Exploring how Health-related Quality of Life (HRQOL) is experienced among patients living with HIV associated TB in Khayelitsha, South Africa.

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A mini dissertation submitted in partial fulfilment of the requirements for the degree of Master of Public Health division of Social and Behavioural Sciences, School of Public Health and Family Medicine, Faculty of Health Sciences

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PREAMBLE

DECLARATION

I, *John-Henry Hickman, student number HCKJOH002*, hereby declare that the work on which this dissertation is based on my original work, except where acknowledged otherwise. Neither the whole work offered here, nor any part of it has been, is being, or is to be submitted for another degree in this or any other tertiary institution. I entitle the University of Cape Town to reproduce, for the purpose of research, either the whole or any portion of the information contained in this dissertation.

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DEDICATION

To my wife, Heske, for your continued support in my constant pursuit of knowledge and for the love you kept showering unto our son on the lonely nights I had to work, even when your cup was empty. To my son, John-Nicolas, for your playful smiles and oblivious observations of me at work. May this one day too inspire you to pursue your dreams. Lastly, to my unwavering parents for the courage you instilled in me to follow through on the paths I choose.

THESIS ABSTRACT

Health-related quality of life (HRQOL) is a construct that has received attention in research for nearly four decades. However, renewed interest in this field came about with advances in medical technology and health policies. Better treatment options and policies, which enables greater access to health care, have improved health outcomes, such as leading to an extension in life expectancy. This rings particularly true for Human Immunodeficiency virus (HIV) and associated illnesses such Tuberculosis (TB). However, improvements in health outcomes are not necessarily accompanied by satisfactory patient experiences of HRQOL. Health-related quality of life is predominantly studied through quantitative research methodologies. However, the measures used are not entirely tailored to the South African context. Consequently, this mini-dissertation aims to explore HRQOL using qualitative methodological inquiry within the South African context.

This mini dissertation is structured around the three following components: A research protocol (Part A) which addresses HRQOL in a South African context with particular focus on HIV and TB. Part B is a literature review examining existing HIV, TB and HRQOL literature, with emphasis on the South African context. The final section (Part C) is a manuscript for a journal article prepared to be published. Part C focuses on the social experience of HRQOL and how it is the central construct to experiencing HRQOL in South Africa as opposed to an individualised view in Western settings.

The findings from this mini dissertation can add to the limited existing HRQOL literature in South Africa, by providing a perspective on how HRQOL is experienced in this country. The knowledge obtained here can further aid in the development or improvement of interventions and policies which aim to not only improve patient health outcomes, but HRQOL as well. Lastly, it can provide valuable information to those focused on developing quantitative HRQOL tools that are appropriate for use in South Africa.

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LIST OF ACRONYMS AND ABBREVIATIONS

AIDS Acquired Immunodeficiency Syndrome

ARV Antiretroviral

ART Antiretroviral Therapy

DRC Departmental Research Committee

HIV Human Immunodeficiency Virus

HREC Human Research and Ethics Committee

HRQOL Health-related quality of life

PredART Trial Prednisone Antiretroviral trial

StatsSA Statistics South Africa

TB Tuberculosis

DR TB / MDR TB Drug Resistant Tuberculosis / Multi Drug Resistant TB

QALYs Quality Adjusted Life Years

QOL Quality of life

UNAIDS The Joint United Nations Programme on HIV and AIDS

WHO World Health Organization

Part A: Protocol

Health Related Quality of Life Protocol

Exploring how Health-related Quality of Life (HRQOL) is experienced among patients living with HIV associated TB in Khayelitsha, South Africa.

This proposal aims to address a secondary data analysis of a qualitative component to a completed quantitative study. Research described in this proposal is associated with a larger clinical trial identified as the Prednisone-Anti-Retroviral Treatment (Pred-ART) Trial.

Section One

1. Background and context

Health-related quality of life (HRQOL) has become a significant component to research and treatment interventions of medical conditions, in particular among enduring illnesses. Development and roll out of antiretroviral (ARV) medication has seen HIV infection move from an acute illness to a chronic condition (Degroote et al., 2014; Kastien-Hilka et al., 2016; Pitt et al., 2008; Yang et al., 2018). Consequently, HRQOL research in Human Immunodeficiency Virus (HIV)-associated illnesses has sparked interest among those seeking to understand health outcomes and improve health care responses (Ebrahim, 1995; Kastien-Hilka et al., 2016; Nglazi et al., 2014). This study, utilising a qualitative methodology, looks to explore how HRQOL is experienced in a cohort living with HIV associated Tuberculosis (TB) and add to the HRQOL literature in South Africa.

1.1 HIV and TB South Africa

The prevalence of Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) remain a great concern to public health in South Africa despite substantial progress made in addressing these illnesses (Govender et al., 2015; South African National AIDS Council, 2017; UNAIDS, 2019b). Progress is noted in the reduction of mortality rates as well an increase in life expectancy

among those living with HIV since the upscaling of Anti-Retroviral Therapy (ART) over the last decade (South African National AIDS Council, 2017; UNAIDS, 2019b). Despite positive strides made in South Africa toward 2020 UNAIDS 90-90-90 targets (i.e. 90 % of people living with HIV know their status, 90% of people who know their HIV-positive status are on antiretroviral therapy, and 90% of people on antiretroviral therapy achieve a viral load that is undetectable), unequal performances across provinces has left South Africa to still have 240 000 new infections annually adding to the estimated 7.7 million people living with HIV, placing South Africa as one of the countries with greatest HIV prevalence (*UNAIDS Data 2018*, n.d.). Thus warranting South Africa to scale up its current effort in addressing the spread of HIV if it wants to end the HIV epidemic by 2030 (South African National AIDS Council, 2017).

The HIV epidemic in South Africa compounds and is compounded by the TB burden in this country due to co-infection. Co-infection rates of HIV and TB in South Africa exceed 70% (Mathema et al., 2017). Due to the high co-infection rate of HIV and TB it is important for research pertaining to these diseases to be inclusive of both HIV and TB Thus, underscoring the need for research inclusive of both illnesses. South Africa has a mounting burden of TB and is one of eight countries that contribute to two-thirds of the global TB prevalence (Mathema et al., 2017; World Health Organisation, 2018). This burden is exemplified through South Africa being one of three countries exceeding 500 new TB cases per 100 000 people in 2017 (World Health Organisation, 2018). Despite the remaining high incidence rates, South Africa has observed a 7% decrease in TB-incidence for the period 2010-2017, largely due to upscaling of ART and establishing TB as a notifiable infection (South African National AIDS Council, 2017; World Health Organisation, 2018).

Increased HIV and TB treatment uptake has contributed to improved health outcomes and the consequential progression of HIV infection to a chronic illness (Degroote et al., 2014; Kastien-Hilka et al., 2016; Pitt et al., 2008; Yang et al., 2018). This progression carries with it a new set of challenges for public health and has led to the increasing importance of measuring Health Related Quality of Life (HRQOL) in HIV associated research (Mutabazi-mwesigire et al., 2014). Research in this field is of particular interest considering that clinical outcomes in treatment of infectious diseases, which are significant to patient health, often do not align with patients' subjective experience of treatment and well-being (Kastien-Hilka et al., 2016). Resultingly a gap has emerged in the treatment of HIV associated TB as a chronic condition with challenges to patients' HRQOL as patients become concerned not only about survival, but about their HRQOL as well (Vagiri et al., 2014).

1.2 HIV and TB treatment and management

The recommendations in South Africa for the treatment of HIV with the use of Antiretroviral therapy (ART) sets out to achieve maximal suppression of viral load, restore and preserve patient immune function, reduce risk of opportunistic infections, prevent transmission of HIV, minimise adverse side effects from treatment, prolong life expectancy and improve quality of life (QOL) (Meintjes et al., 2017).

HIV treatment is to start immediately once diagnosed with either a two-drug or three-drug fixed dose regimen and is to be continued for the patients entire lifetime (Meintjes et al., 2017). For patients who have a concurrent TB infection, ART initiation remains urgent, especially in advanced HIV infection. However, it is suggested that ART is started with a two-week delay after initiation of TB treatment to reduce adverse side effects. TB treatment is divided into two phases. Patients start with an intensive treatment phase where a combination of drugs are to be taken daily for two months. During the second, continuation

phase, patients are prescribed two drugs to be taken daily for four months, dose and number of tablets are patient weight dependent (*South African National TB Guidelines - Adults*, 2017; The National Department of Health, 2014).

Large scale continuous treatment for HIV and TB in South Africa has successfully increased life expectancy of those living with HIV and TB to an age similar to those not living with HIV and TB(Johnson et al., 2013). With prolonged treatment regimens, even after improved health status come challenges to HRQOL among those with HIV associated conditions. One such challenge which directly confronts both patient health and HRQOL is adherence. Adherence to treatment has multiple factors as influencers, among which are the psychological and social HRQOL domains (Muessig et al., 2015; Vandermause et al., n.d.). Patients experience psychological challenges to HRQOL as a result of the daily compliance to prescribed medication. They experience the psychological challenges in terms of feeling stripped from their autonomy to make decisions regarding treatment (Muessig et al., 2015). Similarly, patients experience their illness in a social context, with those who receive support from health care practitioners better equipped to deal with the challenges of medicating daily (Vandermause et al., n.d.) and ultimately experience greater HRQOL.

1.3 Health-Related Quality of Life (HRQOL)

Health related quality of life has for years been an area of interest to researchers of various diseases including both non-communicable illnesses such as diabetes and rheumatoid arthritis, as well as communicable diseases like HIV and TB (Busija et al., 2011; Kastien-Hilka et al., 2017; Louw et al., 2012; Nglazi et al., 2014; Raaijmakers et al., 2014). Health related quality of life is a concept that was first recognised in the 1970's in the United States of America in the disciplines of psychology and sociology (Haas, 1999). Interest in HRQOL grew

as technology and medicine progressively became more advanced which ultimately contributed to increased life expectancy, however, soon it became apparent that longer lives are not necessarily desirable if it lacks in quality. In this regard HRQOL research and understanding provided health care practitioners, patients and their families additional information on whether treatment should be pursued (Haas, 1999).

Despite the keen interest in HRQOL across various disciplines, HRQOL is a concept which is notoriously ambiguous with no single generally agreed upon definition or conceptual model guiding instrument development and research (Busija et al., 2011; Ferrans et al., 2005; Karimi & Brazier, 2016). However, a working understanding of what HRQOL constitutes which this research project draws on is, as postulated by Ebrahim (1995), "those aspects of self-perceived wellbeing that are related to or affected by the presence of disease or treatment". This definition places emphasis on those aspects of one's life subjectively experienced to be affected by health (Karimi & Brazier, 2016).

1.3.1 HRQOL in research

Predominantly HRQOL research utilises quantitative measures, of which a multitude exist, to explore the subjective experiences associated with treatment and patient health and well-being through consideration of varying life domains. These domains broadly include but are not limited to physical, mental and social spheres pertaining to the individual patient (Cunillera et al., 2010; Ebrahim, 1995; Kastien-Hilka et al., 2016; Pitt et al., 2008; Robberstad & Olsen, 2010; Ware & Sherbourne, 1992). Two commonly used HRQOL quantitative measures are the EQ-5D-3L and the Medical Outcomes Study (MOS) 36/12-item questionnaires. The EQ-5D-3L is a self-report questionnaire covering five life domains related to health (i.e. mobility, self-care, usual activities, pain or discomfort, and anxiety or

depression). Each domain is listed as a statement with one of three answers for participants to choose from depending on how they experience that domain on the day of assessment (EuroQol Research Foundation, 2018). The popular MOS Short-Form (SF) 36-item and MOS SF-12-item questionnaire measure HRQOL across eight domains namely physical functioning, role physical/role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role emotional/role limitations due to emotional problems, and mental health (Busija et al., 2011; Ware & Sherbourne, 1992). Answers to either the 36 or 12 questions are offered and scaled using the Likert method. The number of answers per question varies and ranges from two to five. The scores derived from the questionnaires provide the researcher with an understanding of what areas of the patients' life related to health do they regard as having quality or where does it lack in self-perceived quality. Based on this information health care practitioners can, together with their patients make decisions on how to proceed with treatment. In larger populations, this information could guide policy and distribution of resources to better HQOL (Ebrahim, 1995; J. Jelsma et al., 2005; Shisana, O, Rehle, T, Simbayi LC, Zuma, K, Jooste, S, Zungu N, Labadarios, D, Onoya, 2014; Ware & Sherbourne, 1992).

1.3.2 HRQOL Domains

Initial HRQOL scholars were rooted in the fields of psychology and sociology (Haas, 1999). As a result, the development of domains in HRQOL came from the perspectives of these disciplines. Although the disciplines of psychology and sociology are rich in theories, initial HRQOL research was not necessarily, to the extent that aspects of quality of life to be included as domains of study were identified by the researcher based on their particular interest and not based on a particular theoretical perspective. This approach is flawed as it lacks

empirically evaluated conceptual models, is biased and exclusive of domains that might be more relevant to the patient (Haas, 1999; Vidrine et al., 2005). Thus, only offering a one-sided view of the patients' HRQOL with the possibility of making errored judgements on how to proceed with interventions, as only a narrow, biased view of the patient is recorded (Vidrine et al., 2005). Since the earlier HRQOL research, subsequent domain development, the inclusion or omission of domains have become more inclusive of theories and built on conceptual models of what constitutes HRQOL (Cummins, 2005; Peasgood et al., 2014).

