle et al*. provides a warning: that recent literature has constructed a negative view on adolescent romantic relationships.[384] A South African reviewing the

construction of intimacy in adolescent relationships found that adolescents constructed their ideas of intimacy in line with mainstream adult discourses and norms that include an emphasis on mutual self-discourse.[385]

Linking relationships to health-seeking behaviours

In a study reviewing anxiety and depression in adolescents, it was found that adolescents that were not in a relationship were more likely to be anxious. While on the other hand, it was a predictor of depressive symptoms if adolescents were in bad relationships.[378] The study also posited that adolescents that experience community violence, unintended pregnancy, absent fathers and single mothers may look towards and identify with more idealized romantic relationships for positive relationship influences – to have futures different from people in their community.[386] Adolescents were found to value time alone to share their opinions and talk about themselves and their relationship – giving them a sense of closeness. This is slightly different from adult relationships, where this closeness or intimacy is more reliant on an emotional and abstract experience, bringing a sense of validation and understanding.[386] Relationship and dating experience is said to influence view on romantic relationship. Inexperience was associated with an idealized construction of romantic relationship and more experience related to seeing love as imperfect.[387] In relatively relationship inexperienced adolescents, this could contribute their willingness to share concerns and trust their partner with their concerns of having TB symptoms as well as taking on a new shared responsibility – to protect their partner from developing TB.

There is significant evidence of the benefits of social relationships to health. This dissertation primarily focuses on adults, but shows a decrease in overall mortality and provides compelling evidence of protection from serious illness such as cardiovascular disease and cancer.[388] Reasons for improved health outcomes and improved prevention of disease relates to behavioural and psychosocial explanations.[388] Relationships and strong social ties have been linked to positive health behaviour over a ten-year period – in part because of an influence on health habits. Spouses have been found to promote partner's health by providing and sharing information and creating health norms. These relationships foster a sense of meaning and purpose in life.[389–391]

Having a TB test and having knowledge of TB, according to a South African study among adolescents and young adults, was associated with being female and having a family member with TB.[392] This brings forward two noteworthy considerations. The first, along with the findings of this dissertation's own work, that TB testing is associated with female ALHIV. It stands to reason that in close relationships, females can influence their male patterns to have a TB test. As TB is attached with its own stigma and fear of displaying symptoms, particularly among men where health seeking and being ill is considered weakness, being able to share their symptoms in a safe, trusting confidential space will likely contribute to TB testing. [162,337–340,393] There is no available research on TB testing and stigma in adolescents, but a paper researching mental health in adolescence, found that adolescent boys have similar apprehensions about their role in society – that they need to be successful and strong. It was also shown that adolescent boys are less candid with sharing their concerns than adolescent girls.[394]

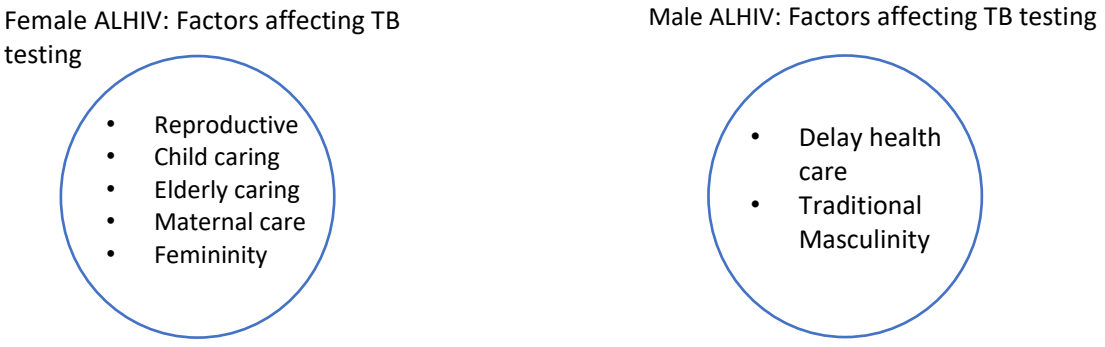
The importance of trust and confidentially has been highlighted to be a crucial aspect of adolescent care, influencing adolescent TB and HIV care and testing. This is exampled by the success of adolescent specific, youth friendly HIV and TB care services where the principles of trust, confidently and non-judgment are the bedrock of the service.[395] Furthermore, adolescence is a time defined by the importance of peer evaluation, social contacts, social status, and social capital.[396] Having someone close to confide in becomes even more important when struggling with symptoms and the social pressure of the age.

Social Action theory and a social contextual view

Max Weber's Social Action theory can be applied to this dissertation. The 3 relatable aspects of his theory are: empathetic study helps to understand human action and social change, it is possible to make generalisations about the basis of human motivation and relationships and societies encourage certain behaviors.[397] A Social Action view underlines a social interdependence and interaction and understands that the relationship between social and personal empowerment affect self-change.[397–399] This theory has been used to successfully inform family-based interventions to address HIV risk and care among adolescents in South Africa.[66]

Ewart explains that a social contextual view asserts that the ability to regulate action is a function of close, personal relationships. [400] It is said that if a valued relationship is thought to be negatively influenced or threatened by disruption, the outcome is dependent on the collaborative and conjoint problem-solving capabilities of both persons in the relationship. Further research on social support shows that having close relations, typical of that between spouses, is central for people to feel adequately supported and to cope with health challenges.[398]

Figure 9 - Relationship status: Whether ALHIV has a boyfriend and or girlfriend



Viral load testing – indication of retention in HIV care:

Having a viral load test each year, for the 2 years across T2 and T3, was associated with TB testing in the multivariate regression model and serves as an indicator of Retention in HIV care. This shows the importance of being retained in HIV care for an extended, sustained period of time as well as at a single time point. Viral load testing was also associated with TB testing at the cross section of T2. Perhaps there is more to this – suggesting that there is a threshold amount of time required to be in HIV care to have an effect on the odds of having a TB testing.

HIV retention in care is defined by the WHO as the "continuous engagement from diagnosis in a package of prevention, treatment and care services".[401] Using the association of viral load testing as proxy for retention in HIV care, neither the individual factor of missing a clinic appointment nor last week adherence was statistically significant in association with TB testing. This uncovers a paradox. As being retained in HIV care, not missing clinic appointments and good ARV adherence is considered protective against developing TB, with ART offering 65% protection against developing TB disease, regardless of CD4 count. [84] Why would there be an association with TB testing in ALHIV who are retained in HIV care and therefore presumably less at risk?

Importantly, factors associated with HIV adherence in ALHIV have a much greater body of research from which to draw on than TB testing in the same group. It is reasonable and justified to explore if the same factors that are predictive and associated with good adherence to ART are translatable to TB testing in ALHIV. There is also this dynamic to be considered – that ART adherence and not missing clinic appointments are part of an essential steppingstone or cascade necessary to have TB testing.

Factors associated with HIV adherence and missed clinic visits

The highest risk of non-adherence of all age groups exists in ALHIV. Factors that are associated with improved adherence are: having a guardian present at each clinical encounter, feeling free to ask questions to healthcare providers and having group sessions lead by professionals. Logistical issues such as costs to get to clinics, waiting times and expectations to have frequent visits were found to have a negative association with ARV adherence in ALHIV. While the logistic concerns were not central to this dissertation, one of the factors pertaining to travel, cost of travel to the clinic, was found to significantly effect TB testing. Poor adherence to ARVs were associated with being male, an orphan, poor mental health and having missed a clinical appointment; while being female, making use of drugs and not being socially supported were associated with missing HIV clinic appointments.[402–405] These factors are relatable to the significant factors associated with TB testing and provide further evidence that TB testing is part of the package of HIV care and should not be neglected in ALHIV.

Health service TB screening

It is standard practice in South Africa that each PLHIV must be screened for TB at each clinic visit and a test ordered if there are any TB symptoms present.[224] While the literature shows

varying levels of TB screening across different age groups, TB screening was found to take place in 75% of all HIV clinic visits in high burned HIV/TB countries in Africa. In ALHIV patients who miss appointments, it is possible that TB screening and active case finding does not take place when they did attend. This is made more worrying by atypical presentation of TB in ALHIV because of HIV co-infection, extrapulmonary TB and their age. It is said that 150 000 TB cases are missed in South Africa each year. In a review of South African adults living with HIV and not on ART, 47% had at least one TB symptom each time they visited a clinic.[51,116,406,407] It is important not to forget that TB testing is required to enter the next step in the TB cascade, starting treatment. In another South African study, 1/5th of TB patients were lost to follow up after their diagnosis.[408] There are fallout points with each link in the TB care cascade chain, but by not attending appointments – opportunities are missed to enter TB care at all.

