QUALITY OF MENTAL HEALTHCARE FOR PEOPLE LIVING WITH HIV AND COMORBID DEPRESSIVE DISORDER IN SOUTH AFRICA

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Quality of mental healthcare for people living with HIV and comorbid depressive disorder in South Africa

A thesis submitted in partial fulfilment of the requirement for the degree of master's in international health

by

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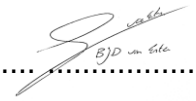
Declaration:

Where other people's work has been used (either from a printed source, internet or any other source) this has been carefully acknowledged and referenced in accordance with departmental requirements.
The thesis "Quality of mental healthcare for people living with HIV and comorbid depressive disorder in South Africa" is my own work.

Signature: ……  ……

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Writing this thesis would not have been possible without the support and inspiration of some people.

First, I would like to thank my supervisors for the guidance and great support they have given me while writing this thesis. I really enjoyed working with them. Their help, kind advice and critical notes have helped me enormously to improve this thesis. I hope our paths will cross again in the future.

Furthermore, I would like to thank dr. Ebuenyi for giving me new insights on mental health in PLHIV in LMIC's.

I also would like to thank my former colleagues from the Shoklo Malaria Research Unit in Thailand. Working for SMRU has been a lifetime experience. Learning from high end researchers and working together to improve the health for disadvantaged people has been a great motivator to continue working in international public health. It has encouraged me to write my thesis on mental health.

In the last year I started with my first year of training in general practice. During this year I also wrote the main part of this thesis. I was lucky to be placed at a great office where my supervisors have given me the opportunity to combine my training in general practice with the master's in international health. Bert and Karin thank you very much.

Also, I would like to thank my family for the continuous support they have given me in my life and career. I have had all the opportunities that I could wish for and I am grateful for that.

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Abstract

Research on mental healthcare in people living with HIV (PLHIV) is scarce. In this thesis the burden of major depressive disorder (MDD) in PLHIV in South Africa (SA) is investigated and a quality assessment of the mental healthcare system in SA for PLHIV with MDD was done.

Methods: A narrative review of the literature was performed using a systematic approach. Quality of mental healthcare in this thesis was studied using Donabedian's framework on structure, process and outcomes of care.

Results: Prevalence of depression in PLHIV in SA differed between 5.2% and 78.2%. Main determinants associated are female gender, younger age, HIV infection, low CD4 count, stigma, lack of support, unemployment and poverty.

Structural factors involved in the quality of care relate to lack of financial and human resources, lack of screening tools, lack of interaction with social services and lack of knowledge in healthcare providers. In the process of care, it seems that psychotropic medicine is available, but psychotherapy is not. Integrated care models are developed and look promising. Outcomes of care in PLHIV with MDD are lower adherence to therapy and lower quality of life.

Conclusion: The burden of depressive disorder in PLHIV in SA is high. The quality of mental healthcare in this population is influenced by different factors in the structure, process and outcomes of care. The interaction of these components needs to be recognized. To improve the mental healthcare for PLHIV with MDD quality assessment need to be incorporated in policies, guidelines and daily practice.

Key words: HIV, Major Depressive Disorder, South Africa, Quality of Care, Donabedian

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List of abbreviations

AIDS	Acquired Immunodeficiency syndrome
AIMS	Assessment instrument for mental health systems
ART	Antiretroviral treatment
ARV	Antiretroviral
CBT	Cognitive behavioural therapy
CMD	Common mental disorder
DoH	Department of Health
DSM	Diagnostic statistical manual of mental disorders
EDL	Essential drug list
GDP	Gross domestic product
GNI	Gross national income
HIV	Human immunodeficiency virus
HrQOL	Health related quality of life
IOM	Institute of medicine
IPT	Interpersonal therapy
LMIC	Low- and middle-income country
MDD	Major depressive disorder
MDE	Major depressive episode
MH	Mental health
MHD	Mental health disorder
MSM	Men who have sex with men
NCD	Non-communicable disease
NGO	Non-governmental organization
OT	Occupational therapist
PHC	Primary healthcare
PLHIV	People living with HIV
PST	Problem solving therapy
QALY	Quality adjusted life year
QOL	Quality of life
SA	South Africa
SADAG	South African Depression and Anxiety Group
SMRU	Shoklo Malaria Research Unit
SNRI	Selective noradrenalin reuptake inhibitor
SSA	Sub-Saharan Africa
SSRI	Selective serotonin reuptake inhibitor
WHO	World Health Organization
YLD	Years lived with disability

Background of the Author

My name is Bert van Enter and I am a medical doctor. After medical school I started with the Dutch course in International Health and Tropical Medicine. During the course I gained clinical experience in surgery (Netherlands) and obstetrics and gynaecology (Curaçao) and attended the core course of the master's in international health at the Royal Tropical Institute in Amsterdam. During my training in Curaçao the country experienced an outbreak of Chikungunya disease. I decided to develop local guidelines on perinatal care for Chikungunya infection and did some small research on this topic. Although my experience in research, epidemiology and writing guidelines was limited I enjoyed working on this and for me this was the start to become interested in doing research and public health. This interest was even more developed while working for the Shoklo Malaria Research Unit (SMRU) at the Thailand-Myanmar border at a later stage. The SMRU is a local field unit doing research in tropical infectious diseases and public health and providing free medical care for migrants and refugees from Myanmar residing in Thailand. My work included clinical work providing obstetric care and training, but I had the opportunity to participate in several research projects and to learn from high-end researchers at SMRU. These experiences have encouraged me to start with the MIH and work in the field of international public health.

My medical interest has always been broad. That is why, after returning to the Netherlands, I decided to start with the specialisation course in general practice. As having a strong primary healthcare system in the Netherlands, I hope that in the future I can use my knowledge and expertise in primary healthcare (PHC) and international health in countries where there is a lack of good PHC.

In my work as a doctor in International Health I have seen the problems of increasing numbers of non-communicable diseases (NCD's) and mental health disorders (MHD's). While working in Thailand we were not able to provide good care for people with cardiovascular problems, diabetes, cancer and MHD's. As mental health problems often coincide with having multiple or comorbid diseases this topic is becoming more important as global numbers of NCD's rise. To improve health systems in the future to deal with mental health problems is therefore something I would like to achieve. One of the persons that has inspired me to work in the field of mental health is Gracia Fellmeth, a former colleague in Thailand. Within a setting where the focus of healthcare provision was on communicable diseases, she made me aware of the burden of mental health problems.