Different HRQOL instruments capture different domains or seemingly similar domains with a different nomenclature (Busija et al., 2011; EuroQol Research Foundation, 2018; Ware & Sherbourne, 1992). Despite the complexity of HRQOL most domains can be pooled to revolve around the physical, psychological and social domains of life (Enimil et al., 2016; Hays & Reeve, 2010). In predominant HRQOL research, physical domains are explored and measured through scoring on quantitative tests where a HRQOL score would be derived from areas such as physical functioning, ability to execute certain roles at work, general health perceptions, pain and energy levels (Yang et al., 2018). Psychological domains pertaining to HRQOL are measured through similar quantitative tools and continue to explore mood and discrepancies in affect such as depression and anxiety (Yang et al., 2018). Social domains are explored along social support, stigma, and participation in social activities (Yang et al., 2018).

1.3.3 HRQOL HIV/TB South Africa

Studies conducted in South Africa among HIV/TB-infected cohorts have shown that treatment is effective in improving HRQOL (Kastien-Hilka et al., 2017; Nglazi et al., 2014). Most South African studies in this field are quantitative deploying measures such as the EQ-5D, EQ-VA MOS SF36 and the WHOQOL-HIV instrument (Jelsma et al., 2007; Nglazi et al., 2014; Peltzer,

2012; Pitt et al., 2008; Robberstad & Olsen, 2010; Vagiri et al., 2014). The greatest improvements in HRQOL for both HIV and TB separately are noted in the initial treatment phases (Jelsma et al., 2007; Kastien-Hilka et al., 2016; Peltzer, 2012). These studies further show that not only does the uptake of treatment influence HRQOL, but adherence to treatment is seen to have an even greater impact on HRQOL. Patients with more than 95% adherence to treatment have better mean HRQOL scores than those below 95% adherence (Vagiri et al., 2014). However, even though HRQOL improves with treatment, HRQOL remains lower than in comparative community groups not living with HIV or TB (Jelsma et al., 2007). The domains of HRQOL reported to be most affected by HIV/TB and its treatment are the physical and mental domains (Kastien-Hilka et al., 2016; Louw et al., 2012).

These studies often observe HRQOL separately from other factors impacting health such as level of education, stigma, socio-economic status or employment (Peltzer, 2012). Thus, placing HRQOL as an isolated entity which can be influenced by these "external" factors, but not factors regarded to be incorporated into HRQOL domains. According to Peltzer (2012) predictive factors in the improvement of HRQOL include low levels of internalised stigma, being employed or earning wages.

Based on these studies it is suggested that more social support is required to improve HRQOL, more efforts made to fight stigma of infectious diseases and that more research should be conducted on the impact of treatment on HRQOL beyond the initial years of treatment (Kastien-Hilka et al., 2016; Nglazi et al., 2014; Peltzer, 2012; Vagiri et al., 2014).

The use of different measures in similar contexts make cross comparisons between findings difficult. These studies further lack in the use of theoretical or conceptual frameworks to discuss findings. As a result, HRQOL domains are ill-defined with health and quality of life

regarded as separate entities to patient context. Concepts such as socio-economic status, stigma, employment and education are regarded to influence HRQOL, but not integrated into a HRQOL domain. Many of these factors can readily be included in HRQOL domains and aid its understanding (Yang et al., 2018).

1.3.4 Challenges with HRQOL

Despite the popularity of HRQOL research, HRQOL has been clouded by the ill-defined and interchangeable use of constructs such as quality of life, health and health-status (Ferrans et al., 2005; Karimi & Brazier, 2016). Refining a definition for HRQOL is challenging because of a lack of clarity around the concepts it deals with and the difficulty in defining seemingly simple terms such as disease, illness, sickness, health and healing (Boyd, 2000). Karimi and Brazier (2016) report that four different definitions on HRQOL can be identified in literature which is separate from the definitions available for QOL and health status. The first of these definitions places focus on the physical ability of a person to complete tasks and a person's self-perceived experience of their state of health. The second definition considers all aspects of life that directly impact on or are part of an individuals' health. However, it excludes factors such as economic status and political factors that can impact health. The third definition considers HRQOL to be those aspects of health that are affected by disease or treatment thereof. The final definition concerns the numerical value assigned to health states which can be used to calculate Quality Adjusted Life Years (QALYs) (Karimi & Brazier, 2016). Quality Adjusted Life Years is a value produced in consideration of the expected years of life and the quality thereof of a person affected by particular health challenges(McGregor & Caro, 2006).

Further clouding HRQOL research is the myriad of theoretical approaches and conceptual models which exist and attempt to explain how the domains encapsulated in HRQOL, quality

of life, health and health status interact (Cummins, 2005; Peasgood et al., 2014). Despite the many discussions and conceptual models on the complexity and interconnectedness of life domains there are little testable theories on the underlying constructs and conceptualisations of HRQOL, with limited comparisons to be drawn between studies (Cummins, 2005; Vidrine et al., 2005). Additionally, many of these conceptualisations have definitions of HRQOL which perceive health in isolation of other domains of life (Karimi & Brazier, 2016).

In light of conceptual challenges it has been noted that qualitative efforts to study HRQOL is needed and that a move away from quantifying subjective experiences is required (Barofsky, 2012a; Till et al., 2019). This move could particularly ring true for HRQOL studies in South Africa as even though HRQOL measures such as the EQ-5D and SF-12 have been used in South Africa, concern does exist around the appropriateness of these measures in use with patients in HIV subgroups for example among adolescents versus adults, women versus men, ART naïve (i.e. have never been on Anti-retroviral medication) versus treatment experienced (Clayson et al., 2006; Kastien-Hilka et al., 2017; Scott et al., 2017). The EQ-5D and SF-12 are generic measures which are not disease specific and does not account for differences in conceptualisation to how opposing subgroups might regard HRQOL (Kastien-Hilka et al., 2017; Scott et al., 2017). The insensitivity of measures to subtle differences between subgroups could result in outcomes not reflecting true HRQOL indicators for these groups. However, additional HRQOL tools for use in HIV/AIDS clinical trials do exist such as the Functional Assessment of HIV-infection (FAHI) and the Patient Reported Outcomes Quality of Life-HIV (PROQOL-HIV) questionnaire. The FAHI, similar to the MOS-HIV, can be self-administered and completed within a relative short time period (5-10 minutes). The PROQOL-HIV poses challenges of its own in patients with acute illnesses as sections of the questionnaire focus on

long-term side effects. Therefore making it irrelevant to certain subgroups. Furthermore, the above measures do not include TB related questions (Meintjies et al. 2010). Quantitative HRQOL measures further tend toward a clinical perspective of patient experience of illness, which is beneficial on the individual level, but often it neglects the utilitarian public health perspective of a patient in a context greater than themselves (Ebrahim, 1995).

Additional apprehension in the use of these instruments in the South African context is understood from the perspective where these HRQOL tools were developed in and for Western contexts and prior to the widespread availability and uptake of ART. It is also noted that many studies in developing countries have used these instruments often without proper validation and reliability testing, bringing into question their appropriateness (Camfield & Ruta, 2007; Martin et al., 2007).

Due to the above challenges in the use of quantitative measures of HRQOL in a South African context dealing with HIV and TB, qualitative research is warranted to help navigate this landscape. The richer nature of qualitative data could provide insight and understanding of what constitutes HRQOL to individuals living with HIV and TB. Qualitative approaches have the potential to allow for the identification of HRQOL experiences that reflect meaningfully contextualised patient experiences as opposed to quantitative measures which are potentially limiting as it introduces predetermined constructs (Azungah, 2018). Thus, as noted earlier, potentially produces information not completely representative of patient experience (Haas, 1999). Fully contextualised patient experiences can foster appreciation of the influence of these experiences on health related behaviour and HRQOL which could affect improvement in interventions and policies (Conrad & Barker, 2010).

Qualitative methods could further guide adaptations to existing HRQOL tools to be more

context and illness specific and could produce a novel HRQOL measure which if demonstrated to work well in this context, can be used in future.

1.4 Pred-ART Trial

The current study formed part of a clinical trial called the Pred-ART trial conducted at the Site B HIV-TB clinic in Khayelitsha, South Africa. This trial set out to determine whether a 4-week course of prednisone in patients who start antiretroviral therapy within 30 days of starting treatment for tuberculosis (TB) and have a CD4 count ≤100/µL, reduces the incidence of paradoxical TB-IRIS (Immune reconstitution inflammatory syndrome), without an excess of adverse events. Patients were followed up on six occasions over a twelve-week period. The trial was powered to determine a reduction in TB-IRIS events. The objective of the clinical trial, should it demonstrate benefit and safety, was to take this intervention forward into a larger phase three clinical trial with a sufficiently large sample size to determine a mortality reduction.

In addition to the clinical arm the Pred-ART trial had a quality of life (QOL) sub-component. An aim of the of the QOL sub-component was to establish a definition of HRQOL that is more appropriate in this context (i.e. setting and illnesses), which can be used in the evaluation of the impact a treatment regime has on short-term health outcomes. The study objective was to develop a definition of HRQOL and produce a novel HRQOL measure through utilising QOL tools adapted to context and illness. If demonstrated to work well in this context, this HRQOL tool could be used in future clinical trials.

2. Purpose of this study

The purpose of this study is to explore the perceptions and experience of HRQOL among patients living with HIV-associated TB in Khayelitsha.

3. Rationale

Health-related quality of life is an ever-increasing significant aspect of health care interventions and research. However, HRQOL research has many challenges which has created gaps in this field. Among these challenges is the limited qualitative research on HRQOL that exist globally and in South Africa. Additionally, quantitative tools used to assess HRQOL are developed in Western settings with limited validation in African contexts. These measures are often generic in terms of disease illness. This study moves to explore HRQOL in a South African context among individuals with HIV associated TB from a qualitative perspective to gain a contextualised understanding of how HRQOL is understood or experienced by participants. This study aims to add to the gap that exists in qualitative HRQOL research in South Africa.

4. Aim, objectives and research question

4.1 Aim

The aim of the study is to gain an understanding of the experience and perception of HRQOL patients enrolled in the Pred-ART trial hold and how this relates to the existing understanding of HRQOL.

4.2 Objectives

The objectives of the study are:

1. To explore the experience of HRQOL among patients living with HIV-associated TB.
2. To examine the domains of HRQOL most pertinent to patients living with HIV-associated TB.

4.3 Research question

Exploring how Health-related Quality of Life (HRQOL) is experienced among patients living with HIV associated TB in Khayelitsha, South Africa.

Section Two: Methodology

1. Study design

This study will make use of a qualitative, exploratory study design. Exploratory study designs are employed when little is known regarding a particular phenomenon and aims to establish inductive derivations of the phenomena under study (Stebbins, 2011).

Furthermore, the majority of existing HRQOL research is quantitative in design with limited studies focussed on HRQOL in co-morbid HIV and TB (Cunillera et al., 2010; Pitt et al., 2008; Robberstad & Olsen, 2010; Ware & Sherbourne, 1992). A qualitative research study design therefore has the potential to address the gap in knowledge of how HRQOL is experienced by patients with HIV-associated TB and possibly provide a perspective not attainable through quantitative measures.

Although HRQOL among HIV and TB is widely researched globally, limited research in this regard has been done in South Africa (Kastien-Hilka et al., 2016; Robberstad & Olsen, 2010). Existing literature on HIV, TB and HRQOL in South Africa has also considered these two conditions separately despite high rates of co-morbidity among these illnesses (Kastien-Hilka et al., 2016, 2017; Nglazi et al., 2014; Robberstad & Olsen, 2010). This HRQOL study has particular focus on Khayelitsha which can be of significance to the HIV/TB burdened area due to the potential information it might produce which could be of value to future interventions in health care. Khayelitsha has the highest HIV prevalence in the Western Cape and has the greatest prevalence of TB in the Cape Town Metro East geographical service area (Mahtab & Coetzee, 2017; Stinson et al., 2017). Khayelitsha is further burdened by health-effecting socio-economic factors such as high rates of unemployment, informal housing and amenities such as water, flush toilets and electricity not available to all (Stinson et al., 2017).

2. Population and sampling

2.1 Study setting: Khayelitsha

The City of Cape Town, which the study setting Khayelitsha forms part of, in 2016 had 132 primary health care facilities which is constituted out of primary health care clinics, community day centres and community health centres. In addition to these facilities, the city has 85 ART and 128 TB treatment sites as well as 2 regional hospitals within the City's boundaries. The City of Cape Town has recently seen an increase in ART treatment sites, but the number of TB clinics have however decreased (Western Cape Government, 2017).