In further support of how clinic attendance and adolescent involvement and ownership of their own healthcare is associated with TB testing, adolescents that answered that they had a viral load test in the past year demonstrated knowledge about important surveillance tests that they had and the significance of those tests. This not only shows education about HIV, and in the same light TB, but also that they were able to book a date to have a blood test done and report to the clinic to have the test performed.

Health care workers, Broken glass concept – personal view

Not taking ART is associated with developing TB symptoms. Yet taking ART and attending clinics are associated with TB testing. The paradox. Experience and work has taught me that healthcare workers are not above the basic human feeling of acknowledgement when their message has been received, understood and acted upon. [409] When discussing ART and imparting their importance, healthcare workers are in effect hoping that what they say or do influences a patient's behaviour, for the better. When a patient comes back to the see the doctor and they have taken on previous advice, there is reward for the healthcare worker, hopefully, although normally – the patient too feels better/their disease markers have improved. This reward is why many people choose medicine as a career path.

When someone returns, not having taken their ART or having missed an appointment, healthcare workers are left feeling a sense of disappointment and often, unfairly, label the patient a "defaulter" – which only further stigmatizes someone. If this happens repeatedly, the onus of taking responsibility for their patient's health falls short on the patient's side, as the healthcare provider knows that they could not do more. When patients adhere to their medication and keep appointments, the patient is doing their part and the onus to find a solution remains with the healthcare worker.

I think of it as similar to the broken glass concept. Wilson and Kelly, 43 years ago, described this concept with an example. "If a window in a building is broken – all the other windows will soon be broken". The broken glass theory was first used in the field of criminology and built on the premise that visible signs of anti-social behaviour, crime and civil disorder encourage ongoing wrongdoing – leading to more serious crimes. There is already evidence to support the application of this theory in fields other than criminology, including healthcare. [410] A recent study of healthcare work settings in Australian hospitals is among

the first to move from a theoretical consideration of this theory to provide empirical evidence. The study concluded that a positive, orderly and productive culture leads to better wellbeing of staff and care for patients. Despite the field of application this theory has, however, been met with criticism as academics have outlined the fault in the lack of a clear causality.[411] To use this theory in unpacking the healthcare patient relationship introduces significant bias and should receive justified critique. It contradicts good clinical practice and treating everyone equally, but in practice I have experience that a patient who defaults and despite their best efforts is unable to adhere to treatment or keep appointments, will fall into the category of the broken window. A patient who does adhere, attend clinics and does their part will experience the opposite. Healthcare workers tend to treat a person with "no broken glass" with greater care and respect and often with more urgency.

Factors with an indirect association with TB testing

Several of the factors which were associated with increased TB testing were most likely to result in more testing via increased risk of TB exposure and infection. These factors included experiencing community violence and living in informal housing.

Migration and rapid urbanization have brought challenges to infrastructure and housing in South African. Creating an environment with immense population density; rife for the spread and airborne transmission of communicable diseases such as TB. Overcrowding, poor ventilation and HIV exacerbate the high level of TB in these environments. In one South African study, a participant described these settings saying; "TB is found in every house". In a systematic review on the impact of upgrading the infrastructure and services in these environments, it was found that there were noticeable improvements in both health and well-being of residents[412]. There is an interplay in these spaces between hazards and vulnerability, where crime, violence, unemployment, and poor social security commonly interact in South Africa – creating a poverty trap.[412–414]

While living in informal housing follows reasoning in explaining an increase in the burden of TB and thereafter the need to test for TB, another aspect may be that healthcare workers serving those areas may also be less reserved in testing, knowing the ALHIV's living condition. Background and living conditions are part of standard history taking and vital in helping to guide testing and diagnosis.[415] A patient's demographics and history are still among the most essential parts of a medical consultation. There is limited research on the influence of experiencing community violence and TB testing. This paves the way for further exploratory research to explain this association. One possible explanation is that experiencing community violence could be a proxy for the community environment, where violence is common and a product of circumstances. Again, signifying a high TB burden area.

Food security

Food security was associated with TB testing at T2, using multivariate logistic regression. ALHIV are particularly affected by food insecurity and resulting hunger, impacting their ability to adhere to ART,[416] which in in turn predisposes them to TB. In a review of South African adolescents, 78% reported medium to high level of food insecurity.[417] Through varying pathways, including malnutrition and an association with high risk behaviours, food insecurity is associated with TB disease. Moreover, undernutrition has been linked to postponing health seeking and delaying treatment initiation. In further support of the importance of food security in accessing healthcare, social protection in the form of nutritional support has shown improved TB adherence and TB treatment completion rates. Studies have demonstrated how cash transfers to a TB population has a positive impact on their ability to access healthcare services.[418–420]

Social protection measures for HIV adherence, retention in care, testing and improving outcomes among adolescents are significantly more researched than TB.[61,62] Leaving an opening for future research. However, *Cluver et al.* provides evidence that social protection is associated with significant risk reduction among adolescents across the Sustainable Development Goals, but specifies that social protection had no effect on tuberculosis burden. [65,98]

Food insecurity has come to fore during the COVID-19 pandemic and ensuing levels of lockdown. In the early months of the COVID-19 pandemic, almost half of respondents in the South African representative NIDS-CRAM survey indicated that they ran out of money for food. Alarmingly, school closures left many adolescents without access to school-provided psychological, social and nutritional support [83], which includes over 9 million South African students who are supported by the National School Nutrition Programme (NSP).[421] While being food insecure, and as a result undernourished, follows reasoning that these ALHIV are more at risk of TB disease; the social implications of being food secure are protective and improve access to TB testing. In this way food security reveals itself as a target for potential social protection interventions.

Access to a sim card/cell phone

Having access to a basic sim card phone was associated with TB testing at T2, using multivariate analysis. There is a growing interest in the use of mobile phones to help adolescents access health information and engage in health services.[422] Many South African adolescents and youth fear HIV clinics and visiting healthcare practitioners, citing stigma and unwelcomed clinical examinations. Even if they overcome these feelings and decide to go the clinic, they encounter barriers to access. Mobile health services offer acceptable, cost effective, easily accessible adolescent tailored services. In a South African study of adolescent and youth, mobile clinics were successful in engaging males and linking them to healthcare services, a cohort conventional clinics have struggled to engage with.[423] Mobile phones are known to improve access to health information and improve awareness of

services. Promisingly, the mobile phone infrastructure is the preeminent infrastructure development in Africa – by far exceeding roads and water.[424]

Success of mHealth

In a randomised control trial undertaken in Cape Town, mobile phone reminders and text messages containing healthy habit information to control blood pressure had a marked effect on the intervention group's clinic attendance.[425] *Maraba et al*. implemented an mHealth study in South Africa where an application was created to capture patients' TB investigation data, give TB test results and monitor treatment initiation. The study showed that the mHealth application was feasible and acceptable to both healthcare users and patients and had the potential to reduce the time delay to initiate TB treatment and prevent loss to follow up from primary health care services. This intervention moderates both patient related factors and clinic factor delays to accessing TB care.[426] Mobile phones have been found to be well suited to promote knowledge on HIV/AIDS and TB – overcoming geographical isolation, stigma and improving access to play a significant role in adherence to ART.[427]

Social cognitive theory

The social cognitive theory proposes that health behaviour, in this case TB testing, can be altered by knowledge of health risk, benefits of change, self-efficacy, outcome expectations and solution finding. It is built on the construct of self-monitoring and self-motivation to influence health behaviour. Having access to a sim card phone provides access to all these aspects. This theory also instils a belief that a person has control over their own health, including finding solutions to perceived barriers and therefore their ability to be tested for TB.

Bandura, the founder of the theory, envisaged that Social cognitive theory would serve as regulatory delivery system for technology-based health interventions. Cell phone use allows access to knowledge of TB, anonymously, without fear or stigma, to engage with multimedia information sharing that has been proven to enhance understanding, establish social connections and learn from the examples of others by reading their comment and remarks.[428,429430]

Transport costs and living rurally

Having to pay more than R10 to get to clinic was associated with NOT TB testing at T2 and Living in a rural area was associated with TB testing at T2 on multivariate logistic regression. These findings are at odds with each other. It would be a fair assumption to think that living in a rural area would be a barrier to TB testing and for those same reasons to apply to having to pay more than R10 to get to clinic as a barrier. In this dissertation this was shown not to be the case.