While looking for research possibilities in the field of International Health and primary care in the Netherlands I met dr. Kerstin Klipstein-Grobusch, who is Associate Professor of Global Health at the Julius Centre for Health Sciences and Primary Care, at the University Medical Centre Utrecht. As dr. Klipstein-Grobusch has experience in integrated care and health systems for HIV and non-communicable diseases in South Africa we started to discuss different topics for this thesis. As there is a lack in mental health system research in people living with HIV (PLHIV) in South Africa and this topic interests me, I decided to write my thesis on this topic. I want to have a closer look on how South Africa is best able to organise its mental health care for people living with HIV and associated depressive disorder. Furthermore, I hope to give pragmatic, but well validated recommendations on how to improve care.

Finally, as, even within my family, people often refer to mental health problems in low- and middle-income countries (LMIC's) as problems mainly caused by poverty, I want to show them that mental health is more than that and that we have to work on these problems to improve health for all.

"There is no health, without mental health".[1]

Republic of South Africa: Country profile

Geography
South Africa (SA) is a country with a geographical area of 1 220 813 square kilometres.[2] The country is divided in nine provinces: Northern Cape, Eastern Cape, Free State, Western Cape, Limpopo, North West, Kwazulu-Natal, Mpumalanga and Gauteng. Northern Cape is the largest province with approximately 30.5 % of the geographical area. Gauteng is the smallest (1.4 % of the total geographical area), but most populated province. Two of the largest cities in the country, Johannesburg and Pretoria, are in Gauteng, while the three other largest cities, Cape Town, Port Elisabeth and Durban, are in Western Cape, Eastern Cape and Kwazulu-Natal respectively. The majority (66,4%) of the people live in urban areas.[3]

Demography
The total population of SA is estimated at 56 522 000 people. Ethnic groups are divided in black African (80,8%), coloured (8,8%), Indian or Asian (2,5%) and whites (8%).[2] The percentage of women is 51% in the country.[2]

Economic situation
With an estimated gross national income (GNI) per capita of $5,430 (US-dollars), SA is classified by the World Bank as an upper middle-income country ($ 3,896 - $12,055). Gross domestic product (GDP in US dollars) in 2017 was $349,42 billion dollars.[4]
18.9 % of the population lives below the international World Bank poverty line of less than $1,90 (US-dollar) a day. Although, according to national poverty lines, 55,5 % of the population live below the poverty lines of having enough money to buy food and non-food items for living and 25,2% of the people live in extreme poverty with not enough money to buy the minimum food for healthy living.[5] Poor households in SA have access to " social wages" such as free primary healthcare, free basic services (water and electricity) and child support.
Unemployment rate (population age group 15 – 64 year old) in the country is approximately 26,5%, with highest numbers in black Africans and lowest numbers for white ethnic groups.[6]

Health
Life expectancy at birth in 2016 was 63 years. Under five mortality rates (per 1,000 live births) declined from 59 in 2010 to 42 in 2017.[4] Total fertility rate (the number of children ever born to a woman at the end of childbearing age) was 2,4 in 2016.[7]
Total health expenditure in 2015 was 8.9 % of GDP.[8] Government health spending per person was approximately $594 US dollars per person.[9]
South Africa has more than 7 million people living with HIV, with an estimated prevalence of 18.8 % (16.2 -20.9) in adults (15-49 year).[10] Almost all (93%) South Africans are aware of HIV/AIDS and 81 % of adolescents aged 15-24 years have ever tested for HIV.
Most deaths and premature deaths are caused by HIV/AIDS, while non communicable diseases (NCD) as ischemic heart disease, cerebrovascular disease and diabetes rank 2nd,4th and 5th as most common death causes.[9]

Introduction

Problem statement and thesis justification

An estimated 38.8 million people are living with HIV worldwide.[11] In the last two decades huge efforts have been made to improve access to antiretroviral treatment (ART) for people living with HIV (PLHIV).[12] UNAIDS 90-90-90 goals for 2020 are that 90 percent of PLHIV will know their HIV status, 90 percent diagnosed will receive treatment and 90 percent on treatment will have viral suppression.[13]

As PLHIV live longer and due to the HIV infection itself PLHIV are at increased risk for comorbid non-communicable diseases (NCD's) and mental health disorders (MHD's).[14–16]

MHD's are one of the leading causes of disability globally and major depressive disorder (MDD) is among the five leading causes of years lived with disability (YLD's). It is estimated that over 300 million people suffer from depressive disorder.[17,18] Global prevalence of MDD is 4.4 % (4.1%-4.7%), with prevalence estimates for PLHIV being twice as high.[19–23] It is believed that in 2030 HIV and depressive disorder worldwide are the main causes for burden of disease.[24,25]

South Africa is the country were the most people with HIV live, with estimations of 7.1 million people being infected.[10] SA has made great progress in the last two decades to improve HIV care. In the year 2000 it was estimated that over 80% of people infected with HIV in SA were not diagnosed.[26] Current estimations are that 90% of PLHIV are aware of their status.[10] Mental health problems rank 3rd in the burden of disease in SA after HIV and other infectious diseases.[27] Prevalence of MDD in SA is estimated at 4.9%.[28]

The burden of MHD's in PLHIV is recognised and international guidelines and programs for integrated care are developed.[27,29,30] Mental healthcare can be integrated in HIV services or vice versa.[11,15,16]

Although awareness is there and guidelines and frameworks are in place limited data from low- and middle-income countries (LMIC's) is available on MDD in PLHIV. Moreover, in many countries it is unknown what the quality of care is that PLHIV with MDD receive and if improvements can be made.

South Africa, the country with the most people globally living with HIV in this regard offers an excellent opportunity to look at the burden of depressive disorder in PLHIV and to assess the quality of mental healthcare for PLHIV with comorbid depressive disorder.

In this thesis the burden of depressive disorder in PLHIV in SA will be investigated. Next to that a situational analysis will be performed to look at the quality of mental healthcare for PLHIV with comorbid depressive disorder.