This study was conducted at the Site B primary public health HIV–TB clinic for outpatients in Khayelitsha (Meintjes et al., 2018). Khayelitsha is a peri-urban informal settlement situated 30km from the CBD of Cape Town, South Africa. Khayelitsha has an estimated population exceeding 500 000 with the highest unemployment rate in the Cape Town Metropolitan and subsequently widespread poverty among its residents (Stinson et al., 2014; Super, 2015; Western Cape Government, 2017). Despite the Western Cape province, in which Khayelitsha is situated, having the lowest HIV prevalence rate at 5% among South African provinces, Khayelitsha still has continued high prevalence rates of HIV (Stinson et al., 2017). Despite extensive HIV and TB prevention strategies which saw impressive reductions in TB incidence rates across South Africa between 2013 and 2017, South Africa continues to have one of the highest global TB burdens with more than 500 TB cases per 100 000 people in 2017 (World Health Organisation, 2018). Additionally, in 2016 Khayelitsha had 17% of all TB cases in Cape Town (Du Preez et al., 2018) and a worryingly high burden of Drug Resistant (DR) and Multidrug-Resistant (MDR) TB (Cox et al., 2014; Cox et al., 2010).

2.2 Population

In this study, the research population will be comprised of patients who are enrolled in the Pred-ART trial. Initial inclusion criteria to the Pred-ART trial was that patients had to be 1. ART-naïve, 2. Be an adult (≥ 18 years) who is HIV-infected, 3. Have a CD4+ blood count of < 100 cells/µL, 4. Diagnosed with active TB and 5. Start ART within 30 days of starting TB treatment. Further, patients had to be eligible for and provide consent to starting ART and written informed consent for trial. Exclusion criteria include: Kaposi's sarcoma, pregnancy, TB meningitis or tuberculoma at TB diagnosis (because these patients receive corticosteroids), known rifampicin-resistant TB, being on corticosteroids for another indication within the past 7 days, on other immunosuppressive medication within the past 7 days and uncontrolled diabetes mellitus.

2.3 Sampling

This study made use of purposive sampling from the patients enrolled in the Pred-ART trial. All patients included in the qualitative arm met the inclusion criteria for the Pred-ART trial and were thus adults able to provide consent. For the HRQOL qualitative arm, patients were selected based on their availability and willingness to participate in interviews related to quality of life concerning HIV-associated TB in more detail. An intended sample number for semi-structured qualitative interviews in this study was 20 – 25 participants.

3. Data collection

Data collection for this study was done using semi-structured one-on-one interviews at patients' follow-up visits as part of the Pred-ART trial. Patients in this trial had six planned followed-up visits from ART initiation (week 0), week 1, week 2, week 4, week 8, and week 12. Interviews were held at any of the above follow-up events as per the patient's preference

and convenience. Interview questions look to explore patients' experience and perceptions of HRQOL. Interviews were conducted in the participants' language of preference i.e. isiXhosa or English. Interviews were conducted by a trained HIV counsellor based at the Site B clinic. The interviews were audio recorded with the consent of participants, transcribed and stored in a digital cloud with restricted access to the quality of life research team. This team include the current researcher, his two supervisors (Ms. N. Sicwebu and Dr. A. Swartz) and two QOL researchers from the Pred-ART trial. A topic guide developed by the original project team was provided to the interviewer with a broad list of questions of interest to the study. The interviewer was trained on the use of the topic guide. The interviewer was encouraged to ask probing questions related to patient responses, while still collecting answers to all the necessary questions. I was not involved with the data collection process, nuanced understandings from interview observations are lost as sources of data, potentially impacting on the analysis and interpretation thereof. I'll present my analysis for input frequently to my supervisors Dr. A. Swartz who's involvement with the PredART trial started at the qualitative data collection phase and Ms. N. Sicwebu who was involved in the data transcription and translation phase, to obtain her insights and to ensure my analysis is respectful and reflections of the data.

Timing of follow-up visits could have influence debriefing interviews in that time passed could have resulted in different health outcomes at different times, patients could have suffered from medication side effects, later follow-ups could mean patients had more time to come across challenges to domains of HRQOL and would have impacted how they experienced HRQOL at that time, lastly later follow-up times could have provided patients with time to develop coping mechanisms to challenges to HRQOL again impacting how HRQOL is experienced at that particular time.

4. Data management: Use and protection of research data

Audio recordings and transcriptions will be uploaded onto password protected computers. These files will also be uploaded to web-based cloud storage for additional safekeeping, indefinitely. Restricted access to these files will only be provided to the research team. All recordings and transcripts will be appropriately labelled, after removal of all identifying information. Patient names will be entered into a study log where after it will be fully anonymised and assigned a corresponding trial number. Anonymising will involve removal of patient identifiers including initials, place of birth, place of residence, day and month of birth. Thereafter, all documentation and recordings will only reflect trial numbers. Original copies of signed consent forms will be stored in a locked cabinet to which the primary Pred-ART clinical trial researcher has access.

5. Data analysis

The data collected from debriefing interviews will be transcribed from audio to text and translated from isiXhosa to English by a co-researcher. A six-phase approach to thematic analysis as postulated by Braun and Clarke (2006) will be utilised in analysis of the data. Thematic analysis aims to move beyond the mere identification and count of themes and aims to describe implicit and explicit ideas and complexities within the data (Guest et al., 2014). Phase one is a process of familiarisation with the data. In this phase the transcripts will be read and re-read with initial notes made on identified patterns in the data on which subsequent analysis can build. Phase two is a process of generating initial codes. In this process an inductive approach will be followed to ensure strong links are kept between the codes and the data (Braun & Clarke, 2006). Phase three is the search for themes. Themes are identified from patterns and grouping of codes. Phase four is a process of reviewing themes. Themes will be reviewed by myself, a supervisor and co-supervisor in relation to coded

excerpts and the greater data set. The following phase is to name, define and refine these themes. The final phase as described Braun and Clarke (2006) is the final opportunity for analysis and the production of a report. A report will be written with an aim to publish in an academic journal and as a dissertation component to Master of Public Health.

6. Ethical considerations

This study is part of the larger Pred-ART clinical trial which has been granted HREC approval (HREC 136/2013). Additionally, the current study has been granted HREC approval (HREC 087/2020).

6.1 Voluntary participation

Although all participants in this study have granted informed consent to be included in the greater Pred-ART trial, participation in this sub-study will remain voluntary at all times with additional consent forms signed for this sub-study. Patients will be invited orally to participate in debriefing interviews. On their arrival for the interview the interviewer will explain the informed consent form in the participant's home language. Followingly, opportunity will be provided for the participant to ask any questions. To ensure patient confidentiality, participants will be reminded of their right to terminate the interview conversation at any point, and the option to refuse to answer any of the questions posed to them without any consequence. The patient will also be asked for permission to audio record the interview so that the conversation can be transcribed and translated from isiXhosa into English at a later stage, should it be required.

6.2 Confidentiality and anonymity

All information that relates to individual participants will be held in strict confidence. All identifying particulars will be removed through a process of anonymising patient details to

trial ID numbers. No information concerning the patient will be released to an unauthorised third party during or after completion of the study.

6.3 Reflexivity

Reflexivity is the process qualitative researchers engage in to explicitly evaluate their own inner subjectivity and its role in data analysis (Finlay, 2002). In this study I will be analysing secondary data which is not exempt from the influence of intersubjective experiences and its influence on data analysis (Jackson et al., 2013). I am aware that as a white middle class 29-year-old South African I'll have to take care in thorough introspection throughout. Therefore, I will remain reflexive through keeping a journal during the process of analysis and writing up to ensure that the outcome reflects and respects the data and the participants who provided it. I will also continuously discuss findings with my supervisor and co-supervisor to gain their insight and understanding of the phenomena.

6.4 Ethical approval

Ethical permission for the greater Pred-ART clinical trial has been obtained from the University of Cape Town Human Research Ethical Committee (HREC), as well as from Institute of Tropical Medicine IRB and the Ethics Committee of Antwerp University Hospital, Belgium, before the trial is initiated (HREC reference number 136/2013). This sub-study has been granted ethical approval from the Departmental Research Committee (DRC) at the School of Public Health and Family Medicine as well as from the University of Cape Town's Health Science Faculty's HREC (HREC reference number 087/2020).

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Part B: Literature Review

1. Introduction

There is a great amount of Health-related quality of life (HRQOL) literature, however there is little literature from qualitative research on HRQOL, especially in South Africa.

1.1 **Literature review structure**

1. Introduction
2. HIV and TB Comorbidity
3. Health-Related Quality of Life
4. Theoretical Approach: Social Constructionism
5. Conclusion

1.2 The objective of the literature review

Comorbidity of HIV and TB place an immense burden on patients, society and health care in South Africa. However, advances in medicine has produced medication that can improve health outcomes in these diseases. Nevertheless, improvements in health outcomes are not necessarily associated with improved experiences of health-related quality of life. Hence, the objective of this literature review is to explore how HRQOL is experienced among those infected by both HIV and TB. To guide this review, I will consider the state of HIV and TB comorbidity in South Africa and how this could relate to HROQL. Secondly, this review will examine HRQOL literature, to understand how it is defined and deployed in research. Lastly, this literature review will discuss available literature on social constructionism in health-related research. This review aims to organise current knowledge on HRQOL and HIV/TB to assess any key gaps in the literature.

1.3 The scope of the literature review

There is an abundance of studies on HIV and TB, as well as numerous articles on HRQOL, however, little research includes all three topics. This literature review will focus on HIV and TB comorbidity in South Africa and potential underlying causes. Next HRQOL will be explored to determine how it is defined and researched in existing literature. Thereafter the construct of HRQOL will be extended to include HIV and TB. This topic is important because with improvements in treatment of infectious diseases such as HIV and TB, these conditions which were formerly acute, become states of enduring illnesses, that last for long periods of time. HIV infection in particular has become a chronic condition with the introduction of antiretroviral (ARV) medication, extending lives to ages similar to those not infected (Degroote et al., 2014; Johnson et al., 2013; South African National AIDS Council, 2017; UNAIDS, 2019b). Consequently, HRQOL research in HIV-associated illnesses has sparked interest among health care professionals seeking to understand health outcomes and improve health care responses (Ebrahim, 1995; Kastien-Hilka et al., 2016; Nglazi et al., 2014).

1.4 Literature search strategy

The literature review process started off with a search for peer-reviewed articles with the key words: “Health-related quality of life” or “quality of life in health” or “HRQOL” and “Human-Immunodeficiency virus” or “HIV” and “Tuberculosis” or “TB” and “South Africa”. These keywords were input into the University of Cape Town library search database PRIMO, Google Scholar, and PubMed. Articles corresponding with the keywords were reviewed and reference lists examined for relevant articles. The literature review also drew on reports from the Western Cape Government, Statistics SA, UNAIDS, and the World Health Organisation (WHO). Information drawn from the aforementioned institutions were related to statistical information on HIV and TB in South Africa. As far as possible, focus for inclusion was placed

on articles published less than ten years prior to the submission of this review for inclusion. The aim thereof was to illustrate awareness of the progressive rate at which scientific papers are published, to offer current views of phenomena and highlight the paucity in the direction of current research (Pautasso, 2013). Exceptions to the ten-year timeline include articles discussing the formulation of HRQOL, its theoretical conceptualisations and early uses.

2. HIV and TB comorbidity

Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) remain major public health threats throughout the world with more than 10 million people estimated to have developed TB disease in 2017 alone (World Health Organisation, 2018) and 1.7 million people acquiring HIV in 2018 (UNAIDS, 2019a). The increasing prevalence of TB has been amplified by the persistent HIV epidemic (Mathema et al., 2017). In 2017 South Africa had 7.9 million people living with HIV with an adult population (aged 15-45 years) prevalence of 20.6% (HSRC, 2018). Sub-Saharan Africa has been impacted most by the comorbidity of these diseases, despite significant strides taken in combatting these infections (Govender et al., 2015; South African National AIDS Council, 2017; UNAIDS, 2019b). Illustrating South Africa's burden is its position as the fifth placed country by TB incidence, and the number one ranked country by coinfection with HIV and TB (Jacobson et al., 2015). Among those diagnosed with TB in South Africa, coinfection with HIV exceed 70% (Mathema et al., 2017; UNAIDS, 2019a).

High rates of coinfection of HIV and TB affect the poor and vulnerable populations of South Africa most. Coinfection rates can be ascribed to the immense burdens each of these diseases place on these populations separately, creating further vulnerability in acquiring the other disease (Loveday & Zweigenthal, 2011). South Africa has a mounting burden of TB, accounting for 2.4% more deaths than HIV in 2015 (STATS SA, 2016). Moreover, South Africa is one of

eight countries that contribute to two-thirds of the global TB prevalence (Mathema et al., 2017; World Health Organisation, 2018). The scale of the TB burden in South Africa is further displayed through the country's position as one of only three countries who exceeded 500 new TB cases per 100 000 people in 2017 (World Health Organisation, 2018).