Living rural associated with TB testing

Living rural is associated with a lack of access to the clinic and a lack of transport and it has shown that barriers to TB care among rural residents is the slow process involved in diagnosing TB.[431] The lack of available transport may explain that adolescents living rurally did not face the transportation costs that proved to be a barrier to TB testing at the same time point. The slow process in diagnosing TB, along with other health challenges such as HIV testing in rural communities, has been addressed by the use of mobile clinics in South Africa. The success of mobile clinics may provide a possible explanation for the association between ALHIV living rural and TB testing. Research shows that mobile clinics are better at reaching youth (less than 25 years) than primary care clinics.[432,433] In a South African study, 90% of adolescents and youth rated their mobile health clinic experience better than conventional clinics.[423] Mobile clinics offer a solution to people living in districts that are difficult to get to. These clinics have been shown to facilitating HIV testing and healthcare accessibility to people in these areas as well as high risk populations.[434–437] In a South African study reviewing linkage to HIV care following HIV testing at a mobile testing unit in underserved areas, 20% of people who tested positive for HIV, screened positive for TB. This demonstrates the value of mobile units in identifying, previously unknown people, who need to be investigated for TB. Furthermore, newly diagnosed HIV positive people who had TB symptoms were more likely to link to care than those without TB symptoms.[434]

There is literature to support that there is considerable effort being made to implement active TB surveillance in the Eastern Cape of South Africa. In a review of active case finding, both governmental and non-governmental organizations adopted the National Department of Health's active surveillance program for high-risk populations. The local government and non-governmental organization have gone as far as employing community healthcare workers to go door to door to identify TB cases.[438] Perhaps these programs are coming to fruition, or it may be political window dressing.

A different viewpoint to understand this finding is that there is less risk of developing TB in rural areas than urban areas, due to overcrowding. Despite the burden of TB being less, loss to follow up from TB care has shown to be higher in rural areas, likewise with the number of people who develop recurrent TB. A study in Zambia found the risk of TB loss to follow up twice as likely in rural residents than their urban counterparts[439,440]. It will require further investigation of the rural residing ALHIV and whether incomplete treatment, loss to follow up and recurrent TB and re-testing as a result thereof plays a role in their association with TB testing.

Cost to get to the clinic and TB testing

Despite TB diagnosis and testing in South Africa being free in public health facilitates there are substantial direct and indirect costs to consider. It is important to grasp the economic burden associated with TB illness in South Africa. Minimising the cost of TB care is a central part of the global strategy to tackle TB the world over. A South African study found that the greatest costs to the patient was incurred before the initiating of TB treatment, including TB screening and TB testing. It was cited that transportation cost became a barrier in TB care as the diagnoses of TB required multiple visits. As such, transport became a significant factor in determining the catastrophic cost to the individual. [441] *Mudzengi et. al,* in a cross sectional

study in South Africa, found that PLHIV and TB incurred greater costs than people with only TB and among the greatest barriers to accessing TB care in vulnerable homes was transportation costs. [442] The cost of transportation in South Africa is said to be significant barrier to care, especially to those reliant on their parents for financial support.[443]

Knowing that transportation cost is a barrier to care, this dissertation has taken a step further by also quantify the amount of money for transportation that was associated with not accessing TB testing. A possible consideration for future social protection measures could consider allowing ALHIV and caregiver with a clinic appointment a transport cost waiver. In "Rurality as a root of fundamental Social Determinants of Health", it is said that *place* contextualises health and that geography plays a role in evaluating access to health services. The Theory of Fundamental Cause draws attention to the interconnected nature of available resources as a product of the historical and sociological persistence socioeconomic status. Living in a rural environment and the cost of transport to access TB testing, meet all four of Link and Phelan's Theory criteria to determine a fundamental social cause. To quote criteria number 3: " It impacts access to resources that may be used to avoid risk or minimize the consequence of disease" – a certainty for the factors of living rurally and the cost of transport to access TB testing for ALHIV. [159,444,445]

TB symptoms

Having TB symptoms was associated with TB testing at T2, T3 and across T2 and T3 using multivariate analysis. Regardless of age, presenting to a healthcare facility with TB symptoms requires further work up for TB – even more so in ALHIV.[219] It is understood, and expected that healthcare providers will use the diagnostic TB algorithm and refer appropriately.

Success and failures – snapshot of a bigger picture

It is encouraging that TB symptoms are associated with TB testing at all time points investigated – indicating a success of healthcare services and of healthcare providers. While this is a success, analysis showed that more than a third of ALHIV who had TB symptoms at T2 and T3 did not access TB testing. Bringing to attention the need to improve current systems and adapt linkage to care mechanisms to protect all ALHIV.

These findings suggest that being ill (having clinical features of TB) either forces or creates an urgency for an ALHIV and their support structures to overcome their barriers to care. This is not possible for all ALHIV who, despite expressing TB symptoms, remain inhibited by their experienced social determinants to access TB testing. This dissertation does not speak to possible delay from TB symptoms to TB testing as well as whether the ALHIV received their result and consequently started on treatment.

Policy to provision

There is a shortcoming in the implementation of TB healthcare policy in South Africa, despite the South Africa Youth Policy's objective of comprehensive and integrated TB services.[91] Three important South African studies evaluated the implementation of the TB diagnostic cascade and guidelines at a primary health care level, where the majority of TB cases typically present. These studies further expose the magnitude of the diagnostic gap in South Africa. *Kewza et al.* estimated that predominately nurse run primary care facilities miss between 62.9% and 78.5% of patients seeking care for TB symptoms.[446] *Claasens et al.* reported that in similar Cape Town clinics, only 8% of individuals with TB symptoms were screened for TB.[447] *Chihota et al.* found that 22% of symptomatic TB patients were requested to send sputum samples.[448] This shortcoming is not isolated to South Africa. The term "know-do-gap" summarises this concept best and has been shown in a study as far afield as rural China – where healthcare workers scored well on clinical vignettes in detecting TB symptoms and referring for testing, but only 41% of patients with TB symptoms were appropriately referred in reality. [449] This was emphasized in a paper by *Naidoo et al.* on the number of drop off patients in the South African TB care cascade. It was shown that an improvement in the implementation of existing polices is required to close the prevalent gaps in TB diagnosis.

In "identifying contextual determinants of problems in Tuberculosis care provision in South Africa: a theory generating case stu*dy", Murdoch et al.* highlights the challenges of aligning policy of the clinical aspects of care with social and structural drivers of TB. The review concluded that the overarching problems of delayed diagnosis, limited psychosocial support for patients and staff are as a result of interdependent contextual determinants, including policy and vertical care provision (where TB services are not integrated into general nor HIV services). The authors urge TB policy to resolve the tension between managing TB as national epidemic and a person centred approach.[273] In a study conducted in South Africa to determine the poorly understood systemic drivers of TB mortality, it was found that TB policies were not enacted due to a lack of leadership, the current organizational structure, unequal financing and limited human resources.[450] Improving implementation of polices is seen as a driver to better TB care in South African. To do this, there is a growing body of evidence to integrate TB services into general and HIV services to improve TB case detection in HIV-TB co-infected patients.[451] This dissertation addresses service integration as it is inherent in the research question. By asking about TB testing in ALHIV, you are really questioning how to bring together HIV and TB services and access.

It is worth contemplating if ALHIV in the dissertation admitted to TB symptoms in the questionnaire, but not to healthcare workers, for fear of stigma or other personal reasons. Furthermore, healthcare workers may have neglected to ask specifically about TB symptoms. In my experiences, it frequently occurs that unless prompted and skilfully navigated to ask important questions, adolescents will not readily offer up symptoms. This happens more regularly because adolescents are pre-occupied on another aspect of their health rather than adolescents not being willing to disclose information. This presents the discussion of responsibility and the healthcare worker – patient relationship.

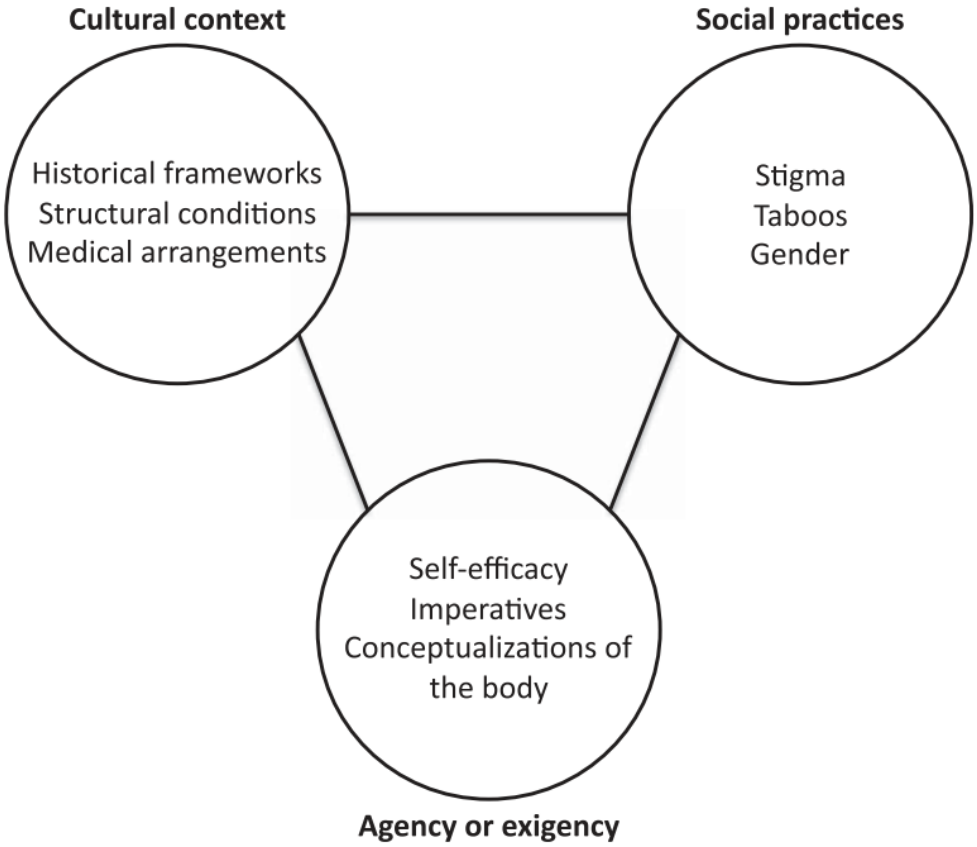
Language and expression of TB symptoms

The vast majority of people living in the Amathole district are Xhosa speaking[194] which could influence expression of symptoms to healthcare workers and the healthcare workers