Results can be used for future quality assessments, possible improvements and recommendations in the care for PLHIV and depressive disorder in SA and other countries.

Objectives

- To describe the burden and major determinants of depressive disorder in PLHIV in SA
  - What is the prevalence of depressive disorder in PLHIV in SA?
  - What are the determinants associated with depressive disorder in PLHIV in SA?
- To assess the quality of mental healthcare for PLHIV with comorbid depressive disorder in SA

The focus of this thesis will be on the quality of public mental healthcare in PLHIV and less on HIV care in mentally ill patients. Also, an evaluation of mental healthcare among HIV infected gay people and prisoners fall out of the scope of this thesis.

The target audience is

- Policymakers in the fields of HIV care, mental healthcare and primary healthcare (PHC) working in governmental or non-governmental organizations (NGO's) in SA and sub-Saharan Africa (SSA).
- Health professionals and lay health workers working in HIV care, mental healthcare and PHC working in governmental or non-governmental organizations in SA and SSA.
- Researchers and organizations involved in HIV/AIDS research and mental health in SA and SSA.
- Media interested in reporting on global health issues.

Methods

Conceptual frameworks

For the description and categorization of the determinants involved in depressive disorder in PLHIV in SA the Lalonde conceptual framework is followed. In this model health is influenced by: human biology, lifestyle, the environment and the healthcare organization.[31] The healthcare organization is discussed in more detail in the part on quality of mental health care.

The Lalonde model is chosen, because it gives the possibility to give a general overview of main determinants that are important in the development of depression in PLHIV. The Lalonde model includes individual patient characteristics and the healthcare system, but also makes it possible to look at sociodemographic determinants. All these factors are important while looking at HIV and mental health. The focus of this thesis is on quality of care, for that reason the Lalonde model will not be discussed in detail.

To assess the quality of mental healthcare for PLHIV and MDD in SA the Donabedian conceptual framework (SPO framework) on quality of care is used.[32]

Donabedian stated that the quality of care is influenced by the structure, process and outcomes of care. The structure has to do with the equipment, instruments and workforce available in a country. While looking at the process it is more important to look at how care is coordinated and how it is delivered to patients. At last outcomes can be measured, such as mortality, recovery, improved quality of life and adherence to therapy. Often structural components influence the process of care and both structure and process influence outcomes of care. Although, sometimes outcome factors affect the structure or process of care. Therefore, it is important to look at all three components, while describing the quality of care.

The Donabedian framework is mentioned in important international guidelines and key publications on mental health.[33,34] In the World Health Organization (WHO) package on quality improvement for mental health, Donabedian's framework is used and components are divided according to the indicators as mentioned in figure 1.[34]

As integrated care models for PLHIV and MDD are being developed and touch on the process of care I will also review examples of integrated care models.

While systematically going through the literature and following the Donabedian SPO framework we can identify and link important indicators involved and perform a situational assessment of the quality of mental healthcare for PLHIV and depressive disorder in SA.

Figure 1 – Donabedian's conceptual framework on structure, process and outcomes of care

As described in the WHO service guidance package on Quality improvement for mental health[34]
* Added to the original description in WHO guidance package

Definition of depressive disorder

Where in this thesis is referred to depression or depressive disorder the definition from the 5th edition of the diagnostic and statistical manual of mental disorders (DSM) from the American Psychiatric Association for MDD is followed as much as possible (Box 1).[35]

Box 1. Major depressive disorder[35]

Presence of at least five of the symptoms mentioned below, including at least a depressed mood most of the day and/or loss of interest or pleasure in daily activities.

- Significant weight gain or weight loss
- Sleep disturbance
- Psychomotor dysfunction
- Lack of energy
- Feeling worthless or having inappropriate feelings of guilt
- Lack of concentration or to think clearly
- Recurrent thoughts about death, suicidal ideation

These symptoms must at least be present for two weeks and causing reduced functioning in daily life (social, occupational, educational). Furthermore, symptoms must not be caused by any other psychiatric or medical illness.

Depression includes both major depressive episode (MDE) and major depressive disorder (MDD) and are based on the definition above. The difference is the chronicity of the disease. A major depressive episode can be a part of MDD, but lacks the chronicity of disease.

In screening tools often an assessment of depressive symptoms is done, which could be indicative for MDD, depending on different cut off points and severity of disease.

Search Strategy

A narrative review of the literature was performed using a systematic approach.[36,37] To find all relevant research on HIV and MDD in SA a search was performed using five different databases (PubMed, Cochrane, Embase, PsycInfo and CINAHL). First relevant synonyms for HIV, MDD and SA were identified and databases were searched using a combination of these different search terms (Table 1).

Articles found in the different databases were checked for duplicates using Mendeley reference management software. Identified duplicates were removed. A multistep process looking at titles, abstracts and full text was followed to identify relevant papers. Inclusion criteria were based on papers that involved depressive disorder in PLHIV in SA.

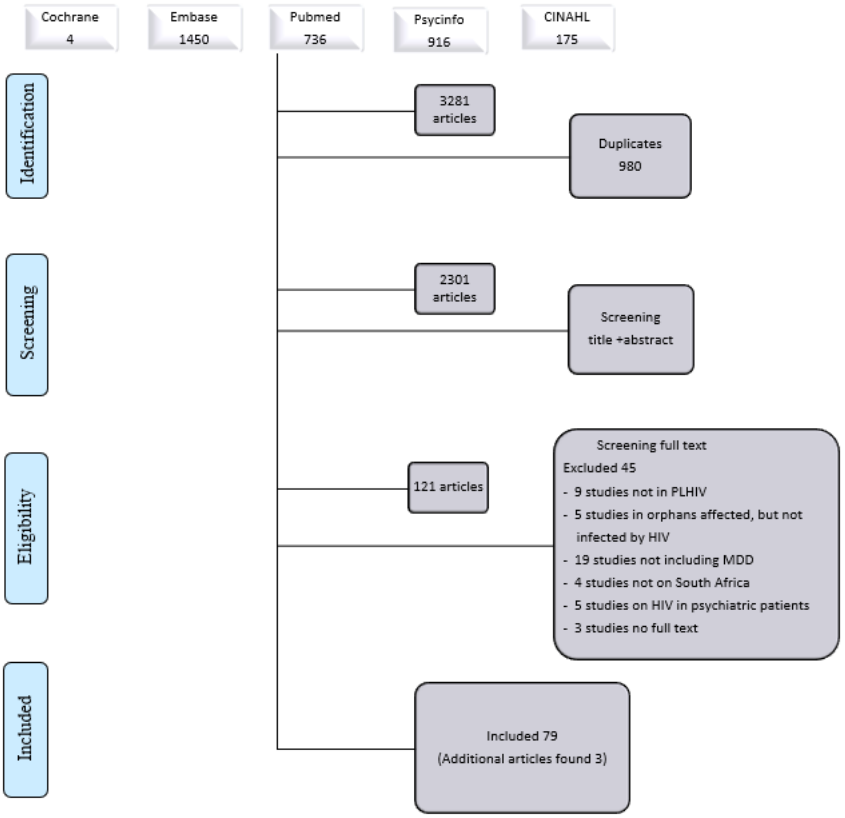
Exclusion criteria were research that did not include SA, HIV and depressive disorders and that focused on HIV in people with pre-existing mental disorder or focused on MHD in patients not yet diagnosed with HIV. Also, articles on mental disorders other than