2.1 Reasons for HIV/TB comorbidity

High rates of coinfection with HIV and TB occur largely through HIV's action in diminishing the efficacy of the infected individuals' immune system, making these individuals more vulnerable for infection by other diseases such as TB (Meintjes et al., 2017). Furthermore, challenges and differences in approaches to treating HIV and TB contribute to prevalence of coinfection (Loveday & Zweigenthal, 2011). HIV requires lifelong adherence to medication and takes a person-centred approach to delivering health care service delivery, focussed on patient education, autonomy and empowerment. In contrast, TB treatment aims to address the illness over a six-month period of direct observation in adherence with little focus on patient education and autonomy building (Loveday & Zweigenthal, 2011). These contrasting approaches could cause confusion and impact adherence negatively (WHO, 2003). Furthermore, patients with a CD4 cell count less than 500 cells/µl still spend a lot of time below this threshold despite initiating ART and resultingly have a greater risk an higher rate of TB incidence (Lawn et al., 2009). It has also been suggested that, adjusting for covariates, the excess TB rates among those with CD4 cell counts less than 200 cells/µl may be due to ART unveiling subclinical TB through rejuvenation of the immune system (Lawn et al., 2008, 2009). Lastly, patients often cease taking their medication when they are either feeling better or see no difference in health prior to the scheduled end of treatment. This cessation of treatment creates the opportunity for infections to return (Munro et al., 2007; WHO, 2003).

2.2 HIV/TB Treatment

Due to the high rates of coinfection between these two diseases, it is difficult to identify participants to enrol in research studies who only have either (Kastien-Hilka et al., 2017). Although the majority of patients in South Africa who have TB are also HIV positive, and despite the difficulty in identifying patients with only either one, most research studies still focus on these two conditions separately (Brown et al., 2015; Kastien-Hilka et al., 2017). Equally, collaborative HIV and TB treatment programmes are met with obstacles in South Africa such as intervention design and implementation, thus seeing to it that in many settings these diseases are addressed separately, despite their comorbidity (Loveday & Zweigenthal, 2011). However, effective management of both HIV and TB require integrated treatment approaches, meaning HIV and TB treatment programmes working in partnership to establish an holistic approach to treatment (Loveday & Zweigenthal, 2011).

Ending the global HIV and TB epidemic is set as a priority by the Sustainable Development Goals (SDGs), in particular goal 3.3 (United Nations, 2015). Key to achieving this goal is early detection of TB, which would initiate a timeous treatment response, which in turn reduces the risk of transmission and increases survival (Berkowitz et al., 2018). TB treatment in South Africa is divided into two phases. Patients start off with an intensive treatment phase where a combination of drugs are to be taken daily for two months. During the second, continuation phase, patients are prescribed two drugs to be taken daily for four months, dose and number of tablets are patient weight dependent (*South African National TB Guidelines - Adults*, 2017; The National Department of Health, 2014).

However, TB focussed treatment alone does not address the epidemic, but has been reported to be effectively supported by HIV treatment interventions (Loveday & Zweigenthal, 2011).

The recommendations in South Africa for the treatment of HIV with the use of ART sets out to achieve maximal suppression of viral load, restore and preserve patient immune function, prevent transmission of HIV, minimise adverse side effects from treatment, and importantly for this context, reduce risk of opportunistic infections, and prolong life expectancy and improve quality of life (QOL) (Meintjes et al., 2017). Due to the influence of persistent ARV treatment, South Africa has observed a 7% decrease in TB-incidence for the period 2010-2017 (South African National AIDS Council, 2017; World Health Organisation, 2018). Once HIV is diagnosed in a patient, treatment is to start immediately with either a two-drug or three-drug fixed dose regimen. This regimen is to be continued daily, for the entire duration of the patients' life (Meintjes et al., 2017).

Equally, for HIV positive patients who have a concurrent TB infection, initiation of antiretroviral (ARV) medication remains urgent, especially in advanced stages of HIV infection. However, it is suggested that ART is started with a two-week delay after initiation of TB treatment to reduce adverse side-effects (Meintjes et al., 2017). Possible side-effects include drug toxicity, increased vulnerability to hospital acquired infections, unveiling of underlying opportunistic diseases such as TB and Kaposi's sarcoma, and tuberculosis-associated immune reconstitution inflammatory syndrome (TB IRIS) (Lai et al., 2016; van der Plas et al., 2013).

2.3 TB IRIS

TB IRIS has an increased risk of developing after the early initiation of ART among individuals living with HIV who have low CD4 cell counts and an associated TB infection (Meintjes et al., 2018). TB IRIS is an inflammatory response characterised by recurrent or worsening TB associated symptoms such as fever, coughing, lymph node enlargement (recurrent or new),

or worsened radiography (Meintjes et al., 2020). Systematic reviews, report TB IRIS to occur in 16%-18% of patients diagnosed and treated for TB-associated HIV (Müller et al., 2010; Namale et al., 2015). TB IRIS is further reported to have an average lethality of 3.2% in cases (Müller et al., 2010). To reduce the incidence of TB IRIS, patients could be prescribed a four week course of a drug called Prednisone during the first weeks of initiating ART (Meintjes et al., 2017, 2018; The National Department of Health, 2014).

2.4 Improved Health Outcomes

Despite associated risks to treatment of comorbid HIV and TB it remains paramount that treatment be initiated timeously. While the prevalence of HIV and TB remains high in South Africa, there has been significant progress in the reduction of AIDS related mortality rates, and increases in life expectancy for those who are HIV positive (South African National AIDS Council, 2017). These improvements are due to increased distribution, availability and uptake of HIV and TB treatment and has resulted in the consequential progression of HIV infection to a chronic illness (Degroote et al., 2014; Kastien-Hilka et al., 2016; Pitt et al., 2008; Yang et al., 2018). Sustained progress in addressing the HIV and TB epidemics in South Africa is underlined by its commitment to the 90-90-90 goals in addressing HIV set for 2020, and the 2030 SDGs aiming to eradicate HIV and TB (UNAIDS, 2014; United Nations, 2015).

The 90-90-90 targets set for HIV are to have 90% of people living with HIV know their status, to have 90% of people who know their HIV-positive status on ART, and achieve an indetectable viral load in 90% of people on ART (UNAIDS, 2014). South Africa is reported to have reached goal one through the intense upscaling of ART, but still falls short of goals two and three which is largely assigned to the variability in performance toward these goals across provinces (Johnson et al., 2017; UNAIDS, 2019b). However, despite poor inter-provincial

performance on goals two and three, the value of achieving goal one is notable in two particularly significant measure of progress in health outcomes – the observed reduction of mortality rates and an increase in life expectancy among those living with HIV. Life expectancy has increased among the South African male population from 56.5 years in 2010 to 61.9 years in 2015 (South African National AIDS Council, 2017). Female life expectancy rose by a similar margin from 61.2 years to 67.7 years over the same time period (South African National AIDS Council, 2017). Life expectancy for HIV-positive individuals with CD4 cell counts ≥ 200 cells/µl were reported to be 70%-86% that of counterparts with the same sex and age who are HIV-negative (Johnson et al., 2013). Life expectancy was seen to increase among HIV infected people by 10%-15% two years after initiating ART (Johnson et al., 2013).

2.5 Health Outcomes and Health-Related Quality of Life

The progress made in terms of improved health outcomes carries with it a new set of challenges for public health and has led to the increasing importance and interest in measuring HRQOL in HIV associated research (Mutabazi-mwesigire et al., 2014). Research on HRQOL is of particular value as clinical outcomes in treatment of infectious diseases, which are significant to patient health, often do not align with patients' subjective experience of treatment and well-being (Azoulay et al., 2008; Haas, 1999; Kastien-Hilka et al., 2016). For example, the HIV treatment regimen places a significant burden on patients as it requires patients to consume up to three pills daily, from the day of diagnoses, for the remainder of their life (Vagiri et al., 2014). In addition, these medications are accompanied by side-effects, potential toxicity, and the increased susceptibility to opportunistic infections or unveiling of latent diseases, and inflammatory responses such as TB IRIS (Meintjes et al., 2017, 2018; Tam et al., 2012). Hence, the concern with survival among people living with HIV is accompanied

by the navigation of these side-effects and the HRQOL patients are able to experience amidst a lifetime of treatment (Biadgilign et al., 2012; Vagiri et al., 2014).

Considering the above literature, with the progression of comorbid HIV and TB to a chronic condition, a gap has emerged in the treatment thereof. In particular in relation to patients' HRQOL as patients become concerned not only about survival, but about their HRQOL as well (Vagiri et al., 2014). Consequently, urgent research concerning both of these conditions are needed in the South African context to understand HRQOL among people living with both HIV and TB (Brown et al., 2015).

3. Health-related quality of life (HRQOL)

The World Health Organisation defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (World Health Organisation, 1946). This definition starts to illustrate the multiple components there are to health. Important to note in this definition are the components of social well-being, as well as the ending statement "not merely the absence of disease or infirmity". These aspects create emphasis that health is not merely a binary condition of being ill or not that is experienced individually (Karimi & Brazier, 2016).

Despite the influential and encompassing definition of health, the biomedical approach predominantly used to treat illness has as its priority, patient survival and improved health outcomes (Azoulay et al., 2008), which offers a very narrow view of health. Although the importance of biomedicine is not denied, it is noted that health, illness and treatment have a significant experiential component to it, often overlooked by biomedicine (Azoulay et al., 2008; Conrad & Barker, 2010). The medical model assumes that diseases are universal and never changing in relation to time or place and is only focussed of improved patient health

outcomes (Azoulay et al., 2008; Conrad & Barker, 2010; Kaplan, 2003). Conceptual models of HRQOL recognises but move beyond the biological health status (Wilson & Cleary, 1995). The most frequently used HRQOL conceptual model postulated by Wilson and Cleary (1995), places the biological variables at the distal end of the HRQOL model and recognises the influence of other experiential variables, such as different types of support i.e. psychological, social, and economic, on HRQOL (Bakas et al., 2012; I. B. Wilson & Cleary, 1995).

3.1 Defining HRQOL

There is recognition of the personal experiential aspect of health and subsequently vast interest therein which started with research into health status and quality of life (Karimi & Brazier, 2016). The term HRQOL has its origins in the fields of psychology and sociology (Haas, 1999) and was first used in the 1980's in literature on the measurement of health status (Karimi & Brazier, 2016). Health-related quality of life was introduced by Kaplan and Bush (1982) in a debate on the assessment of the value of one healthy life year i.e. Quality-Adjusted Life Years or as they preferred; "well-year". Prior to the use of HRQOL, the terms quality of life and health status were already in use in the preceding decade (Karimi & Brazier, 2016). Health-related quality of life is preferred to quality of life and health status, although the interchanging use of these three concepts in literature has made distinctions between, and defining each difficult (Ferrans et al., 2005; Karimi & Brazier, 2016). Health status is deemed to only be concerned about the physical health of a patient in terms of symptoms and functional ability and is thus considered to be a component of HRQOL (Ferrans et al., 2005). Health-related quality of life and quality of life are more difficult to distinguish (Ferrans et al., 2005; Karimi & Brazier, 2016). Health-related quality of life is focussed on how health, illness and treatment impact quality of life and is not primarily concerned about other factors

influencing quality of life such as level of education, standard of living, transportation, environmental resources and politics (Ferrans et al., 2005). However, these aspects do at some level impact health and it has become difficult to draw a line to separate what constitutes HRQOL versus QOL (Ferrans et al., 2005; Karimi & Brazier, 2016). Defining HRQOL is further complicated by ambiguity in constructs related to, and underlying HRQOL such as health, healing, disease, illness and sickness have long been difficult to pin down and remain topics of debate (Boyd, 2000; Ferrans et al., 2005; Karimi & Brazier, 2016).

Defining HRQOL is further impacted by the many theoretical approaches and conceptual models that have been formulated to provide explanations of how commonly used HRQOL domains interact and come to produce HRQOL (Cummins, 2005; Peasgood et al., 2014). As most HRQOL research is quantitative in design, few theoretical frameworks have been developed that address the underlying constructs of HRQOL, the formulation of associated domains, or the phenomenology of HRQOL (Cummins, 2005; Peasgood et al., 2014).

3.2 HRQOL Domains

The quantitative measures used to evaluate HRQOL typically do so along set domains of life. Domains are those areas of life that are of interest to patients, health care practitioners and researchers, which can be addressed to improve HRQOL (Wilson & Cleary, 1995). These domains vary across measures as conceptualisations of HRQOL differ among tool developers (Busija et al., 2011; EuroQol Research Foundation, 2018; Ware & Sherbourne, 1992). However, they can broadly be condensed into physical, mental and social spheres pertaining to the individual patient (Cunillera et al., 2010; Ebrahim, 1995; Enimil et al., 2016; Hays & Reeve, 2010; Kastien-Hilka et al., 2016; Pitt et al., 2008; Robberstad & Olsen, 2010; Ware & Sherbourne, 1992). The physical domains are explored and measured through scoring on

quantitative tests where a HRQOL score would be derived from areas such as physical functioning, ability to execute certain roles at work, general health perceptions, pain and energy levels (Yang et al., 2018). Psychological or mental domains pertaining to HRQOL explore mood and discrepancies in affect such as depression and anxiety (Yang et al., 2018). Social domains are explored along social support, stigma, and participation in social activities (Yang et al., 2018).