interpretation of those symptoms. It was found in a South African cohort of Xhosa speaking parents of children admitted to hospital, that language and cultural barriers were more of a challenge to healthcare than structural and socioeconomic barriers. Patients in South Africa are not often seen by practitioners that share a language, making it difficult for patients to understand medical advice, to express themselves or to ask questions.[452] Patients then blame themselves for the breakdown in communication which leads to parents being concerned of the negative effects on their children's care. African languages have a low literacy achievement in comparison to English and Afrikaans [152] and the Eastern Cape has the 2nd lowest literacy achievement amongst grade 4 leaners in South Africa. This is of concern as the WHO and National TB guidelines, posters, informational handouts, algorithms and videos are all presented in English. Any distribution of this information in African languages is not readily available and subject to the effort of the healthcare facility or healthcare personnel to translate the work. This can create disparities and inconsistencies between the use of guidelines and the health information given to healthcare workers and patients. This could negatively affect TB screening and the treatment cascade to TB testing and treatment.

Relationship with healthcare workers

Figure 10 - Theories of patient care



Mason PH, Roy A, Spillane J, Singh P. SOCIAL, HISTORICAL AND CULTURAL DIMENSIONS OF TUBERCULOSIS. J Biosoc Sci. 2015;48(2):206-232

Mason et al. uses the above image to show that the failings of TB case detection are due to varying interconnected factors.[453] Remarkably, these factors are imperative ingredients in the healthcare worker patient relationship, which is essential to TB case detection.

The description of "doctor-patient" relationship is commonly used in literature, but it needs expansion to include all healthcare workers, as varying levels of care are provided throughout healthcare in South Africa. This relationship has evolved and transitioned along with society – once paternalistic has now become person-centred. Three models proposed by Szasz and Hollander describe this relationship: *Activity-passivity*, which is entirely paternalistic; *guidance-co-operation*, being aware that a patient is more than an illness and is a person with a consciousness and feelings; *model of mutual participation*, based on equality, power sharing and mutual independence. This model is the patient centred model and is the ideal model strived for today, whereby responsibility is shared between patient and healthcare worker – exposing a potential flaw.[454,455] If it is a shared responsibility, who is responsible for eliciting the sharing or identification of TB symptoms – the ALHIV or the healthcare worker? If an ALHIV does not share that they experienced TB symptoms, does it fall on the healthcare worker to take on more of the responsibility? Another consideration is presented: is responsibility age-dependent and does the degree of responsibility entrusted differ with age, socioeconomic factors and insight? In my experience, adolescents will not willingly withhold information. The very more likely reason is a preoccupation with a related but not telling feature of disease, for example loss of appetite. This ethical conundrum is resolved by applying the guidelines and policies with discipline. Responsibility should perhaps be trumped by duty – which falls on all healthcare workers to screen ALHIV for TB and to ensure they are tested or referred appropriately.

Concise policy and program recommendations

This research shows the importance of TB screening in ALHIV. Furthermore, it exemplifies the value of slightly broader screening questions that include all levels of the ecological framework. Examples of these questions include: How do you obtain health information, how do you get to the clinic, what is the cost of coming to the facility, do you have enough food to eat at home, are you in a relationship?

A number of social factors that ALHIV experience that influence their ability to test or their vulnerability to developing TB have been identified. Investigating or incorporating these factors into the standard TB screening can offer a more sociological approach to TB screening. It will also allow for social factor focused TB risk stratification, guiding which measures to put in place to protect at risk ALHIV and provide support in overcoming challenges of access. This may help to contextualise the ALHIV. This coincides very well with the aim of the People Centred model, of putting the individual at the forefront of TB care by addressing health needs, tackling determinants, empowering and engaging patients. This research lays the foundation for both a policy shift and as a result, development in the TB program package offered to ALHIV. At the very least, bringing attention to ALHIV and TB.

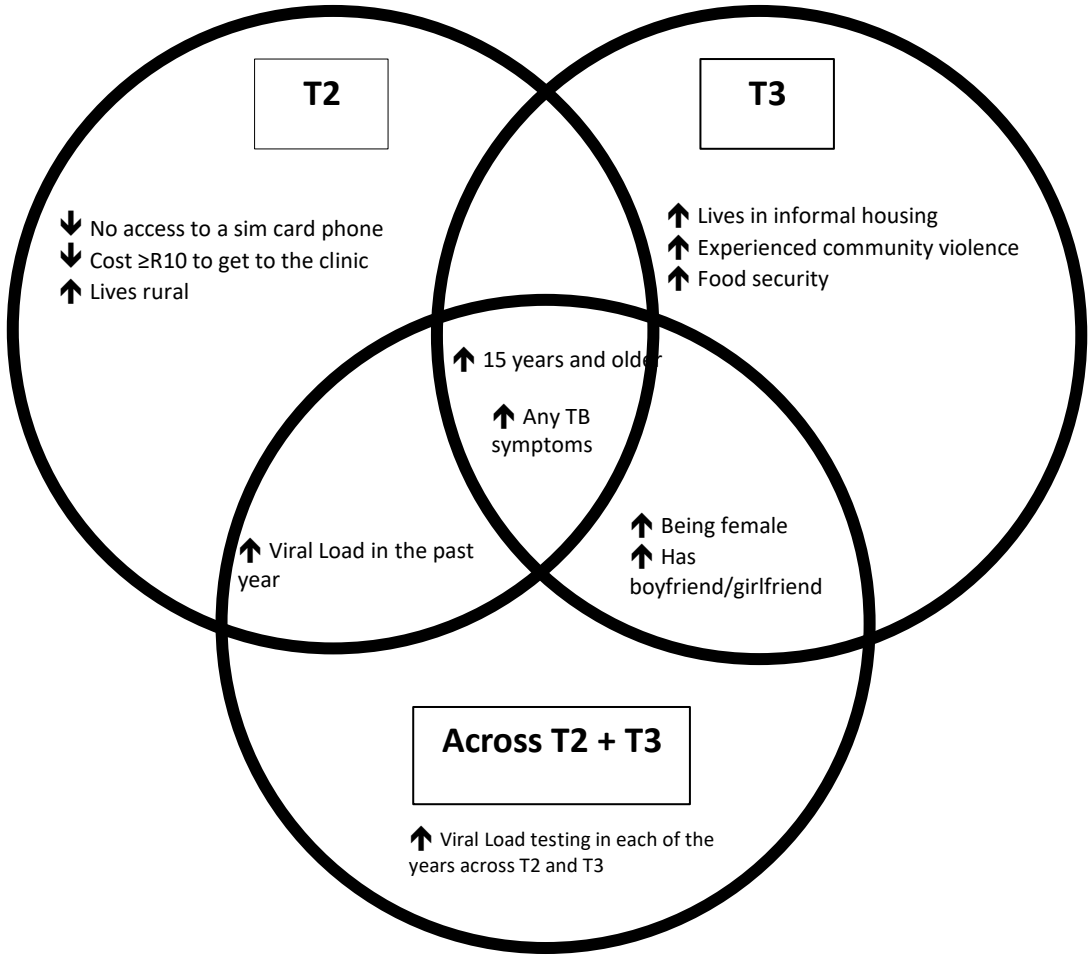
This research put the individual at the forefront, endeavouring to identify challenges to TB care access both at cross sections and across time. ALHIV with an increased HIV viral load have a greater risk of developing TB and should be flagged, followed up and if needs be mobile tracer units created to re-engage ALHIV with HIV care. Identifying the cost incurred by ALHIV to get to the clinic and whether or not the ALHIV has access to a sim card – are examples of barriers to TB testing that were not proven before. We have shown that individuals at high risk can be identified through questioning about experiencing community violence and living in informal housing. This research provides evidence to support these risk stratification questions which will allow for targeted programmatic interventions.