depressive disorders and not including depression were excluded. No exclusion criteria were made for year of publication or research that focused on depressive disorders in specific subgroups, such as children or pregnant women (Figure 2).

Table 1 – Search Strategy

HIV (MESH)	**South Africa**	**Depressive disorder**
aids (MESH) HIV infection acquired immunodeficiency syndrome HIV antibodies CD4 lymphocyte human immunodeficiency	Republic of South Africa (MESH) Union of south Africa (MESH) South-Africa Southern Africa	Depression Dysthymia Dysthymic disorder mental health (MESH) mental disorder (mesh) mood disorder (mesh)
Example search strategy PubMed	Search **((((((((((depression[MeSH Terms]) OR mood disorder[MeSH Terms]) OR mental disorder[MeSH Terms]) OR mental health[MeSH Terms]) OR depressive disorder) OR Dysthymic) OR Dysthymia) OR depressive disorder)) AND (((((south Africa[MeSH Terms]) OR southern Africa) OR South-Africa) OR republic of south Africa[MeSH Terms]) OR union of south Africa[MeSH Terms])) AND (((((((HIV[MeSH Terms]) OR AIDS[MeSH Terms]) OR HIV infection) OR acquired immunodeficiency syndrome) OR HIV antibodies) OR CD4 lymphocyte) OR human immunodeficiency)**	

Figure 2 – Flow chart search strategy



* Guidelines, policies and articles not including SA, but relevant for the topic are not included in this flowchart

References of included articles were checked for relevant articles missed in the initial search. First the different articles found were analysed if they mentioned prevalence numbers or determinants of health. The determinants that were identified in the different studies were categorized as being part of human biology, lifestyle or environmental factors according to the Lalonde model.

The following step was to look at indicators that involved quality of care for PLHIV and MDD. Within this step also more general reports and research on the mental health system and HIV care in SA and integrated care were included. Indicators found were grouped according to the Donabedian SPO framework.

Results were complemented by looking at major guidelines and policies on HIV, mental health and integrated care by WHO, UNAIDS and the Department of Health (DoH) in SA (Table 2).

Key research and publications, such as published in the Lancet Mental Health series were also included if relevant. Next to that major articles on mental health and quality of mental healthcare in SA and SSA countries were reviewed.

At last also experts in the field of HIV and mental health were interviewed to identify if any important issues were missing (see: Appendix 1).

Table 2 – International and national guidelines and policy reports on HIV and MH

Organisation	Guideline
WHO	• Depression and Other Common Mental Disorders: Global Health Estimates. Geneva. World Health Organization; 2017.[18] • World Health Organization. Mental health & HIV/AIDS therapy series. Geneva. World Health Organization, 2005.[38] • World Health Organization and WONCA. Integrating Mental Health into primary care: a global perspective. World Health Organization and World Organization of Family Doctors (WONCA) 2008.[39] • World Health Organization and Calouste Gulbenkian Foundation. Integrating the response to mental disorders and other chronic diseases in health care systems. Geneva. World Health Organization, 2014[15] • World Health Organization. Mental Health Action Plan 2013-2020. Geneva. World Health Organization, 2013[40] • World Health Organization. Improving Health Systems and services for Mental Health. Geneva. World Health Organization, 2009[41] • World Health Organization and Calouste Gulbenkian Foundation. Policy options on mental health: a WHO-Gulbenkian Mental Health Platform collaboration. Geneva. World Health Organization, 2017.[42] • World Health Organization. mhGAP Intervention Guide for mental, neurological and substance use disorders in non-specialized health settings: Version 2.0. World Health Organization 2016[43] • Mental health atlas 2017. Geneva. World Health Organization, 2018[44] • World Health Organization. Assessment Instrument for Mental Health Systems. Geneva. World Health Organization, 2005[45] • Quality improvement for mental health. Geneva. World Health Organization, 2003 (Mental Health Policy and Service Guidance Package)[34] • Monitoring and evaluation of mental health policy and evaluation plans. Geneva. World Health Organization, 2007 (Mental Health Policy and Service Guidance Package)[46]
USAIDS	• Gutmann, Mary and Andrew Fullem. 2009. Mental Health and HIV/AIDS. Arlington, VA: USAID | AIDSTAR-ONE PROJECT, Task Order[47]
South Africa	• National Mental Health Policy Framework and Strategic Plan for 2013-2020[27] • National Strategic Plan on HIV, STI's and TB 2012-2016[48] • Mental Health Care Act 2002[49] • Primary Care 101 – Symptom-based integrated approach to the adult in primary care[50] • Ideal clinic manual, Version 18[29]

Results

Out of 2301 articles that were found in the initial search, 121 articles were selected. 76 of 121 articles were included in this thesis as being relevant for the different objectives. Three articles were added while checking for references (Figure 2).