HRQOL domains represented in the various quantitative instruments capture different domains or seemingly similar domains with a different nomenclature (Busija et al., 2011; EuroQol Research Foundation, 2018; Ware & Sherbourne, 1992). Clear overlap exists between these domains across measures, resultingly, most domains can be aggregated to create encompassing domains reflecting HRQOL and align with those aspects associated with health as encapsulated in the WHO definition of health. However, due to the variation in domain conceptualisation between measures it is difficult to make comparisons, draw conclusions and apply findings in practice (Ferrans et al., 2005).

3.3 HRQOL Significance

Over time HRQOL has remained an area of interest to researchers across a broad spectrum of fields and diseases, including both non-communicable diseases such as diabetes mellitus, Huntington's disease and rheumatoid arthritis, and infectious diseases such as HIV and TB (Busija et al., 2011; Carlozzi & Tulsky, 2013; Guo et al., 2009; Kastien-Hilka et al., 2017; Louw et al., 2012; Nglazi et al., 2014; Raaijmakers et al., 2014). Interest in HRQOL grew as advances in technology and medicine accounted for improvements in health outcomes and consequently, increases in life expectancy (Johnson et al., 2013). However, in many diseases longer lives were not guaranteed lives without health related difficulties or lives of quality

(Azoulay et al., 2008; Haas, 1999; Kaplan, 2003; Kastien-Hilka et al., 2016; Tomlinson et al., 2009). This is typically experienced in chronic conditions, including HIV managed by ART, where treatment has to be adhered to for a prolonged period of time, often without cure but only less deterioration in health (Kaplan, 2003; Loveday & Zweigenthal, 2011). These patients have to struggle with the psychological and social burden of not being cured and having to adhere to treatment often with severe side effects (Kaplan, 2003). Similar experiences are reported on for people living with TB (Guo et al., 2009). In their review Guo et al. (2009) report that although across studies TB treatment improves physical health, mental well-being lags behind and that after patients are microbiologically healthy, they still experienced significantly lower levels of quality of life compared to those in the general population.

In consideration thereof, the recognition and understanding of HRQOL research contributed to the body of knowledge revolving around patient care. The utilisation of HRQOL research enabled health care practitioners, patients and their families to make informed decisions on if and what treatment should be pursued or how interventions should be tailored, to not only ensure improved health outcomes but improved HRQOL as well (Azoulay et al., 2008; Haas, 1999; Vidrine et al., 2005). A South African based study by Jelsma, Maclean, Hughes, Tinise, and Darder (2007) evaluated HRQOL over a 12-month period among an HIV infected cohort receiving ART. Their findings indicated that ART is successful in improving HRQOL and that drug side-effects and toxicity did not have a pertinent impact on HRQOL. However, they report that these participants scored lower in HRQOL measures than healthy cohorts. They were then able to identify the need for support services as part of the ART program to promote adherence.

On a larger scale HRQOL information could guide treatment interventions, policy

development and distribution of resources to better HRQOL (Ebrahim, 1995; Jelsma, Maclean, Hughes, Tinise, & Darder, 2007; Kastien-Hilka et al., 2016; Shisana, Rehle, Simbayi, Zuma, Jooste, Zungu, Labadarios, Onoya, 2014; Ware & Sherbourne, 1992). In South Africa longitudinal data on HRQOL and medication adherence among those diagnosed with TB is not available and is argued to have the potential to aid in identification and assessment of sustainable interventions for TB (Kastien-Hilka et al., 2016). Health-related quality of life information in this regard can identify successes and gaps in current treatment approaches and motivate for tailored strategies for certain patient populations (Kastien-Hilka et al., 2016).

3.4 Assessing HRQOL

Predominant HRQOL research relies on quantitative measures to assess HRQOL (Bernheim, 1999). Numerous quantitative measures are available to paradoxically explore subjective, qualitative patient experiences of treatment, health and well-being (Azoulay et al., 2008; Bernheim, 1999). The irony in the quantitative approach has been noted as this approach attempts to quantify subjective patient experiences of health and treatment. These subjective patient experiences are the areas of focus in qualitative research and becomes difficult to fully grasp once quantified (Azoulay et al., 2008; Hammarberg et al., 2016).

Two commonly used quantitative HRQOL measures are the EQ-5D-3L and the Medical Outcomes Study (MOS) 36/12-item questionnaires. The EQ-5D-3L is an easy to administer (Cunillera et al., 2010) self-report questionnaire covering five life domains related to health, namely: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. In the EQ-5D-3L each domain listed above is presented as a statement with one of three possible answers for participants to choose from. Answers reflect possible patient experiences of the particular domain (EuroQol Research Foundation, 2018). The EQ-5D has been translated in

many languages and used in various contexts including South Africa (J. Jelsma & Maart, 2015). A version of the EQ-5D has been translated into isiXhosa and reported to have acceptable validity and reliability (Jelsma, Mkoka, Amosun, & Nieuwveldt, 2004).

The popular MOS Short-Form (SF) 36-item and MOS SF-12-item questionnaire measure HRQOL across eight domains namely physical functioning, role physical/role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role emotional/role limitations due to emotional problems, and mental health (Busija et al., 2011; Ware & Sherbourne, 1992). Answers to either the 36 or 12 questions are offered and scaled using the Likert method. The number of answers per question varies and ranges from two to five. The shortened MOS SF-12 has significantly decreased completion burden placed on the respondents (Cunillera et al., 2010). Domains on the SF-12 are pooled together in scoring to comprise a physical and mental component. Population norms are used to interpret scores however, no population norms are available for South Africa nor other African countries (Kastien-Hilka et al., 2017). As noted, there is variability among HRQOL measures in terms of the number and description of domains assessed.

Quantitative measures are generic in terms of disease and does not account for differences in conceptualisation on how subgroups might experience HRQOL (Kastien-Hilka et al., 2017; Scott et al., 2017). The insensitivity of measures to subtle but potentially significant differences between subgroups could result in findings not representative of their true HRQOL experience. However, HRQOL tools developed for use among those living with HIV do exist such as the Functional Assessment of HIV-infection (FAHI) and the Patient Reported Outcomes Quality of Life-HIV (PROQOL-HIV) (Degroote et al., 2014; Mthiyane et al., 2016). The FAHI, similar to the MOS-HIV, can be self-administered and completed within a relative

short time period (5-10 minutes). The PROQOL-HIV posts challenges of its own in patients with acute illnesses as sections of the questionnaire focus on long-term side effects. Thus, making it irrelevant to certain subgroups. Furthermore, the above measures do not include TB related questions (Meintjies et al. 2010).

Literature further reflects concern over the use of these instruments in South Africa as many of the measures were developed in western countries with use in these contexts. A lack in validity and reliability testing of these tools in developing countries bring into question the appropriateness of their use in non-western contexts (Camfield & Ruta, 2007; Martin et al., 2007). Moreover, concern is situated around the appropriateness of these measures in use with patients in HIV subgroups. For example among adolescents versus adults, women versus men, ART naïve (those who have never received ARV medication) vs treatment experienced (Clayson et al., 2006; Kastien-Hilka et al., 2017; Scott, Ferguson, & Jelsma, 2017)

Quantitative HRQOL measures further tend toward a clinical perspective of patient experience of illness, which is beneficial on the individual level, but often it neglects the utilitarian public health perspective of a patient in a context greater than themselves (Azoulay et al., 2008; Ebrahim, 1995). Qualitative approaches have the potential to address this and allow for the identification of HRQOL experiences that reflect meaningfully contextualised patient experiences as opposed to these quantitative measures which are potentially limiting as it introduces predetermined constructs in its' assessment of HRQOL (Azungah, 2018). Fully contextualised patient experiences produced by qualitative research can foster appreciation of the influence of these experiences on health-related behaviour and HRQOL which could affect improvement in interventions and policies (Conrad & Barker, 2010).

3.5 HRQOL in South Africa

HRQOL research conducted in South Africa among patients living with both HIV and TB have shown that available treatment for these conditions are effective in improving global HRQOL (Kastien-Hilka et al., 2017; Nglazi et al., 2014). The majority of HRQOL research conducted in South Africa are quantitative and utilise measures such as the EQ-5D, EQ-VA MOS SF36 and the WHOQOL-HIV instrument (Jelsma et al., 2007; Nglazi et al., 2014; Peltzer, 2012; Pitt et al., 2008; Robberstad & Olsen, 2010; Vagiri et al., 2014). In these South African studies, scores on HRQOL are seen to improve most during the initial stages of treatment of both HIV and TB (Jelsma et al., 2007; Kastien-Hilka et al., 2016; Peltzer, 2012). These studies further show that marked improvements in HRQOL is noted during uptake of treatment, but that adherence to treatment have an even greater positive influence on HRQOL. Vagiri et al. (2014) report that HIV positive patients who adhere to more than 95% of their treatment regimen have better mean HRQOL scores than those with less than 95% adherence.

Interestingly, even though HRQOL improves with treatment, HRQOL remains lower than that of comparative community groups not living with HIV (Jelsma et al., 2007). The domains of HRQOL reported to be most affected by HIV, TB and its treatment are the physical and mental domains (Kastien-Hilka et al., 2016; Louw et al., 2012). A South African study based across three TB burdened settings in the Northern Cape, KwaZulu-Natal and the Eastern Cape quantitatively assessed HRQOL among TB and HIV-co-infected participants (Louw et al., 2012). Louw et al. (2012) report that among these participants, significant positive effects of HRQOL were observed in the mental domain and that significant negative effects were observed in the physical domain. A quantitative study conducted by Peltzer (2012) in three districts in KwaZulu-Natal found that predictive factors in the improvement of HRQOL include

low levels of internalised stigma, being employed or earning wages.

The limited available literature on HRQOL in South Africa indicating improvements in HRQOL, among those living with HIV and TB and receiving treatment, warrants further study. Qualitative methodological studies in particular, are warranted to determine what this noted improvement means to patients, how it is experienced and what other factors beyond treatment are at play in influencing HRQOL. This information can aid in addressing the gap that remain in HRQOL between those who are infected and non-infected comparative groups.

4. Theoretical Approach: Social Constructionism

Social constructionism is one of a few postpositivist positions developed in the human health sciences (Cruickshank, 2012). Positivist positions assume reality to be an objective entity which transcends all individual perspective and manifests as observable, empirical patterns in behaviour (Wildemuth, 1993).This approach acknowledges and uphold the natural sciences as truth and recognises the power it has to drive progress among humans (Cruickshank, 2012). In health, this is to mean the application of knowledge generated by the natural "hard" sciences to advance technology and medicine (Cruickshank, 2012). Positivism further extends their view that empiricist approaches used in the natural sciences can directly be translated to explore and explain the social sciences (Wildemuth, 1993).

Social constructionism rejects positivism and takes a stance to create scepticism to what is put forward as truth by this approach (Potter, 2003). In the health context, social constructionism critically assesses knowledge claims made by health professionals (Cruickshank, 2012) and offers an alternative understanding to phenomena. This approach gave rise to the social sciences, particularly sociology. It is this approach that also recognised that social sciences are often more complex than natural sciences (Cruickshank, 2012). Social

constructionism further hold that researchers should question and replace empirical approaches claiming to offer certainty in knowledge. They suggest that empiricism be replaced with realism and fallibilism i.e. the notion that even in empiricism truth cannot be proven or accepted.

These approaches acknowledge that medical information or associated knowledge are not natural entities and that claims thereof to be true are socially constructed notions of power to uphold particular views or interests (Burr, 2003; Conrad & Barker, 2010). Moreover, social constructionism believes that all illnesses and the experience of illness are socially constructed through the patients' ascribed understanding of the illness (Conrad & Barker, 2010). Furthermore, social constructionism posits that individuals and their understanding of health or illness is formed through the social environment and that researchers cannot transcend and ignore the social environment to produce objective information (Cruickshank, 2012). Since the development of the social constructionism view, it has significantly contributed to the understanding of the social dimensions of health (Conrad & Barker, 2010). It is from this perspective that the literature review recognises the overwhelming empiricist approach to conducting HRQOL research, and that throughout, subjective human experiences are quantified. This review further acknowledges that power is situated with quantitative approaches over use and acceptance of qualitative methods. Therefore, the analysis approach in this study will be underscored by social constructionism to create scepticism around the existing dominant approaches and understanding of HRQOL and to offer views that potentially differ to the hegemonic opinion (Conrad & Barker, 2010). Furthermore, this approach has additional value as it has shown to aid in development of effective medical practice and development of health policies which improve access to treatment (Conrad &

Barker, 2010).