Future research areas

This work has laid the foundation for future, subsidiary research projects. While the factor selection in this work was guided on a broader research of adults and children, as there was little known about ALHIV before this dissertation, future studies will be able to cite this research as adolescent specific and compare findings. Perhaps an interesting research paper would be to compare which factors influence TB social testing among vertically and horizontally infected ALHIV. Alternatively, the data available continues further in the TB cascade to include TB testing and the results thereof. This may lend itself to creating a socially-aware screening tool that can support identifying positive TB cases by better targeting TB testing, in conjunction with TB symptoms.

CONCLUSION AND OVERARCHING THEMES

Figure 11 - Summary graphic of statistically significant factors after multivariate regression



Decreased association with TB testing

Increased association with TB testing

If one compares the social factors identified at the cross sections of each interview, having TB symptoms and being 15 years and older were the only significant factors at both time points. This could suggest that factors that prevent access to TB testing change at different time points in an ALHIV life. This alludes to the fact that even though certain factors are present or encountered they may be overcome at one point, but at another they may not – then preventing access to TB testing. It is the adolescent's access to resources: social, financial, environmental, family, community and relationships at a specific moment in time that supports and enables them to manage barriers; while at another point, they may lack the means. Their structures of social protection measures are interconnected with their family, relationships and their community. The ability of the individual ALHIV to meet and overcome these potential barriers is linked to the available support of these structures. When ALHIV are unable to access TB testing, it is a combination of certain imbalance of "prevention" factors and a lack of "promotion" support factors experienced and accessed by ALHIV that pass a unique threshold that renders an ALHIV incapable of navigating a barrier to TB testing.

A Life Course approach

The Life Course approach offers an encompassing view and allows an incorporation of the themes identified from this dissertation. ALHIV have been moulded by their experiences and what they have learnt from their families, communities, environments and societies. The norms, expected reactions and ways to govern themselves and manage their lives are a product of the sum of their experiences. Their development into young adults has been shaped primarily by close relationships. Either by their own relationships, or the relationships they have witnessed growing up. As ALHIV mature, the culture and viewpoint of their families and close relations are instilled in them. For the good or bad.

CONCLUSION: The story and next steps

In this Eastern Cape cohort of ALHIV, factors linked to where ALHIV live (living rurally, cost to get the clinic more than R10, informal housing and experience community violence), who they are (age, sex,) and their close peer support (being in a relationship) have shown to strongly influence TB testing. TB exposure risk related factors (rural residence, informal housing, unsafe communities) was associated with TB testing while protective factors that improve TB testing such as having access to a cell phone and being in a relationship came to the fore. The instilled South African culture of gender norms and how we live explaining healthcare access was evident in ALHIV. The independence of older age found importance in ALHIV ability to access TB testing.

This dissertation brings to light essential knowledge on social factors that promote or prevent TB access in ALHIV and provide reasoning grounded in sociological theories to explain their significance. This knowledge can be used to support efforts to target TB testing in ALHIV, promoting entry into TB care and preventing ongoing transmission of TB in South African homes, schools and communities. This dissertation has the potential to enhance the current HIV services package offered to adolescents by creating an awareness and a risk profile of adolescents that may or may not be able to reach TB testing services

The work of this dissertation is steppingstone to reaching the targets set out by WHO's END TB strategy and the STOP Partnership Global Plan, as well as fulfilling the mantra of the combined global effort lead by the WHO to Find.Treat.All. It responds to the call, set out in the WHO's "Roadmap towards ending TB in children and adolescents", to make adolescent TB a priority in high burden countries. This dissertation can also guide interventions and social protection to meet key objective 3, relating to TB testing, of South Africa's National adolescents and Youth policy.

This dissertation has laid the foundation for further study in each of the factors identified. I have ended with more questions than answers. The why of each identified variable can be explored in relation to this data set and the aforementioned sociological frameworks can be used as an approach to understanding the importance of each variable. Furthermore, the discussion section presents hypothesized links between factors from other relatable studies – it will be well worth revisiting those hypotheses and either supporting or offering a different explanation for their importance.

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ADDENDA:

All variables included as factors influencing TB testing are easily understood. However, certain variables may need brief elucidation.

Table 11 - Explanation of certain variables used as factors

Variable/Factor	Explanation
Food secure past week	Had access to 3 meals a day, had enough food each day in the past week
Missed school for more than one week	Missed more than a week of school in the last year
Experienced internal Stigma	Experienced any internalized stigma
Experienced External Stigma	Experienced any enacted stigma
Mental Health Issues	Any of the following: Children's Depression Inventory (CDI) above 2, Revised Children's Manifest Anxiety Scale above 3, PTSD above threshold
Retention in HIV care	Past week ART adherence and did not a clinic appointment in the last year
Orphan Any	Either mother or father passed away
Necessities All	Household can afford all 8 basic necessities: 3 meals a day, school fees, visit to the doctor when you are ill, and all the medicines you need, school uniform, enough clothes to keep you warm and dry, toiletries to be able to wash every day, school equipment, more than one pair of shoes
No treatment buddy	Does the ALHIV have a treatment buddy
No support group	Has the ALHIV attended a support group
High social support	Did the participant report highest score for all time: Derived from responses to MOSSListen(Someone you can count on to listen when you need to talk) MOSSAdvice(Someone to give you good advice about a crisis), MOSSFears(Someone to share your most private worries and fears with), MOSSProblems(Someone to turn to for suggestions about how to deal with personal problems), MOSSBedRidden(Someone to help you if you were confined to bed), MOSSDoctor(Someone to take you to the doctor if you needed it), MOSSMeals(Someone to prepare your meals if you were not well)
No sim card phone	The participant does not have access (own/share) a "sim" phone
Cell use Health Information	Use cell phone to access general health information
Family did not receive a grant	Family receives at least one grant
TB Symptoms for T2+ T3 regression	TB Symptoms for at T2 OR T3 – it was felt that TB symptoms at T2 and T3 would suggest TB across 2 years, which is unlikely.

Specific steps and reasoning:

Table 12 - Summary of Data analysis

Data analysis		
#	Step	Reason
1	Review Codebook and questionnaire from the Mzanzi Wakho database	Identify factors: Guided by literature, ecological and people centered TB model, experience and logic. Factors are categorised according to the ecological model. Although factors can be defended when placed in different sections of the ecological model, every effort was made

		to contextualize each variable in the setting of ALHIV.
2	**Create Frequency Tables**	Important to get an overview of TB testing in ALHIV
3	**Table 2:** Basic demographics of participants at wave 2 and wave 3	• Appreciate the basic characteristics of the cohort
4	**Table 3:** TB symptoms in all ALHIV at Wave 2,3 • Include each respective WHO TB symptom screening question for all ALHIV at T2 and T3 • Create a variable defined as any of the TB symptoms the participants were screened for during the interviews	• Appreciate the frequency of each experienced TB symptom (WHO defined) • Describe the number of ALHIV who experienced ANY TB symptom, and thus would need to be tested for TB
5	**Table 4:** TB tests used in all ALHIV at Wave 2,3 Include each respective TB TEST used at T2 and T3 for all ALHIV	• Appreciate the frequency of each TB TEST used • This will indicate how many ALHIV were tested for TB and specifies which TB test was used. This is important as a GeneXpert is a tailored test for TB disease, while a Tuberculin test is a test of TB infection. It is essential to know which TB test was performed.
6	**Table 5:** TB tests in ALHIV in who had any TB symptoms at cross sections of T2 and T3	• Appreciate the frequency of the number of ALHIV who had TB symptoms and did or did not have a TB test
7	**Table 6 and 7:** Vertically infected ALHIV at wave 2 and wave 3 • All ALHIV vertically infected at each wave	• Appreciate the mode of HIV infection in the cohort • Appreciate if acquiring HIV from vertical infection is associated with TB testing • Describe the number of ALHIV older and younger than 15 years • Use univariate regression to identify association of vertical infection and age, gender and TB testing • Describe the number of ALHIV who were vertically infected and the number who were horizontally infected • Describe the sex with the greatest number of horizontal/acquired HIV infection
8	**Create 3 cross tabulation tables: Table 13 - 15**	• Describe the data and TB testing in ALHIV using factors guided by literature, ecological and people centered TB model, experience and logic.