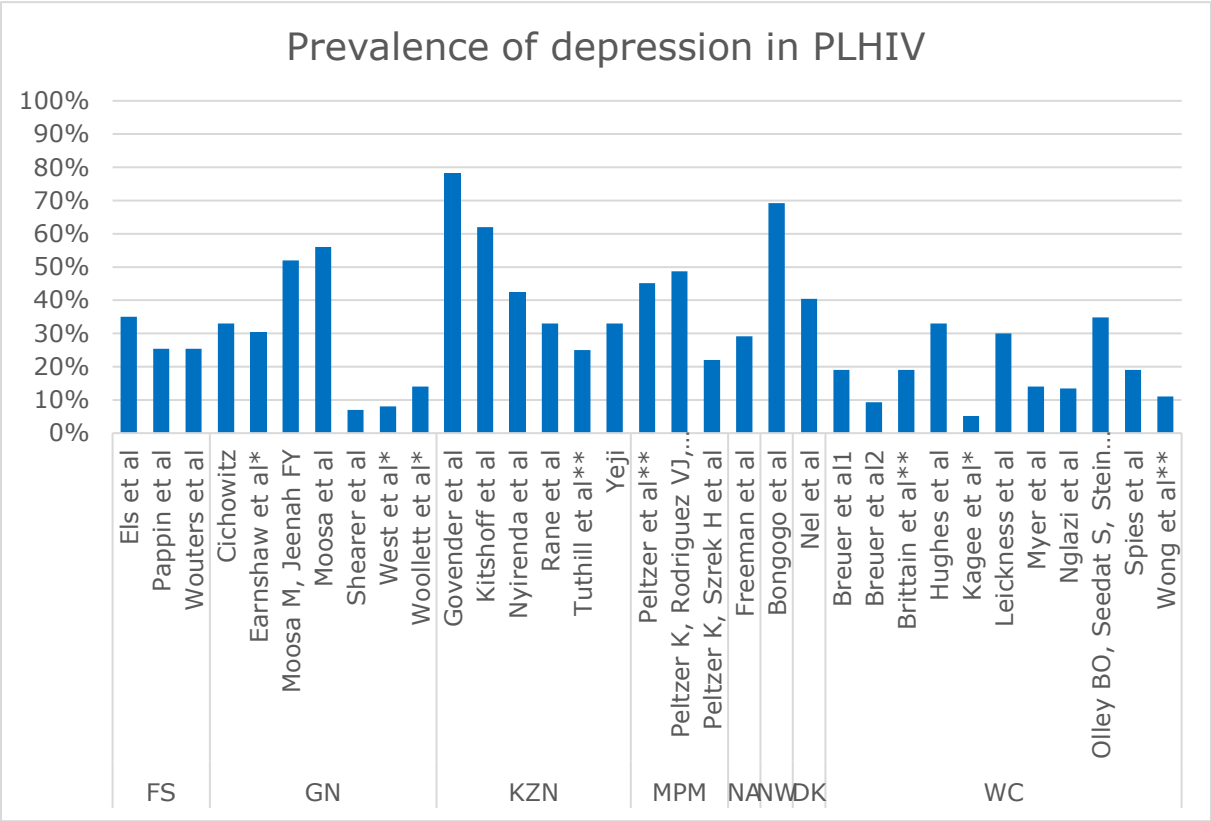
In chapter 1 results will be given for the studies that did report on prevalence of MDD in PLHIV in SA. In chapter 2 major determinants are described that were found in the studies that increase the risks for MDD in PLHIV in SA. The determinants are structured according to the Lalonde model; human biology, lifestyle and environment. At last in chapter 3 the quality of care for PLHIV and MDD will be evaluated. Next to the studies included in the initial search in this third chapter also more general reports on the healthcare system in South Africa are included. The first part of this chapter will focus on the structure of care and the resources available. The second part will look at the process of care and integrated care models. In the last part of chapter 3 outcomes, such as quality of life, reduced symptoms and adherence to therapy will be described.

Chapter 1: Prevalence of depressive disorder in people living with HIV in South Africa

In this chapter an overview is given for studies that reported prevalence numbers of depression in PLHIV in SA.
In total 33 studies were found that reported on prevalence numbers of depression in PLHIV in SA (see: Figure 3). *In Appendix 2 a more detailed description of the studies on prevalence of MDD in PLHIV in SA is given.*

Prevalence of depression in PLHIV differed between 5.2 %[51] and 78.2 %[52]. Out of 33 studies, three studies reported prevalence numbers between 5-10%[51,53,54], eight studies between 10-20 %[55–62], 14 studies 20-40%[25,63-75], five 40-60%[76–80], and three studies reported prevalence exceeding 60%[52,81,82]. In most cases the study groups had an overrepresentation of women and underrepresentation of men. The proportion of females in the studies ranged between 49% and 100% (see Appendix 2).
Four studies in adolescents between 9 and 24 years old showed prevalence numbers between 5.2 % and 30.3%.[51,60,62,63] In one of these studies by West et al. overall prevalence was 8%, with higher prevalence of 17.8% in adolescents with older age (16-19 years old).[62]
Studies by Brittain et al., Wong et al., Tuthill et al. and Peltzer et al. showed prevalence numbers between 11% and 48.7% in prenatal women.[56,59,71,80] Postnatal prevalence of depression in women living with HIV were 11.8% and 45.1%.[71,79] In a study by Tuthill et al. scores suggestive for moderate depression declined when prenatal depressive scores where compared to postpartum scores (25 % prenatal to 11.8% postpartum).[71]
Although in one study by Govender et al. prevalence numbers were high (78.2%) for patients six weeks after diagnosis of HIV, in three other studies in patients with recent diagnosis of HIV prevalence numbers were lower (22%, 25.4% and 34.8%).[25,52,64,65,67]
In the 33 different studies 14 different screening and diagnostic tools were used for diagnosis of depressive disorder or depressive symptoms. The MINI[83], CES-D[84] and BDI[85] were most used.