5. Conclusion

HIV and TB continue to be highly threatening diseases to public health globally and in South Africa. These diseases have long been studied separately and focus should be shifted to research inclusive of both. This is especially true within the South African context with extremely high rates of co-infection of HIV and TB. With effective treatment of HIV and TB, life expectancy has increased, and patients can live long lives in line with the life expectancy of the general population. Therefore, efforts should be made to ensure that these lives are experienced as lives of quality. Research on HRQOL remain of great interest and has the potential to offer valuable information to health care. The majority of HRQOL research is however quantitative and a qualitative approach is needed in South Africa to develop a contextualised understanding of HRQOL among those living with HIV and TB. Qualitative HRQOL research, together with a social constructionist perspective, can shed light on the influences of patient experience of HRQOL on health-related behaviour, which could aid in improvement or development of interventions and policies aimed at improving not only health outcomes but HRQOL as well. Qualitative research could further aid in the development of a quantitative HRQOL instrument primed for the South African context.

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PART C: Journal Ready Article

"To live a good life is different from good health": An exploration of patients' experiences of Health-related quality of life (HRQOL) with HIV-associated TB in Khayelitsha, South Africa.

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Abstract

Background: Health-related quality of life (HRQOL) is an important construct measured in health research, however little qualitative research exists in this field in South Africa. The research setting, Khayelitsha, is one of the largest informal settlements in South Africa and is one of the global locations with the highest HIV and TB burdens.

Methods: Using a deductive analysis approach, we explored qualitative interviews on HRQOL among participants living with HIV-associated TB to examine the experience of HRQOL most pertinent to them. Sixteen interviews were conducted with both male and female adult participants. Data were synthesised into three main interrelated themes to reflect the ways that HRQOL is commonly explored, namely the physical, social and mental domains. These domains are not exhaustive to HRQOL but are regarded as the starting point to all HRQOL discussions and aligns with the World Health Organisation definition of health.

Findings: Experiences of HRQOL are discussed along predominant themes in HRQOL research These themes include, the physical experience of HRQOL, the social experience of HRQOL, and the mental experience of HRQOL. However, we further identified and argue that

irrespective of domain, underlying social experiences of HRQOL underscore the presentation of HRQOL along the presented popular domains. From a social constructionist approach, we illustrate that HRQOL domains are not experienced in isolation but are interconnected through social experience. The social experience of HRQOL was identified as the common denominator which connect all domains and around which HRQOL revolve for these participants.

Conclusion/Significance: Health-related quality of life is experienced socially with the interpersonal connections patients have with significant others presenting as significant to HRQOL among patients living with HIV-associated TB. Recognising the social experience of HRQOL we hope to add to the existing literature of HRQOL and that future programmes can draw on this perspective to better HRQOL among patients.

Introduction

The introduction of antiretroviral therapy (ART) brought improved health outcomes for those living with Human Immunodeficiency Virus (HIV). Large scale rollout of antiretroviral (ARV) medication further saw HIV infection develop into a chronic illness with extended life years (Degroote et al., 2014; Johnson et al., 2013, 2017; South African National AIDS Council, 2017; UNAIDS, 2019b). Subsequently, the measurement of Health-related quality of life (HRQOL) has become an increasingly significant component of HIV-associated research (Degroote et al., 2014; Kastien-Hilka et al., 2016; Pitt et al., 2008). Although the clinical outcomes in treatment of infectious diseases are significant to patient health, the patients' subjective experience of treatment and well-being often does not align with clinical improvements (Kastien-Hilka et al., 2016). Health-related quality of life research utilise quantitative measures to explore these subjective experiences associated with treatment, patient health, and well-being often through consideration of physical, mental and social life domains pertaining to the individual (Ebrahim, 1995; Kastien-Hilka et al., 2016). The value of these explorations lie in the additional information it offers to the process of decision making relating to product approval, pricing, health care interventions, health strategies and health policy development (Kastien-Hilka et al., 2016; Robberstad & Olsen, 2010; Till et al., 2019).

Typically, HRQOL is measured through the use of a quantitative tool, of which a multitude exist (Cunillera et al., 2010; Pitt et al., 2008; Robberstad & Olsen, 2010; Ware & Sherbourne, 1992). However, it has been noted that qualitative efforts to study HRQOL is needed and that a move away from quantifying subjective experiences is required (Barofsky, 2012a; Malterud, 2001; Till et al., 2019). This move comes as awareness grows around the limitations of quantitative research to fully grasp the meanings people attach to social phenomena related

to health (Collingridge & Gantt, 2008; Macur, 2013), as well as the understanding that qualitative research has an integral role to play in the expansion of health related knowledge (Lützén, 2017; Malterud, 2001). Qualitative research specific to HRQOL can address the paucity in qualitative research that exist globally and in South Africa. Furthermore, it can aid in developing a contextualised view of HRQOL which is neglected by quantitative tools (Conrad & Barker, 2010).

Quantitative HRQOL instruments are often generic in their design, meaning that these tools are developed to be applied to various diseases or illnesses (Barofsky, 2012b; Degroote et al., 2014). Thus, their use creates sections that are irrelevant to patients with particular conditions and neglects aspects of HRQOL which are relevant. Additionally, the quantitative tools used to assess HRQOL are developed in Western settings with limited validation in African contexts. Qualitative research can help contribute to the development of quantitative tools that are more firmly rooted in specific contexts related to disease and environment.

Existing qualitative HRQOL research corroborates the notion that an oversight in HRQOL research exist. A Canada-based qualitative study argue that the impact of TB on quality of life (QOL) has for long been underestimated and neglected (Marra et al., 2004). The aforementioned study conducted among patients living with active TB has identified four themes impacting QOL. These themes include “diagnosis issues”, “medication issues”, “social support and functioning”, and “health behaviour” (Marra et al., 2004). Furthermore, a qualitative study among people living with HIV in Uganda report on the complex nature of a subjective construct such as HRQOL. They illustrate how, for these individuals, HRQOL was based on environmental conditions such as work and money, perceived usefulness to others, contentment with one’s predicament, ability to cope in the face of stigma, disclosing health

status and lack of social support, and satisfaction with life in general (Mutabazi-mwesigire et al., 2014).

The objective of the present study is to explore HRQOL in a South African context among individuals with HIV-associated Tuberculosis (TB). A qualitative research approach is taken to gain a contextualised understanding of how HRQOL is understood or experienced by this population. Health-related quality of life experiences are explored among patients who live with HIV-associated TB who were enrolled in an antiretroviral therapy trial.

Qualitative data collected for the present article formed part of the greater Prednisone antiretroviral therapy (PredART) trial. The qualitative sub-study to the trial set out to acquire information on HRQOL among South African populations living with HIV-associated TB and in the use of a prescribed drug called Prednisone. Prednisone is prescribed to lower the incidence of tuberculosis-associated immune reconstitution inflammatory syndrome (TB IRIS) (Meintjes et al., 2017, 2018; *South African National TB Guidelines - Adults*, 2017). TB IRIS is a condition that can occur in patients diagnosed with HIV who are receiving treatment for TB. An increased risk of developing TB IRIS exist after early initiation of ART among individuals living with HIV, who have low CD4 cell counts, and an associated TB infection (Meintjes et al., 2018). The trial found Prednisone to lower the incidence of TB IRIS compared to a placebo group (Meintjes et al., 2018). As stated above, evaluating HRQOL in HIV-associated research as in the PredART trial has become increasingly important to better address patient HRQOL, in addition to improving health outcomes.

Health-related quality of life is widely argued to be an individual construct (Carr & Higginson, 2001; Ebrahim, 1995; Mutabazi-mwesigire et al., 2014). This view is framed by the underlying consideration that measures used to assess HRQOL should be person centred in design, i.e.

focussed on the individual, to capture the individual experience (Carr & Higginson, 2001). The individual experience of HRQOL is frequently discussed along central domains namely the physical, social and mental domains (Cummins, 2005; Mutabazi-mwesigire et al., 2014).

In this article, we illustrate that participants spoke about HRQOL along these existing domains but argue that the experience of HRQOL in this context was profoundly social rather than individual. We offer that, in this context, HRQOL should be understood as reflecting a set of social experiences. These experiences encapsulate the social interactions, interpersonal relationships, and the positioning of oneself as a being in relation to others. We further hold that there is value to be added to interventions and policies when the social perspective is considered in addressing HRQOL.

Methods

Context & Setting:

PredART Trial

Qualitative data collected for this paper formed part of the PredART study which was conducted at the Site B primary public health HIV–TB clinic for outpatients in Khayelitsha (Meintjes et al., 2018). The PredART trial was a randomised, double-blind, placebo-controlled trial which set out to determine if the incidence of TB IRIS can safely be reduced with the administration of a drug called Prednisone. The trial enrolled 240 patients (120 in each arm i.e. placebo versus control) living with HIV and who have never used ART and had CD4 counts of lower than 100 cells per microliter. These patients were also living with TB and started treatment for TB within thirty days prior to starting ART. Patients were followed up on over a 12-week period to monitor the development of TB IRIS and drug safety (Meintjes et al., 2018).

Location

Khayelitsha is a peri-urban informal settlement situated approximately 30km from the central business district of Cape Town, South Africa. Khayelitsha has, in addition to an extensive health burden, numerous socio-economic challenges. It has the highest unemployment rate in the Cape Town Metropolitan, and subsequently, widespread poverty among its residents; it also has high rates of substance abuse, including excessive consumption of alcohol (Saban, Morojele, & London, 2017; Stinson et al., 2014; Stinson et al., 2017; Super, 2015; Western Cape Government, 2017). These socio-economic challenges have negative impacts on population health (Ataguba et al., 2011).

While the Western Cape province has the lowest HIV prevalence at 12.9% among South African provinces (HSRC, 2018), Khayelitsha still has continued high prevalence rates of HIV with antenatal prevalence rates of 34.3% reported in 2012 (Stinson et al., 2017). In comparison, the national antenatal HIV prevalence for 2015 was 18.9% (The National Department of Health, 2015). Additionally, despite extensive HIV and TB prevention strategies which saw impressive reductions in TB incidence rates across South Africa between 2013 and 2017, South Africa continues to have one of the highest global TB burdens, with more than 500 TB cases per 100 000 people in 2017 (World Health Organisation, 2018). Additionally, in 2016 Khayelitsha had 17% of all TB cases in Cape Town (Du Preez et al., 2018), 37% of all TB cases in the Cape Town East Metro (Kastien-Hilka et al., 2017), and a worryingly high burden of Drug Resistant (DR) and Multi Drug Resistant (MDR) TB (Cox et al., 2014; Cox et al., 2010).

Sampling/Participant selection

A total of 20 patients who were already enrolled into the PredArt study were purposefully selected based on age, sex and TB-IRIS diagnoses to have broad representation of participants

in the qualitative sub-study. Patients were selected based on their availability and willingness to engage in interviews concerning quality of life related to HIV-associated TB. A total of 16 interviews were successfully recorded, translated and transcribed. Of the interviewees, ten were males, six females, with ages ranging from 24 to 56 years of age. All patients had concurrent HIV and TB infections.

Data collection

Interviews were conducted by a mother tongue isiXhosa speaking clinic counsellor trained in the usage of a semi-structured interview guide. Semi-structured interviews are beneficial and appropriate for the exploration of participant experience of complex topics such as HRQOL; they allow researchers to probe for more information or clarification of responses during interviews (Louise Barriball & While, 1994). Additionally, due to the wide range in age and life experiences, semi-structured interviews were better suited than a set interview schedule to allow for and capture differences individual experience.

Interviews were held in a private room at the Site B HIV-TB clinic. As part of the PredART trial patients had six planned follow-up visits. Follow-up visits were scheduled at week 0, week 1, week 2, week 4, week 8, and week 12 from ART initiation. Interviews were conducted at any of the above follow-up events as per the patient's preference and convenience. Further, interviews were conducted in the patients' preferred language. For all participants, the preferred language was isiXhosa. Interviews were audio recorded and later translated and transcribed from isiXhosa to English. The duration of interviews varied, with an average duration of 27 minutes.

Data analysis

A deductive framework analysis was utilised in analysis of translated, and transcribed participant interviews. A framework analysis is a five stage systematic iterative approach to data analysis (Pope et al., 2000). First, the analysis process was initiated by familiarisation with the data. Then followed by identification of a thematic framework. Next, a codebook was developed through an iterative process by one researcher and reviewed by two independent researchers. Thereafter, the codebook was used in the process of indexing transcripts, where text sections were linked to themes via codes. Similar indexed sections were charted, pooling thematic sections with verbatim text and summaries of experiences. Here a deductive analysis approach was introduced where the pooling of thematic sections was guided by domains frequently used in HRQOL research. Charted themes were mapped together and scrutinised for links and connections leading to interpretation and explanation of the findings (Pope et al., 2000).