		• Create cross tabulation frequency tables for T2, T3 and T2 + T3. • T2 for a cross sectional view at T2 • T3 for a cross sectional review at T3 <u>After the cross-sectional analysis at T2 and T3</u> Review findings of the cross tabulation done for T2 and T3 to reassess which variables are included in the T2 + T3 cross tabulation. Inclusion for this table was again based on literature, ecological and people centered TB model, experience and logic, but a further filter was applied based on the similarities between T2 and T3. • T2 +T3 were used together to demonstrate how experiencing a certain social factor over time will affect TB testing. <u>Why T1 was not included</u> • T1 was excluded due to a number of salient variables not being available for this time point as well the duration of time that was reviewed in T1. T1 looked at if you had ever had a TB test, unlike T2 and T3 that looked specifically at the preceding year. T1 also did not differentiate what TB test was done. It was decided that T1 would distort the findings of our data analysis and was thus excluded.
9	**Table 13:** <u>Cross Tabulation of ALHIV with outcomes of</u>: HAD A TB TEST or DID NOT have a TB TEST at Wave 2 with factors that are known to shape TB TESTING at Wave 2	• Appreciate the proportion changes with each variable and testing • Appreciate the frequencies • Apply Chi-Squared to test if there is a relationship between the categorical variable and the outcome
10	**Table 14:** <u>Cross Tabulation of ALHIV with outcomes of</u>: HAD A TB TEST or DID NOT have a TB TEST at Wave 3 with factors that are known shape TB TESTING at wave 3	• Appreciate the proportion changes with each variable and testing • Appreciate the frequencies • Apply Chi-Squared to test if there is a relationship between the categorical variable and the outcome

	Table 15: Cross Tabulation of ALHIV with outcomes of: HAD A TB TEST or DID NOT have a TB TEST at Wave 3 with factors that are known to shape TB TESTING across wave 2 and 3	• Appreciate the proportion changes with each variable and testing • Appreciate the frequencies Apply Chi-Squared to test if there is a relationship between the categorical variable and the outcome
11	**Variable reduction for T2 & T3**	• Cross tabulation and application of chi squared test • Selection of factors that have a reasonable frequency, in relation to the number of ALHIV • Selection of factors with a P value of **<0.1**
12	**Create 3 Regression I-III: 3 Step Logistic regression** Outcome: Having a TB Test among ALHIV	• Use only factors selected after variable reduction • Use logistic regression, Multivariate analysis, OR and Confidence interval
13	**Table 8: Regression I** 3 Step Logistic regression for T2 Outcome: Having a TB Test among ALHIV	• Use logistic regression, Multivariate analysis, OR and Confidence interval to determine the influence/significance of each variable on TB testing while controlling for other significant variables • Explore the relationship between the hypothesized social variables and the outcome of TB testing
14	**Table 9: Regression II** Three Step Logistic regression for T3 Outcome: Having a TB Test among ALHIV	• Use logistic regression, Multivariate analysis, OR and Confidence interval to determine the influence/significance of each variable on TB testing while controlling for other significant variables
15	**Table 10: Regression III** Three Step Logistic regression for T2 + T3 Outcome: Having a TB Test among ALHIV	• Use logistic regression, Multivariate analysis, OR and Confidence interval to determine the influence/significance of each variable on TB testing while controlling for other significant variable
16	**Figure 8 and Table 16: Marginal effects Model T2 + T3 for Males and Females** Outcome: TB testing among ALHIV	• Test potential cumulative effects of statically significant combinations of individual and interpersonal factors identified from the stepwise regression • Plot with a 95% Confidence Interval
17	**Table 18:** Cross tabulation of age and having access to a sim card phone	• Appreciation proportion of younger and older ALHIV with access to a sim card phone • Univariate analysis

18	**Table 19:** Cross tabulation of age and relationship status	• Appreciation proportion of younger and older ALHIV in a relationship • Univariate analysis

Table 13 - TB TEST at Wave 3 with factors present at T2

	ALHIV who had a TB TEST (N=594)	Missing	ALHIV who DID NOT have a TB TEST (N=339)	Missing	Total ALHIV (N=933)		Expected or Unexpected (in line with literature and/or logic)
Factors	N(%)		N(%)		N(%)	Chi Squared P-value	
Individual factors							
Age ≥ 15 years	366(61.6)		149 (44.0)		515(55.2)	<0.001	Expected
Male	247(41.6)		172(50.7)		419(44.9)	0.0084	Expected
Not Food secure past week	170(28.6)		98(28.9)		268(28.7)	0.99	Unexpected
Not enrolled in school	78(13.1)		24(7.1)		102(10.9)	0.006	Unexpected
Missed school >= 1 week	60(10.1)		32(9.4)		92(9.9)	0.8323	Unexpected
Experienced Stigma Internal	405(68.2)	14	223(65.8)	15	628(67.3)	0.81	Unexpected
Mental health issues	115(19.4)		66(19.5)		181(19.4)	1	Unexpected
Missed clinic appointments	470(79.1)	81	258(76.1)	55	728(78.0)	0.81	Expected
WHO Stage 3/4	69(11.6)		39(11.5)		108(11.6)	0.72	Unexpected
Any TB symptoms	365(61.4)		179(52.8)		544(58.3)	0.01218	Expected
No TB symptoms	229(38.6)		160(47.2)		389(41.7)		
TB Symptom – Any Cough	9(1.5)		3(0.9)		12(1.29)	0.63	
TB Symptom – Cough with Blood	87(14.6)		45(13.3)		132(14.15)	0.60	
TB Symptom – Cough with Sputum	154(25.9)		62(18.3)		216(23.15)	<0.001	Expected
TB Symptom – Fever Often	15(2.5)		12(3.5)		27(2.89)	0.49	
TB Symptom – Nigh Sweats	127(21.4)		72(21.2)		199(21.33)	1	
TB Symptom – Weight Loss	117(19.7)		47(13.9)		164(17.58)	0.03	Expected
TB Symptoms - Tiredness	196((33.0)		106(31.3)		302(32.4)	0.64	
Alcohol + Drug use ever	13(2.2)		36(10.6)		49(5.3)	0.19	Expected
Retention to Care	363(61.1)		192(56.64)		555(59.49)	0.204	Expected
Last CD4 count in past year	278(46.80)		114(33.63)		392(42.2)	<0.001	Expected
HIV viral load in the past year	230(38.72)		82(24.2)		312(33.44)	<0.0001	Expected
Have not disclosed Status	14(2.36)		15(4.42)		29(3.12)	0.12	Expected
Orphan any	370(62.29)		190(56.05)		560(60.02)	0.07	Expected

Necessities ALL	131(24.30)		76(22.42)		207(22.19)	0.96	Unexpected
Missed school to attend clinic	347(58.42)		201(59.29)		548(58.74)	0.85	Unexpected
Pregnant last year	38(6.74)		10(2.95)		48(5.144)	0.02	Expected
Disclosure to no one	14(2.36)		15(4.42)		29(3.11)	0.12	Expected
Missed ARV dose in the last week	391(65.82)		214(63.13)			0.45	
Interpersonal factors							
Experienced Stigma External	34(5.7)	14	15(4.2)	15	360(38.6)	0.53	Unexpected
No support group	503(84.7)	25	272(80.2)	26	775(83.1)	0.59	Unexpected
No Treatment Buddy	248(41.8)		117(34.5)		365(39.1)	0.06	Unexpected
Unaccompanied to clinic	264(4.4)		16(4.7)		280(30.0)	0.94	Unexpected
Female Care giver	539(90.7)		313(92.33)		852(91.32)	0.48	Unexpected
High Social Support	465(78.29)		270(79.64)		735(78.77)	0.684	Unexpected
In a relationship boyfriend/girl friend	205(34.51)		72(21.24)		277(29.69)	<0.001	Expected
Community factors							
Used Traditional medicine in Past Year	10(1.7)		10(2.9)		20(2.1)	0.24	Unexpected
UnSafe at clinic	33(5.55)		22(6.49)		55(5.89)	0.66	Unexpected
Experienced Community violence	260(43.77)		147(43.36)		407(43.63)	0.96	Unexpected
Organizational factors							
>1Hour Travel Time to Clinic	29(4.8)		16(4.8)		42(4.5)	1	Unexpected
Cost to get to clinic above R10	183(30.8)		128(37.76)		311(33.33)	0.04	Expected
Environmental Factors							
No sim card phone	281(47.3)		210(61.9)		491(52.6)	<0.001	Expected
House hold type informal	88(14.81)		46(13.57)		134(14.36)	0.66	Unexpected
Lives Rural	158(26.6)		72(21.2)		230(24.7)	0.07	Unexpected
Cell Health information	63(10.60)		32(9.44)		95(10.18)	0.79	Unexpected
Structural Factors							
Not confident in confidentiality at clinic	437(73.6)		242(71.4)		679(72.8)	0.52	Expected
Macro Factors							
Family **did Not** receive a Grant	56(9.4)		28(8.3)		849(91.0)	0.63	Unexpected

Individual factors:

Being a female, an adolescent 15 years and older, and being an orphan (either mother or father passed away) had a strong association with having a TB test, p-value <0.001, 0.0084 and 0.07 respectively. Pertaining to female adolescents and maternal care, although the frequency was low, being pregnant in the last year was associated with TB testing (p 0.02).