Figure 3 – Prevalence of major depressive disorder in PLHIV in SA



FS: Free State, GN: Gauteng, KZN: Kwazulu-Natal, MPM: Mpumalanga, NA: National, NW: North West province, DK: Unknown province, WC: Western Cape; PLHIV: People living with HIV, SA: South Africa

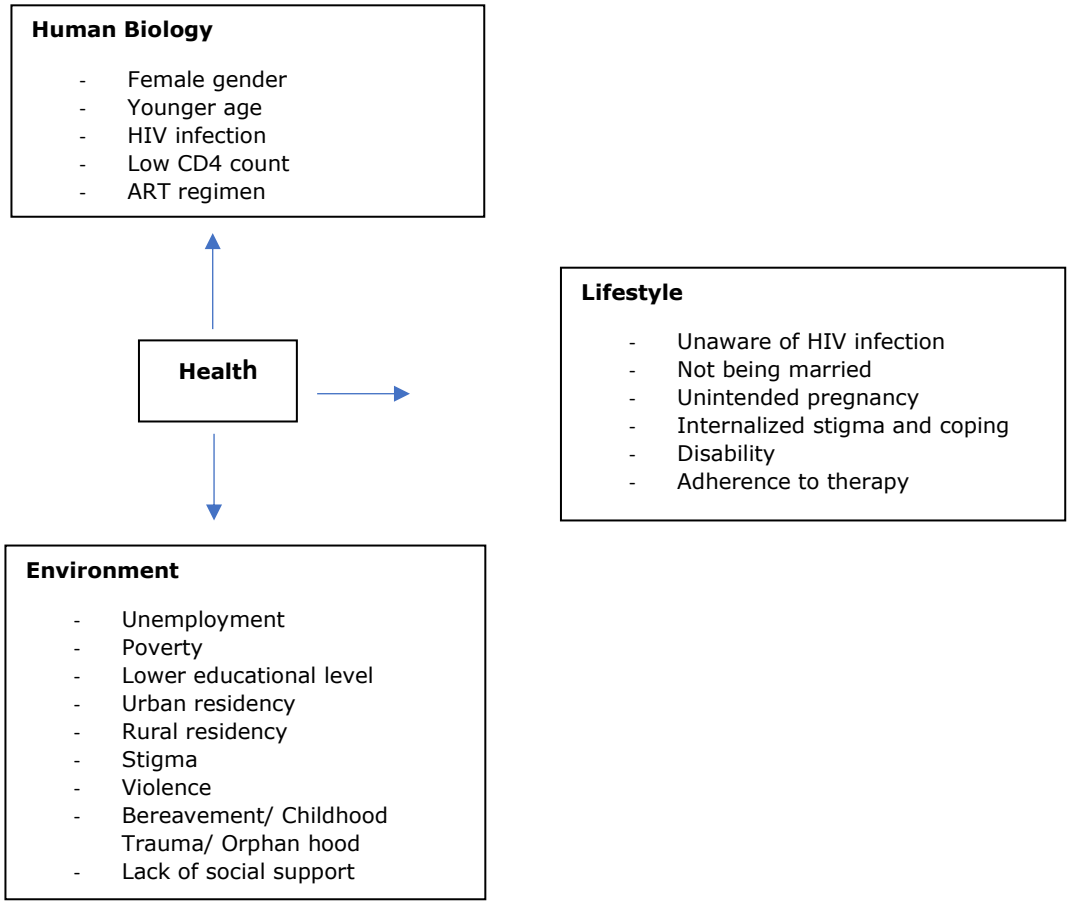
* Studies in adolescents

** Studies in prenatal and postnatal women

Chapter 2: Determinants associated with depressive disorder in PLHIV in South Africa

In this chapter an oversight is given of identified determinants that are related to depression in PLHIV in SA. The structure that was used to describe the different determinants involved, was according to the Lalonde model on health. Health in this model is defined by human biology, lifestyle, the environment and the organization of healthcare. The latter will not be discussed in this chapter, but will be part of the chapters on quality of care. In total 34 studies were found that measured determinants involved in the development of depressive disorder in PLHIV.
In figure 4, factors, related to higher chances for MDD in PLHIV in SA, are presented. *Appendix 3 shows a more detailed version of the results.*

Figure 4 – Major determinants involved in depressive disorder in PLHIV in SA



Human biology and lifestyle

Nine studies found that female gender was related to increased risk for depressive disorder in HIV populations in SA.[54,60,64,66,74,75,86–88], Another important factor for women in three studies was having an unintended pregnancy.[56,89,90]

Internal factors, such as behaviour and coping styles are related to depression in PLHIV in SA. Having an avoidant coping style, non-disclosure of HIV disease and higher rates of internalized stigma increase risks for depression.[56,63,66,74,79,80,90,91]

The HIV virus itself and the stress that PLHIV often endure in daily life influence the immune system and the central nervous system. Changes in cytokine release and altered function of the hypothalamus-pituitary axis in these patients are related to depression.[92] Eight studies in SA describe HIV infection itself to be related to MDD.[25,54,62,90,93–96]

Disease specific conditions in PLHIV and their chances to develop depressive symptoms are related to antiretroviral (ARV) treatment and CD4 counts.[54,81,97,98] In three studies low CD4 count was associated with major depressive disorder.[54,97,98]

The use of certain ARV's and especially the use of Efavirenz was previously found to be related to mood disorders in PLHIV. Although a recent study did not find that Efavirenz increases the risk for depression when compared to another ARV regimen.[99] Of the studies included in this thesis one study[81] noted higher prevalence of MDD in people using Stavudine, Lamivudine, Efavirenz regimens.

Environment

In six studies a lack of received social support from the community or the family was associated with depression in PLHIV.[56,59,62,64,74,100] Furthermore the impact of HIV in families is often considerable for the development of MHD's. The way family members react to diagnosis of HIV is important in the way PLHIV cope with their disease. In a study by Wouters et al. family dynamics were described as where a family's ability to adapt to changing circumstances had a positive effect on mental health outcomes. Rigid family structures increased the risks for mental health problems.[91] Next to the influence of family dynamics, the destruction of families by HIV and loss of family members is of importance for mental health outcomes in families and communities. Bereavement and orphan hood due to HIV were identified as determinants for depression in PLHIV in SA in ten studies.[58,62–64,75,80,87,97,101,102]

In HIV positive orphans the interaction with caregivers is important in dealing with the diagnosis of HIV and probable mental health problems. In their study, Petersen et al. showed that relationships with caregivers who are HIV positive also creates opportunities, as is shown in Box 2 by one of the caregivers in the study who is HIV positive.[102]

Box 2[102]

"When I started to talk to him, I give him the example using myself, I said you see I am HIV and I am living. I was young when I was diagnosed with HIV. I am telling him this so that he can accept it better by knowing that HIV is not a death sentence. It does not mean that when you are HIV positive you are already dead, but you can live longer if you accept your condition. He has accepted it; he does not have a problem. (Participant 36, caregiver, aunt)."