Conceptual framework

Defining HRQOL, and related constructs such as health, healing, disease, illness and sickness have long been elusive and continue to be topics of debate (Boyd, 2000; Ferrans et al., 2005; Karimi & Brazier, 2016). Health-related quality of life research is marked by confusion due to the interchanging use of concepts such as Quality of Life (QOL) and HRQOL and health status (Boyd, 2000; Ferrans et al., 2005; Karimi & Brazier, 2016). Karimi and Brazier (2016) report that four different definitions on HRQOL can be identified in literature which are distinct from the definitions available for quality of life (QOL) and health status. However, the definition of HRQOL which the current article finds to be the most inclusive in identifying constructs related HRQOL is one postulated by Ebrahim (1995). Ebrahim (1995) states that HRQOL is a

combination of self-perceived aspects which are related to well-being in the presence of disease or treatment. The self-perceived aspects Ebrahim (1995) refers to include constructs of HRQOL which align with the World Health Organisation (WHO) definition of health and comprise of physical, mental, social, impairment, disability and handicap as dimensions to health. We therefore argue that well-being as Ebrahim (1995) refers to it should in this context be understood as the WHO definition of health i.e. "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".

Health-related quality of life is often discussed in terms of life domains. These domains vary throughout literature and broadly include, but are not limited to, the physical, mental and social spheres of life pertaining to the individual (Cunillera et al., 2010; Ebrahim, 1995; Kastien-Hilka et al., 2016; Pitt et al., 2008; Robberstad & Olsen, 2010; Ware & Sherbourne, 1992). The physical domain is considered to include areas such as physical functioning, ability to execute certain roles at work, general health perceptions, pain and energy levels (Yang et al., 2018). The mental domain pertaining to HRQOL is explored in relation to the mood of the participant and discrepancies in affect such as depression and anxiety (Yang et al., 2018). Lastly, social domains are explored along categories such as social support, stigma, and participation in social activities (Yang et al., 2018). Additionally, a myriad of theoretical approaches exist which attempt to explain how the domains captured in HRQOL, quality of life, health and health status interact (Cummins, 2005; Peasgood et al., 2014). Many of these conceptualisations have definitions of HRQOL which perceive health in isolation of other domains of life such as economic position, religious or spiritual domains (Karimi & Brazier, 2016).

Despite many theories describing the interaction between domains associated with HRQOL

and how these interactions come to present as HRQOL, little testable theory on the underlying constructs and conceptualisations that make up these HRQOL domains exist (Cummins, 2005). Among those with enduring illnesses such as HIV and TB, the domains of physical, social and mental serve as broad terms for the exploration of underlying constructs related to quality of life such as self-care, participation in usual activities, work and employment, finance, and care and financial support of significant others.

Ethical considerations

Patients were recruited for individual interviews as part of a study which has been granted ethics approval from the Human Research Ethics Committee at the University of Cape Town's Faculty of Health Sciences (HREC reference number 136/2013). Participation in individual interviews were voluntary with research objectives explained to participants in their home language (isiXhosa) prior to obtaining informed consent. Informed consent was obtained from all participants. Measures were set in place to ensure participant confidentiality and anonymity. All patient identifiers were removed from interview schedules and interview transcripts and replaced with participant reference numbers. Interview audio recordings and transcriptions are stored on password protected computers as well as in web-based storage for additional safekeeping. Access to data in web-based storage is restricted to researchers involved in this project.

Results

During individual interviews on HRQOL, participants openly shared their experience of living with both conditions. Based on the data collected from the individual interviews, three broad main themes were identified. These themes align with the predominant domains utilised in HRQOL research - physical, social and mental.

Each of these themes are comprised of sub-HRQOL constructs of participant experience. The physical domain was typified by physical well-being, loss of physical strength and self-care. The social domain comprised of partaking in usual activities, the experience of stigma or the absence thereof and care for those other than oneself. The mental domain entailed concern or anxiety over the care and well-being of significant others and strategies of coping. Furthermore, these themes were seen to be strongly interrelated, illustrating the complexity of HRQOL.

Physical experiences of HRQOL

Physical experiences of HRQOL were most often the first point of discussion among participants in relation to living with HIV and TB. Physical experiences revolved around simple ideals of HRQOL and were focussed on health. Other physical experiences were complex as the physical domain started to merge into other domains.

Physical well-being

An integral identified part of HRQOL was health, particularly physical health. Participants raised physical well-being as the first point of discussion in response to interview questions on HRQOL. Participants had a binary experience of physical well-being as either being healthy or not; falling ill or not: “he/she is healthy, and hardly gets sick. She/he is alright and well”; “when you are not sick” and “Good health, like in the body”. It appeared essential to participants, bar one, that to have good HRQOL, one must have good physical health. The one exception was a participant who expressed that to them a clear distinction exists between physical health and HRQOL and that one can have good HRQOL despite living with a disease.

Loss of physical strength

Health-related quality of life was experienced as a loss of physical strength. The loss of physical strength meant many participants could not participate in their occupations. Among individuals who were employed prior to falling ill, the debilitating effect of advanced HIV/TB infections forced participants to cease working: “I do not quite have the same strength to work as I used to”; “I have stopped now because I am sick, I have no energy that’s needed to work”. Loss of the physical ability to conduct work was a threat to HRQOL as it threatened participants’ livelihood. A loss of employment meant loss of income and an increased dependency on others. All participants spoke about being dependent on others for financial or material assistance once falling ill.

Self-care

Living with HIV and TB made patients more cognisant of their health and awakened a sense of responsibility to their health. Phrases such as “It is to look after yourself and taking good care of yourself”; “I must look after my health” and “I need to look after my life and health” were common. HIV and TB have extensive treatment regimens and part of participant self-care meant adhering to medication. Not all participants were certain about what medication they were taking or for how long they should take them. They were, however, aware that taking medication is important to their health and HRQOL.

To have good HRQOL, participants were aware that some lifestyle changes were required and was reflected in self-care where. For participants lifestyle changes meant changes in dietary intake and abstinence from alcohol. Self-care was frequently discussed in the context of participating in usual activities which often meant social interaction, which were often centred around alcohol consumption. Self-care in the form of abstinence from alcohol was a

threat to HRQOL because being able to consume alcohol with friends was seen as an activity which promotes a life of good quality and the lack thereof acted as a reminder that their quality of life is diminished because of health.

Social experiences of HRQOL

The social domain was often discussed in close relation to the physical experiences of HRQOL. The physically debilitating effects of HIV/TB infections had rippling effects to social experiences of HRQOL. Social experiences of HRQOL were identified to be present in two main ways. The first related to partaking in usual activities and second, the experience of stigma, or the reported absence thereof.

Usual activities

Usual activities revolved around two aspects: one, employment and two, socialising with peers. Employment was a notable experience of HRQOL in the social domain; as one participant noted in response to the question how they understood HRQOL "I would say it's a person that doesn't have any problems, that lives their own life, who has a job, like you for example". For participants, the social experience of employment revolved around the social responsibility of taking care of others with income received. Being employed represented a source of income. Without income, participants were unable to fulfil their social role as breadwinners and felt despondent: A participant expressed "life is stuck now" when reflecting on the loss employment and income.

In the absence of steady income, participants were forced to increasingly depend on others for financial support. This took away independence and autonomy in daily decision making regarding, for example, acquiring food or planning meals. Participants further experienced this as a personal failure to provide for their families and maintain a household. The pressure

of social responsibility was also reflected in obtaining employment, as a participant who had to stop working because of his failing health expressed the initial pressure to work. “I was the first one to get a job, I left school, and I didn’t even go to high school. I was in standard 7 but dropped out halfway through and came to work here; because I saw that my brother was struggling”. In addition to a loss in autonomy over usual activities regarding employment, autonomy was also taken from participants regarding socialisation through stringent guidelines on treatment of HIV and TB.

Usual activities of socialising with friends over the consumption of alcohol was a major factor for participants. The use of alcohol along with HIV/TB treatment is not recommended and participants reported attempting to adhere to this. However, participants searched for loopholes in alcohol consumption along with treatment. Throughout interview discussions participants frequently probed the interviewer on the use of alcohol along with being on treatment. Participants discussed scheduling of medication and attempted to identify time periods were the consumption of alcohol would not limit the effect of the medication or induce severe side effects. It became evident that much of socialising behaviour revolved around the use of alcohol. One participant discussed his life prior to falling ill as: “It was nice, I enjoyed my life, we would drink and get drunk every weekend, I would enjoy myself would always be around girls but things changed when I realised I was ill”.

Participants expressed changes in lifestyle with HIV/TB and increased cognisance of health: “It (my life) has now changed because I used to be someone who used to go to parties, drink alcohol and on weekends I would enjoy myself by drinking alcohol but now I know that I cannot drink, I have to look after my health”. Another reflected a similar experience: “For example if I was at a party, drinking with friends; I could drink for as long as I wanted or when

the alcohol finishes but now even if I am out, I must always be mindful of the time I am supposed to take my treatment so that I do not miss it".

Stigma

Stigma was a theme present within the social domain in the context of employment, disclosure to family, and perceived stigma in the larger community. Employed participants were required to discuss their condition with their employers and faced the potential risk of experiencing HIV/TB associated stigma. Fortuitously, their disclosure was well received by employers and there were attempts to accommodate them and their health states. "I had to tell my boss about the situation (illness and treatment) and he was understanding". Moreover, participants indicated that they experienced similar responses and treatment when they disclosed their health status to their families.

Participants' disclosure to family members, such as parents/caregivers and spouses/partners were also well received. As one participant stated after disclosing his HIV status: "Nothing has changed at home, things are still good". Participants all experienced support from those close to them. Support came in the form of moral support, assistance with travel and material needs as well as financial aid. "…my child takes care of me and gives me things like money"; "Yes she and her husband [support me]. So, I did not see any difficulties sis because each month they give me money. They try to ensure that I am not stressed. They do everything for me when I have a need". One should note that the act of disclosing to family and employers placed the participants in positions where they had to confront their states of health in relation to a broad range of people, exposing them to responses that could have been experienced as stigmatising.

While participants received acceptance and support from close associates, the role of stigma was present in the participants' narratives in various ways. Some of the statements that participants made indicated that they did not experience stigma, as effective treatment allowed those infected to present as others do: "I mean to say you cannot separate from those who do not have these things (HIV and TB). I am okay, I also look like them (people not living with HIV/TB). The only difference is that I eat treatment, and no one can tell that I do". However, secrecy regarding consumption of treatment indicates that fear of discrimination and stigma was experienced. Perceived stigma was further experienced in the larger community. In fear of being stigmatised one participant moved closer to and preferred to receive treatment at the Site B clinic as opposed to the HIV treatment facility close to her home. "That side they still view HIV people as.... so, I feel like they will make me not feel okay whereas this side I feel like people are more open". "They look down on someone with HIV, make them feel ashamed".

Mental experiences of HRQOL

Mental concern

Mental concern as experienced by participants manifested as anxiety and apprehension. This concern is situated in participants anxiety over their children, siblings, and caregivers. Participants expressed apprehension over the care and financial support of their loved ones should they not recover from their illness. As one participant expressed her fear: “My concern was leaving my child behind at a young age so those are the kind of thing I would think about. But it was explained to me that if I take my treatment regularly then I would be able to see my child grow. That is what was concerning me”. Another participant posed a question of care to the interviewer: “The one thing I would like to know is that, should I get sick again, would you be able to assist with my siblings who are in school?”. Another female participant struggled to cope with the worry she witnessed in her children once they knew about her condition to the extent that she sent her children to live with her mother: “I was very worried about them and I would also just cry because I felt hurt and most times I would send them to stay with my mom because they would always cry when they saw how I was; so I wanted to remove them from that environment”.

Coping

Within the mental domain, coping with diagnoses was identified as an experience of HRQOL. Some participants found their coping strategy in the notion that they are not the only one infected by HIV and TB:

> “I learned to accept and told myself that these diseases do not belong to animals, they belong to people, and I am not the only person who has them. It will be different and problematic if they were rare

> diseases, a case whereby nothing is known about them and they are still being researched. Mine are well known so I have no problem, I just accepted things as they are for me to live with them and take treatment".

Others coped with their illness with the knowledge that medication can help them live lives of similar quality to those not living with HIV/TB: "…living with both HIV and TB is not the end of the world. There is a lot that one can still do and take medication regularly it is manageable, and I can live the same life as anyone else". Interestingly, despite the high rates of alcohol consumption in Khayelitsha, alcohol consumption was not reported as a means of coping with the trauma and effects off illness, or the possible side effects of treatment for most participants.

Discussion

Health-related quality of life is frequently studied in health research, however little research is conducted from a qualitative perspective to offer a contextualised view of HRQOL specific to certain diseases, particularly in Africa. In this study we analysed qualitative interviews to explore how HRQOL is experienced among individuals living with HIV associated TB in the peri-urban informal settlement of Khayelitsha, South Africa. Using a deductive analysis approach, themes related to HRQOL were identified in the data. Our study has shown that HRQOL, among our participants, is experienced across three themes aligned with the predominant HRQOL domains of physical, social and mental. Each theme is shown to be comprised of associated sub-themes. Across these domains, we identify the overwhelming presence of a social thread in how HRQOL is experienced. Interactions between HRQOL domains illustrate that these domains do not present in isolation. Rather, the interactions

highlight the restrictions such set domains bring in the understanding of HRQOL. Hence, we hold that the social domain, particularly social relationships, are at the forefront of the existing connections between domains in the experience of HRQOL. Therefore, this article posits that these domains are suited to be explored from a social constructionism position.