While having had a CD4 count in past year, p-value <0.001, or a HIV viral load test in the past year p-value, <0.0001, were associated with TB testing; missing a clinic appointment (p > 0.1) was not associated with not TB testing and being retained in HIV care (p > 0.1) was not associated with testing.

Although not being enrolled in school was associated with TB testing p-value 0.006, neither missing school for a week (p > 0.1) nor missing school to go to the clinic (p > 0.1) was associated with TB testing.

Experiencing Any TB symptom was significantly associated with TB testing, p-value 0.012. Of the TB symptoms coughing with sputum p-value <0.001 and weight loss p-value 0.03 were most associated with TB testing. A WHO HIV staging of ¾ was not associated with TB testing.

Interpersonal factors:

Being in a relationship was associated with TB testing while, p <0.001, but having an HIV treatment buddy was associated with not having a TB test (p 0.06). Having experienced externalized stigma, having a high level of social support, having a support group, being an accompanied to a clinic and having a female care giver was not associated with TB testing (p >0.1)

Community factors:

No measured community factors were associated with TB testing, although this may be due to small samples sizes in the factors measuring Traditional medicine use and being unsafe at the clinic.

Organizational factors:

Incurring a cost of more than R10 to get the clinic was associated with not testing for TB (p 0.04), while travelling for more than hour was not (p > 0.1).

Environmental factors:

Living rural (p <0.001) and not having a sim card cell phone (0.07) were associated with not testing, household type and using a cell phone for health information were not (p > 0.1)

Structural and macro factors:

An adolescent's family receiving a grant was not associated with TB testing (p > 0.1), neither was the level of confidentiality experienced at the clinic (p >0.1).

Table 14 - TB TEST at Wave 3 with factors present at T3							
	ALHIV who **had a TB TEST** (N=502)	Missing	ALHIV who **DID NOT have a TB TEST** (N=431)	Missing	**Total ALHIV** (N=933)		Expected or Unexpected (in line with literature and/or logic)
Factors	**N(%)**		**N(%)**		**N(%)**	**Chi Squared P-value**	See above Chosen Lit expected **barrier factors**
Individual factors							
Age ≥ 15 years	371(73.9)		252(58.5)		623(66.78)	<0.001	Expected
Male	202(40.2)		217(50.3)		419(44.91)	0.002	Expected
Not Food secure past week	103(20.5)		112(26.0)		215(23.04)	0.06	Expected
Not enrolled in school	101(20.1)		51(11.8)		152(16.29)	<0.01	Unexpected
Missed school >= 1 week	399(79.5)		319(74.0)		718(76.96)	0.02	Unexpected
Missed school to attend clinic	214(42.63)		192(44.55)		406(43.52)	0.601	Unexpected
Mental health issues	83(16.53)		49(11.4)		132(14.15)	0.03	Unexpected
Missed clinic appointments	425(84.7)	50	357(82.8)	50	787(84.35)	0.96	Unexpected
WHO Stage **3/4**							
Any TB symptoms	221(44.0)		130(30.2)		351(37.62)	<0.001	Expected
No TB symptoms	281(56.0)		301(69.8)		582(62.38)		
TB Symptom – Any Cough	46(9.2)		23(5.3)		69(7.40)	0.04	
TB Symptom – Cough with Blood	4(0.8)		3(0.7)		7(0.75)	1	
TB Symptom – Cough with Sputum	56(11.2)		19(4.4)		75(8.04)	<0.001	Expected
TB Symptom – Fever Often	17(3.4)		6(1.4)		23(2.47)	0.08	
TB Symptom – Night Sweats	63(12.5)		42(9.7)		105(11.25)	0.21	
TB Symptom – Weight Loss	72(14.3)		47(10.9)		119(12.75)	0.14	
TB Symptoms - Tiredness	115(22.9)		60(13.9)		175(18.76)	<0.001	Expected
Retention to Care	355(70.71)		295(68.44)		650(69.67)	0.495	Expected
Last CD4 count in past year	219(43.63)		155(35.96)		374(40.09)	0.01	Expected
HIV viral load in the past year	201(40.04)		144(33.41)		345(36.98)	0.13	Expected
Have disclosed Status	3(0.60)		3(0.70)		6(0.64)	1	Unexpected
Orphan any	348(69.32)		292(67.75)		640(68.60)	0.66	Unexpected
Experienced Stigma Internal	62(12.4)	17	65(15.1)	18	127(13.61)	0.24	Expected
Alcohol + Drug use ever	32(6.4)		20(4.6)		52(5.57)	0.31	Unexpected
Necessities ALL	174(34.66)		129(29.93)		303(32.48)	0.142	Expected
Missed ARV dose in the last week	380(75.70)		320(74.25)			0.66	
Pregnant last year	33(6.57)		20(4.64)		53(5.68)	0.14	Expected

Interpersonal factors							
Experienced Stigma External	17(3.4)	17	13(3.0)	18	30(3.22)	0.91	Unexpected
In a relationship boyfriend/girl friend	187(37.25)		102(23.67)		289(30.98)	<0.0001	Expected
High Social Support	413(82.27)		342(79.35)		755(80.92)	0.3	Expected
Female Care giver	443(88.25)		400(92.81)		843(90.35)	0.03	Unexpected
No support group	440(87.6)	17	388(90.0)	18	828(88.75)	0.09	Unexpected
No Treatment Buddy	199(39.6)	17	164(38.1)	18	363(38.91)	0.74	Unexpected
Unaccompanied to clinic	18(3.6)		24(5.6)		42(4.50)	0.20	Expected
Community factors							
Unsafe at clinic	12(2.39)		21(4.87)		33(3.54)	0.061	Unexpected
Experienced Community violence	163(32.47)		95(22.04)		258(27.65)	<0.0005	Expected
Used Traditional medicine in Past Year	28(5.6)		27(6.3)		55(5.89)	0.80	
Organizational factors							
>1Hour Travel Time to Clinic	21(4.2)		22(5.1)		43(4.61)	0.61	Expected
Cost to get to clinic above R10	114(22.71)		112(25.99)		226(24.22)	0.40	Unexpected
Environmental Factors							
No sim card phone	221(44.0)		212(49.2)		433(46.41)	0.13	Expected
Household type informal	82(16.33)		49(11.37)		131(14.04)	0.039	Unexpected
Cell Health information	58(11.55)		34(7.89)		92(9.86)	0.08	Expected
Lives Rural	116(23.1)		107(24.8)		223(23.90)	0.53	Expected
Structural Factors							
Not confident in confidentiality at clinic	208(41.4)		200(46.4)		408(43.73)	0.14	Expected
Macro Factors							
Family **did Not** receive a Grant	65(12.9)		49(11.4)		114(12.22)	0.53	Unexpected

Individual factors:

Being an ALHIV 15 years and older has a strong association with having a TB test, p-value <0.001, while being male does not (p 0.002). Pregnancy in the last year and being an orphan (either mother or father was passed away) not associated with TB testing (p > 0.1).

Food insecurity among ALHIV was associated with not testing for TB (p 0.06). Potential individual level factors that promoted TB testing was: Not enrolled in school (p <0.001), missing school for a week or more (p 0.02), having a CD4 count in the past year and having a mental health condition (p 0.03).

Experiencing Any TB symptom was significantly associated with TB testing (p-value < 0.001). Having a cough with sputum (p < 0.001), a fever often (p < 0.001) or experiencing fatigue and tiredness (p 0.001) was associated with TB testing.

Interpersonal factors:

ALHIV who had a boyfriend/girlfriend were associated with TB testing p <0.0001, likewise with having a support group (p 0.09). Having a female care giver or having a high level of social support was not associated with TB testing (p > 1)

Being in a relationship was associated with TB testing while, p <0.001, but having an HIV treatment buddy was associated with not having a TB test (p 0.06). Having experienced externalized stigma, having a high level of social support, having a support group, being an accompanied to a clinic and having a female care giver was not associated with TB testing (p >0.1)

Community factors:

No measured community factors were associated with TB testing, although this may be due to small samples sizes in the factors measuring Traditional medicine use and being unsafe at the clinic (p > 0.1). Experiencing community violence was strongly associated with TB testing (p <0.001).

Organizational factors:

Having to pay more than R10 to get to the clinic was dissociated with not testing for TB (p > 0.1) and travelling for more than hour was not (p > 0.1).

Environmental factors:

Living in an informal house type and using cell phone for health information was associated with TB testing, p 0.039 and p 0.08 respectively.

Structural and Macro factors:

An adolescent's family receiving a grant was not associated with TB testing (p > 0.1) nor was the level of confidentiality experienced at the clinic (p >0.1).