As researched by the South African Depression and Anxiety Group (SADAG) in a study on mental health in the workplace (1064 participants), 1 in 4 employees was suffering from depression and employees with depressive disorder took on an average 18 days off. Furthermore, while depression was prevalent, managers often did not feel confident in giving support to people with depressive disorder. As discussed by SADAG, stigmatisation of MHD's in the workplace are common and people with depression often do not talk about their mental health problems. Reasons that were given are discrimination, fear of missing promotion, sign of weakness, embarrassment, fear of getting fired, fear to be made fun of or being gossiped about. People felt supported by their managers when they asked how they could help and offered professional help or disclosed similar diagnosis.[103] In addition, unemployment has been described as one of the worst factors for development of depression (six studies). [58,79–82,93]

Next to stigma and discrimination being related to depressive disorders, PLHIV experience the same problems. These problems increase the risks for MHD's in PLHIV in a vicious cycle. In eight studies stigma was related to higher depressive rates in HIV positive study populations. [56,59,63,64,79,91,102,104]

Findings from South Africa seem comparable to the international literature.[105,106] Country specific for South Africa was that two studies found higher depressive scores in Afrikaans speaking study participants compared to Xhosa speaking participants.[107,108]

Chapter 3: Looking at the quality of mental healthcare in South Africa as provided for PLHIV with comorbid depressive disorder

This chapter is divided in three parts; structure of care, the process of care and the outcomes of care. Every part is subdivided in different themes as was given as example in the WHO package on quality improvement for mental health.[34]
In the first part the structure of care is evaluated according to *staff ratios, staff qualifications, financial resources* and the *infrastructure*. Reports and policy documents on the healthcare system in SA form a substantial part of the sources used.
In the second part, the process of care is divided in *medication types and amounts* and *examples of integrated care.* In the WHO package on quality improvement of mental health also *types of services* and *hospitalisations* are mentioned. No specific data was found for hospitalisations and information on types of services overlap with integrated care models. Therefore, it was decided to not mention these separately. South Africa is reorganising its mental health care system with a shift from institutionalized care to community healthcare. Also the PHC system is undergoing changes and models for integrated care for chronic diseases, HIV, MHD's and multimorbidity are developed.[29] It is important to look at individual studies that have evaluated integrated care models specifically for PLHIV and MHD's.
At last the outcomes of care are described in outcomes on *quality of life for PLHIV with comorbid depression, reduction of depressive symptoms in PLHIV* and *adherence to therapy in PLHIV with MDD in SA*. The latter was added, because in the international literature on MHD's in PLHIV adherence to therapy is often mentioned as being less in PLHIV.

Part 1. Structure of care for PLHIV with comorbid depression in South Africa

Staff ratios
It is estimated by WHO and the South African DoH that in SA there is 0.28 - 0.39 psychiatrist available per 100 000 people and that around 9.3 health workers per 100 000 people work in mental health.[109,110] In comparison, estimations by WHO are 11.9 psychiatrists and 23.5 nurses working in mental health / 100 000 people in high income countries.[44]
Moreover, one study found 0.45 other medical doctors (working in mental health), 0.32 psychologists, 0.40 social workers, 0.13 occupational therapists, 10.08 nurses and 0.28 other health workers per 1000 000 people working in mental health in SA.[111] The same author modelled that for a population of 100.000 you would need 25.1 nurses, 0.6 occupational therapists (OT's), 1.9 occupational therapist assistants (OTA's), 2.2 social workers, 1.2 clinical psychologists, 1.55 psychiatrists and 1.95 medical officers to treat severe psychiatric conditions.[112]
Other findings are that around 20 percent of all psychiatrists in SA emigrate to another country within 5 years after graduation. [111]

Staff qualifications
In the WHO-AIMS (Assessment Instrument for Mental Health Systems) study in South Africa data was available for training for doctors and nurses on mental health. Around 5.5 % of all training for doctors in Gauteng and KwaZulu - Natal is on mental health and 21% of undergraduate training for nurses.[111,113]

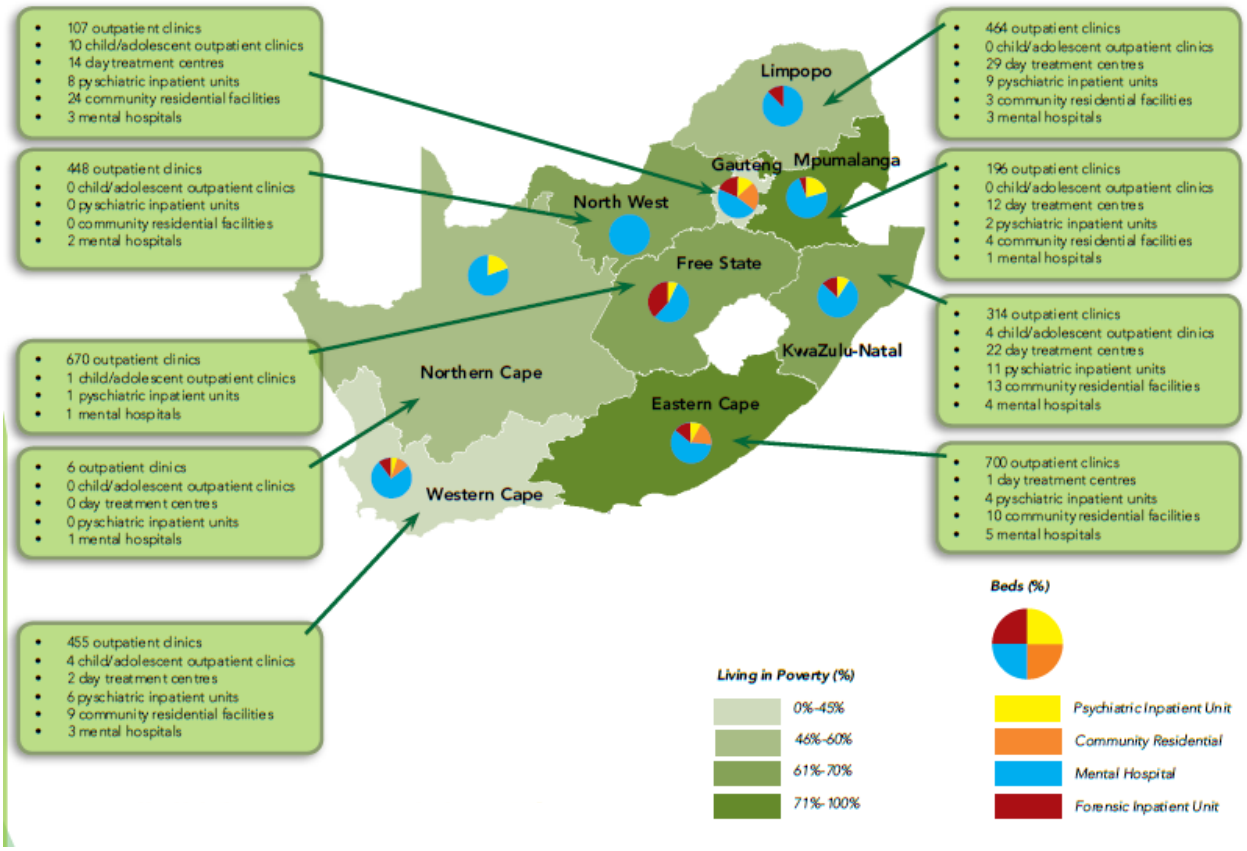
Financial resources
Financing for mental health care is done at the provincial level, while provinces receive budgets from the national government. Health budgets received are mainly tax based. Only in three provinces data on budget allocation for mental health was available as