Social constructionism proposes that the experience of all illnesses is socially constructed. The social construction of illness-experience is situated in how individuals make sense of and live with their illness (Conrad & Barker, 2010). The biomedical perspective often views illness as a fixed feature in nature and often neglects the social domain of health states and the subjective experiences of these health states. The social construction of illness and health is noted in various aspects thereof including the creation, spread, treatment (or lack or avoidance thereof) and the social response to the disease (Conrad & Barker, 2010; Singer, 2004). For example, Singer (2004) postulates that conditions such as HIV have strong biological components to it, but that HIV and its progressed state AIDS, cannot be entirely understood from a biomedical perspective alone. HIV and AIDS have far reaching implications in social settings and the social relationships they are comprised of. The social construction of these conditions have impacts on the spread and distribution of the disease as well as the social response in terms of support, stigma and subsequently help seeking behaviour and treatment adherence (Conrad & Barker, 2010; Singer, 2004). Patients are not passive passengers on a treatment voyage but rather enact their illness and assign meaning to it (Conrad & Barker, 2010) which formulates their experience of HRQOL. Hence, the exploration of patient experience of HRQOL along social constructionism is of significance as it produces differing views to the often deterministic and unilateral approach taken by biomedicine and the conditions it treats. Social constructionism can provide perspectives that aid effective

medical practice and policy (Conrad & Barker, 2010). From this perspective the social experience of HRQOL within other domains become more apparent and illustrates how central these social experiences are in HRQOL.

Physical as social

The physical domain was characterised by the loss of physical strength and the increased awareness of having to tend to one's health. The consequences of these physical effects were experienced socially and were the most pertinent in interview discussions. These physical HRQOL elements were experienced socially as a loss of or pause in employment which had vast impacts on HRQOL across all domains.

The loss of physical strength is regarded different to physical well-being as it started to illustrate some of the connections between HRQOL domains. Physical well-being dealt with a binary view of health of either being ill or not. In contrast, loss of physical strength revolved more around the consequences, in particular the social and economic impact thereof. The social experience of loss of physical strength was typified in the inability it caused to continue working. Employment is known to serve as an integral part to people's lives. It offers structure to life, a network of social support, a sense of belonging, a role to fulfil and adds meaning to life (Hoffman, 1997). Being employed is associated with improved HRQOL (Degroote et al., 2014; Peltzer, 2012) as it encourages interaction with peers and establishes social life growth while strengthening social support (Barreira et al., 2011). The loss of physical strength thus does not only represent the physical experience but rather, the greater experience thereof lies in the loss of social support from peers, confusion concerning life roles and uncertainty about the meaning of life. It is here where the complexities of HRQOL emerge and awareness regarding the interconnectedness start to become apparent.

Loss of physical strength further interacts with stigma in the social domain through the consequence of not being able to work due to ill health. In this study, those who were not self-employed had to inform their employers of their ailing health once they were unable to continue to work. These discussions created potential stigmatising situations which in turn could impact a wide range of aspects related to health. The effect of stigma on people living with HIV have been widely documented and has been seen to negatively impact access and adherence to treatment (Dlamini et al., 2009; Li et al., 2011), physical and mental health (Li et al., 2011; Logie & Gadalla, 2009; Wolitski et al., 2009) and has been noted to reduce HRQOL (Li et al., 2011; Logie & Gadalla, 2009). Care should thus be taken to understand that physical experiences of health have profound effects on HRQOL due to the interwoven social experience of possible stigma.

Concurrently disclosure increased participants' dependency on others within their social contexts. Unemployment meant a loss of income, placing an increased economic burden on those opting to care for participants in an already impoverished environment. The continued support from significant others can be understood through the socially constructed notion of ubuntu, i.e. a sense of humanity with an openness and connectedness to others (Maree & Westhuizen, 2011). Studies conducted in the same setting have reported on the presence of ubuntu in Khayelitsha (Super, 2016) as well as patients' experience of ubuntu in relation to health and how they attributed social support as originating from ubuntu (Cremers et al., 2018). This social cohesion among family and friends established support networks which were able to absorb the challenges of having to care for another.

Equally, the increased awareness of health status and self-care to preserve health was experienced socially. Increased awareness served as an enduring reminder to participants

that they were not healthy, that they were not like “other” people, although some attempted to change that dialogue through reference to the health they can have, should they adhere to treatment and that no one would know whether they take medication or not. This illustrates how a person’s physical body is not only physical but also experienced socially in relation to other people through identifying whether they are sick or not and if so, what that comes to mean to that person. Additionally, taking medication served to remind participants that they are ill, and that life is, and will remain different.

Taking medication took away the autonomy participants had in terms of interacting with others. Again, awareness of participant health status and loss of social autonomy occur in relation to other people and could not emerge in isolation. Social interaction with frequent consumption of alcohol was a pivotal pastime which was restricted with the use of medication. Participants sought to find ambiguities in the guidelines of medication use and alcohol consumption in attempts to keep social ties and maintain an experience of being connected to peers and a life reminiscent of status quo. All this serves to illustrate illustrates how HRQOL is not an individual entity but that individual experience of HRQOL is formed through interaction with and in relation to others, forming the social construction thereof.

Mental as social

Similar interactions are to be observed between the social and mental domains. Alcohol consumption was not reported as a means to deal with life stressors in this high consumption environment (Cremers et al., 2018; Saban et al., 2017). However, although not disclosed, use of alcohol may still serve as a strategy to help cope with the challenges and changes experienced. In a high alcohol consumption setting such as Khayelitsha, the use of alcohol as a coping mechanism is not restricted to illness, but a possible product of the impoverished

circumstances and socio-economic challenges it poses(Louwagie et al., 2014). Alcohol consumption may act as a coping strategy in two ways, by firstly, through the self-medicating use of alcohol for its suppressant effects (Corbin et al., 2013).Second, in a social context as a link to a life previously lived through the social experience producing a sense of well-being (Cremers et al., 2018).Creating a sense of familiarity through established routines and providing a sense of belonging. A similar experience was noted by Cremers et al., (2018) in the same setting among patients living with TB. Although no participant reported current alcohol consumption, many attempted to establish whether using alcohol and medication was at all possible. Despite ambiguity in literature regarding the protective effects of social support and alcohol consumption (Corbin et al., 2013) most participants did express good social support suggesting that, in this setting, social support might act as a protective measure to alcohol consumption among those living with HIV and TB.

Another interaction between the mental and social domains is the experience of not being the only person living with HIV/TB served as a further coping strategy. The sense of universality was a strong motivator for some participants to help shape their view of themselves and regard HRQOL not as an isolated experience of being ill or not, but sharing a commonality with others, even when those are unknown to them. Universality is commonly found in group therapeutic settings where people living with HIV experiencing the same challenges of rejection or stigma share a safe space and creates a sense of being connected to others (Solórzano & Glassgold, 2010). Participants in this context might experience universality outside therapeutic settings due to high prevalence rates of HIV/TB possibly creating increased awareness that it is not a rare condition. This could further be explained, as seen in other studies based in Khayelitsha (Cremers et al., 2018), by the limited reported

experienced stigma, which may still have offered challenges to participants, as well as the social support offered in the spirit of ubuntu (Cremers et al., 2018; Super, 2016).

Further along the mental domain, participants experienced anxiety in relation to their HRQOL not in a manner concerning their own recovery or reclining health but were anxious about the care and financial provision of those they could potentially be survived by. This mental concern is rooted in social experience and the relationships participants have with others, particularly with their children Again, this emphasises that HRQOL is not an individual experience but is socially experienced in that high HRQOL is not only dependent on the wellbeing of self, but on the well-being of significant others as well.

Coda

We have shown that not only do interconnection between domains exist, but that the social interactions, relationships and social experience of being situated in relation to other people, is the golden thread that connects the other domains of physical and mental. Additionally, we have illustrated that HRQOL cannot be viewed in isolation to other life domains (Karimi & Brazier, 2016), but rather place emphasis on the understanding that, in this setting, the social relationships and interactions are central to HRQOL regardless of which domain is considered. Consequently, an individualistic view of HRQOL is not fitting for the South African context, because of the illustrated social experience and the lived experience of interconnectedness and shared humanity among people. Social relationships cannot be excluded from HRQOL evaluations and need to be incorporated into measures of HRQOL assessment. Similar conclusions have been drawn by others stating that to promote health and well-being, health care providers should be cognisant of the significance interpersonal relationships can have on

interventions (Hawe & Shiell, 2000); and that such relationships can serve as a resource in resilience building and treatment adherence (Cremers et al., 2018).

As underpinned by social constructionism, the experience of health-related conditions are formed socially through the developed understanding of the illness by those living with the condition (Conrad & Barker, 2010). We therefore argue that HRQOL is similarly formed through its social experience. It is well established that social relationships are valuable in health promotion especially when those relationships can establish a sense of belonging and empower people to be self-efficacious (Berkman, 1995). In addition to the health promoting value of social experiences of health, these social interactions have also been found to mediate HRQOL (Degroote et al., 2014). Across various countries and medical conditions, good social relationships have been shown to be a positive predictor for good HRQOL. Existing literature has shown that HRQOL is experienced to be higher among those with social support, in the physical domain in particular, followed by the mental domain (Préau, Marcellin, et al., 2007; Préau, Protopopescu, et al., 2007; Zhou et al., 2020). Furthermore, other researchers have documented that social connections, interactions and social support can improve resilience among patients living with TB (Cremers et al., 2018) and mental health among patients living with HIV (Narsai et al., 2016).

We thus emphasise the potential value for contextualised HRQOL research to help develop a view of HRQOL tailored to setting and illness which can aid in intervention development and policy creation (Conrad & Barker, 2010; Hawe & Shiell, 2000) to better HRQOL along with improved health outcomes. Subsequently, we would like to add to the emphasis placed by others that future interventions aimed at addressing HIV/TB and improvements in HRQOL

should consider the social aspect thereof as it may prove crucial to the sustainability of patient health and well-being (Cremers et al., 2018; Hawe & Shiell, 2000).

Limitations and suggestions for future research

The findings of this paper should be interpreted with the following limitations in mind. Participants were recruited purposefully from a single medical facility. Therefore, the sample may not be representative of the larger population living with HIV-associated TB in Khayelitsha. Interviews were conducted over a 12-week follow-up time frame which might have influenced participant responses as health status potentially changed across twelve weeks on treatment. A further factor which need to be considered in interpreting the results is the physical health of participants recruited. Qualifying criteria to patient's enrolment into the PredART trial stipulated that patients had to have a CD4 cell count of less than 100 cells per microliter. Individuals with such low CD4 cell counts are severely immune compromised and potentially more physically and socially disadvantaged than those with higher CD4 cell counts.

Regarding study design the nature of qualitative research does not readily lend itself to generalisability of findings to larger populations and more research strategies may need to be employed to further solidify the findings in the greater population. Due to the ambiguity and abstract nature of HRQOL, it was a difficult construct to communicate through to participants in interviews. Added difficulty in this regard was experienced because the interview questions and concepts had to be translated from English to isiXhosa. The interviewer was a clinic counsellor stationed at the data collection facility which often saw her regress into her role as counsellor and advise participants on issues concerning treatment consumption and adherence. The interviewer had to navigate a thin line between being informative and

suggestive in conversation. Due to the interviewers' position as a counsellor, the possibility exists that participants might have responded in a manner they believe to be appropriate in terms of treatment and self-care which could have had an unknown impact on HRQOL responses. Furthermore, as a white middleclass male, the first author has taken care to reflect on potential biases brought to the analysis process. In support, frequent communication ensued between the first and subsequent authors. Lastly, despite the popular use and view of the identified HRQOL domains, limitations could emerge because these distinct categories may not fully capture the complexity of HRQOL.

However, despite the noted limitations, the findings do cast light on HRQOL as an interconnected experience and aimed to illustrate that social underpinnings of all domains are what constitutes HRQOL. More research focussing on the value of social experience to HRQOL should be performed. We suggest an increased focus on social aspects of HRQOL in medical and public health decision making as well as development of patient empowering guidelines and resources to address social aspects of health. Increased emphasis on social aspects of HRQOL would assist in achieving South Africa's National Development Plan 2030 objective of establishing a primary health care initiative to offer care to families and communities (National Planning Commission, 2012). Additionally, we recommend conducting research exploring the changes in HRQOL once social experiences and associated ramifications are taken into consideration in interventions and policy development should be conducted. Lastly, we recommend selective incorporation of a social perspective into widely used HRQOL measures such as the EQ-5D-3L to better capture patient experiences of quality of life.

Conclusion

This study qualitatively explored how HRQOL is experienced by patients living with HIV-associated TB. The findings further our understanding of HRQOL among those living with HIV-associated TB in Khayelitsha. This study illustrated the centrality of the social domain in the experience of HRQOL among participants. Hence, we argue that all domains and characterisations of HRQOL are experienced socially and that the many social connections play a significant role in patient HRQOL. We hope to contribute to the existing body of knowledge and that those conducting future interventions could draw on this information to better programmes to improve patient HRQOL along with patient health.

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