Table 15 - TB TEST at Wave 3 with factors present at T2 and T3

	ALHIV who **had a TB TEST** (N=502)	Missing	ALHIV who **DID NOT have a TB TEST** (N=431)	Missing	**Total ALHIV** (N=933)		**Expected or Unexpected (in line with literature and/or logic)**
Factors	**N(%)**		**N(%)**		**N(%)**	**Chi Squared P-value**	
Individual factors							
Age ≥ 15 years	314(62.55)		199(46.17)		513(54.98)	0.0001	Expected
Male	300(32.15)		214(49.65)		514(55.09)	0.002	Expected
Food secure past week	306(32.80)		244(56.61)		550(58.96)	0.2	Expected
Enrolled in school	392(78.09)		374(86.77)		766(82.10)	0.0007645	Unexpected
Missed school >= 1 week	11(2.19)		3(0.70)		14(1.50)	0.0076	Unexpected
Mental health issues	26(5.18)		10(2.32)		36(3.86)	0.03	Expected
Missed clinic appointments	361(71.91)	81	291(67.52)	90	652(69.88)	1	Unexpected
Retention in HIV Care	240(47.81)		182(42.23)		422(45.23)	0.1	Expected
Last CD4 count in past year	139(27.69)		84(19.49)		233(23.90)	<0.001	Expected
HIV viral load in the past year	106(21.12)		59(13.69)		165(17.68)	<0.001	Expected
In a relationship boyfriend/girl friend	132(30.63)		57(11.35)		189(20.26)	<0.0001	Expected
Missed school to attend clinic	148(29.48)		124(28.77)		272(29.15)	0.87	Unexpected
Orphan any	314(62.55)		246(57.08)		560(60.02)	0.1	Unexpected
Experienced Stigma Internal	43(8.57)	16	47(10.90)	19	90(9.65)	0.25	Expected
Missed ARV dose in the last week	196(39.04)		289(67.05)			0.7297	
Disclosure to no one	1(0.20)		1(0.23)		2(0.21)	1	Unexpected
Necessities ALL	36(7.1)		36(8.35)		72(7.72)	0.58	Unexpected
Pregnant last year	50(9.96)		26(6.03)		76(8.15)	0.01	Expected
Interpersonal factors							
Experienced Stigma External	2(0.40)	13	1(0.23)	13	3(0.32)	1	Unexpected
Alcohol + Drug use ever	7(1.39)		8(1.86)		15(1.61)	0.83	Unexpected
Treatment Buddy	175(34.86)	15	168(38.98)	17	343(36.76)	0.17	Unexpected
Unaccompanied to clinic	3(0.60)		2(0.46)		5(0.54)		Unexpected
Support group	16(3.19)	14	9(2.09)	17	25(2.68)	0.4216	Expected
Female Care giver	422(84.10)		383(88.86)		805(86.28)	0.04	Expected
High Social Support	338(67.33)		272(63.11)		610(65.38)	0.2	Expected
Community factors							
Used Traditional medicine in Past Year	0		1(0.23)		1(0.11)	0.93	Unexpected
Experienced Community violence	86(17.13)		52(12.06)		138(14.79)	0.04	Unexpected
Unsafe at clinic	2(0.40)		4(0.93)		6(0.64)	0.55	Unexpected
Organizational factors							
>1Hour Travel Time to Clinic	1(0.20)		2(0.46)		3(0.32)	0.5203	Unexpected
Clinic Travel more than R10	87(17.33)		70(16.24)		157(16.83)	0.72	Unexpected
Environmental factors							
No sim card phone	356(70.92)		279(64.73)		635(68.06)	0.05	Expected
Household type informal	74(14.74)		47(10.90)		121(12.97)	0.1	Unexpected
Lives Rural	115(22.91)		102(23.67)		217(23.26)	0.83	Expected
Cell Health information	1(0.20)		1(0.23)		2(0.21)	1	Unexpected
Structural factors							

Not confident in confidentiality at clinic	219(43.63)		179(41.53)		398(42.66)	0.563	Unexpected
Macro Factors							
Family **did Not** receive a Grant	366(72.91)		409(94.90)		775(83.07)	0.19	Expected

Individual factors:

Individual level factors associated with TB testing: Being an adolescent 15 years and older (p 0.001), being female (p 0.002), enrolled in school (p <0.001), missing school (p 0.008), being retained in HIV care (p 0.01), being In a relationship (p <0.0001), being an orphan (p 0.1) and having been pregnant in T2 or T3 (p 0.01).

Interpersonal factors:

Having a female care giver was associated with TB testing (p 0.04), all other interpersonal factors were not associated with having or having a TB test (p >0.1).

Community factors:

Very few ALHIV fell into the unsafe at clinic category and made use traditional medicine category. Although experiencing community violence was associated with TB testing (p 0.04).

Organizational factors:

Neither travelling for more than hour nor paying more than R10 to get to the clinic was associated with TB testing (p > 0.1)

Environmental factors:

Living in informal housing (p 0.1) and having no access to a sim card phone (p 0.05) was associated with TB testing, living rural was not (p > 0.1) and using a cell phone with cell health information had 2 participants.

Structural and Macro factors:

No structural or macro factor was associated with having a TB test or not having a TB test (p > 0.1)

Table 16 - Marginal effects table for Wave 2 and wave 3

15 years and older	predicted	std.error	Confidence Interval	Boy Girl	Viral load	Relationship
0	0.390943788467595	0.12	0.34-0.45	0	0	0
0	0.489888204701147	0.17	0.40-0.58	0	1	0
0	0.534478930473049	0.23	0.42-0.58	0	0	1
0	0.632051764932621	0.25	0.51-0.74	0	1	1
0	0.462263203038335	0.13	0.40-0.52	1	0	0
0	0.562584868661342	0.17	0.48-0.64	1	1	0
0	0.605932635871028	0.23	0.50-0.71	1	0	1
0	0.697018674237822	0.25	0.59-0.79	1	1	1
1	0.478274936395229	0.15	0.41-0.55	0	0	0
1	0.578334256973334	0.16	0.50-0.65	0	1	0
1	0.621172232547954	0.19	0.53-0.71	0	0	1
1	0.710419190078212	0.20	0.62-0.78	0	1	1
1	0.551110107626387	0.14	0.48-0.62	1	0	0
1	0.647496097714327	0.15	0.58-0.71	1	1	0
1	0.687109144136555	0.19	0.60-0.76	1	0	1
1	0.766657496496058	0.19	0.70-0.83	1	1	1

Table 17– Older ALHIV – access to sim card			
	Older ALHIV (≥15 years old) Across Wave 2 and 3 (N=513)	**Younger ALHIV (≤ than 15 years old) Across Wave 2 and 3 (N=420)**	**P value**
Factors	N (%)	N (%)	
Access to sim card	408(79.53)	227(54.05)	<0.001

Table 18– Older ALHIV – being in relationship			
	Older ALHIV (≥15 years old) Across Wave 2 and 3 (N=508)	**Younger (≤ than 15 years old) ALHIV (N=420)**	**P value**
Factors	N (%)	N (%)	
Being in a relationship	180 (35.43)	9(2.14)	<0.001

The Data Access Request form was completed on the 22/03/20.

Table 19 - The Data Access Request form	
Research outline	
Academic lead/supervisor:	Dr Elona Toska, Dr Faisal Garba
Project:	The Mzantsi Wahko
Data type:	Anonymized
Purpose:	Analysis of factors shaping access to TB testing and treatment in HIV positive adolescents.
Research area/	Barriers to TB screening and treatment with specific focus on challenges face by HIV positive adolescents.
Research question(s)/objectives:	What are the factors shaping access to TB testing and initiating TB treatment in adolescents that are HIV positive with symptomatic TB.
Variables/measures:	All factors related to access to TB testing All factor related to initiation of TB treatment TB screening questions Anonymized information of the following regarding participants: → Demographics → Social factors → Details related to health and well being → HIV status and treatment difficulties/adherence status → TB symptoms, screening, diagnosis and treatment status → Facilitators and barriers to accessing health care facilities → Personal experience of health care facilities → Caregiver information → Schooling and level of education → Factors regarding mental health → Involvement in community → Friends, relationships, technology → Drug and alcohol use
Analysis plan:	R and Stata as well as excel will be used to analyze the data and draw inferences.
Timeline:	The aim is to complete the analysis and dissertation by the end of 2021.
Research team:	Supervisor – Dr Elona Toska Masters Student – Quintin Andre van Staden
Proposed journals, books or other fora for publications:	At advice and discretion of supervisors with options including: > Global Public Health > Medical Humanities > African Journal of AIDS Research > And other related journals
Authorship plan:	At the advice of supervisors and the inclusion of any collaborators to produce a better body of work.

Acknowledgement plan:	Acknowledgement will go to the Mzantsi Wakho team for the privilege to analyze and use their data for this dissertation.
Completed on 22/03/20	