reported in a study by Lund et al..[111] Northern Cape spends 1 percent of the health budget on mental health and Mpumalanga around 8 percent. Based on data from four provinces, the authors conclude that around 86 percent of the mental health expenditure is received by mental health hospitals.[111]
Government grants in South Africa are available for poor people who cannot work due to disability.[114,115]
No studies were found that researched financial resources available for care of depression in PLHIV.

Infrastructure
In the country there is a national mental health authority which has 1 director, three deputy directors, assistant directors and administrative staff. Policy on mental health is made by the mental health authority and delegated to the provinces. Provincial mental health authorities are responsible for services, management, coordination and quality. All provinces are following national policy to integrate mental health into primary health care.

Distribution of health services that provide mental healthcare is shown in figure 5.[111]

Figure 5 – Distribution of mental health services in South Africa



Lund C, Kleintjes S, Kakuma R, Flisher A, the MHaPP Research Programme Consortium. Public sector mental health systems in South Africa: inter-provincial comparisons and policy implications. Social Psychiatry and Psychiatric Epidemiology 2009. [111]

There are differences between provinces for hospital-based care and community services. Overall, 25% of mental health staff work in the community (in KwaZulu Natal this is 5%, while in Northern Cape this is 70%). Data on distribution of psychiatrists between rural and urban areas were available for Free State and North West. Distribution around the largest city was 3.6 times higher than in the entire provinces.[111]
SA has a mandatory community service program and young health professionals need to work in rural areas for at least on year.[116]
Different national policy plans and guidelines on mental health and HIV were researched if these documents include depressive disorder in PLHIV. In the National Mental Health Policy Framework and Strategic Plan 2013-2020 in chapter 7 the attention for mental health needs of PLHIV is specifically mentioned *"Certain vulnerable groups will be targeted for specific mental health needs. These include women, children, adolescents, the elderly, and those living with HIV and AIDS".* In the National Strategic Plan for HIV, STI's and TB it is stated " *The full package of screening, to be available in all clinical settings, will include: HCT; TB symptomatic screening, linked to TB testing for those with symptoms; as well as screening for diabetes, blood pressure, anaemia, mental illness and alcohol abuse, with referral to psychological and social support".*[27] While SA's health system is undergoing changes to improve PHC systems and to integrate care for chronic diseases, specific guidelines are in place.[50,117,118] Guidelines for PHC in SA (PC 101, Ideal clinic) have separate chapters on screening and treatment for depressive and anxiety disorders.[29,50] In the chapters on HIV it is specifically mentioned to assess the mental health status of PLHIV at time of diagnosis and when adherence is low. At last the society of Southern African HIV clinicians provide a guideline specific for the management of MHD's in PLHIV.[23] In these guidelines a brief screening for depressive disorder in PLHIV is recommended by asking for depressed feelings. Extra screening is necessary at the first ART-visit, in non-adherent patients and in patients who look worried. The PHQ-9 is given as an example for screening.[23]

In ten studies out of 79 found in the initial search a need for adequate screening tools for depressive disorder in PLHIV was highlighted.[55,65,81,108,119–123] Six different studies were found that investigated brief screening tools for MDD in PLHIV in SA (Table 3).[53,61,108,121,123,124]

Looking at the infrastructure, the coordination of care between social services and health services is also of importance in mental healthcare.
In six out of 79 studies it was found that often there is a lack of coordination between the social welfare system and the healthcare system.[56,75,90,94,125,126] In one qualitative study among health care workers by Burgess et al.[125] this problem was addressed by one of the study participants in the next phrase:

"S: Yes, where the cause [of depression] is poverty, we recommend food parcels, or DG (disability grants)….. But the problem is the working relationships because if you refer a patient to home affairs to get these documents, ... they [home affairs staff] will ignore the patient and tell them to wait... so, they wait wait ... but ultimately, it's a waste of time for us to go with them, because other patients are waiting here to see us (laughs)."

Table 3 – Evaluation of screening tools for major depressive disorder in PLHIV in South Africa

Article	Study population	Screening tool	Reference test	Sensitivity	Specificity	PPV	NPV
Breuer et al.[53]	356 PLHIV	SAMISS	MINI	94 % (95% CI 88-98%)	58% (95% CI 52-65%)		
Saal et al. [121]	500 patients (HIV testing)	BDI	SCID	67%	67%	0.25	0.92
Singh et al.[124]	20 PLHIV ART - CD4 < 200	CES-D	DSM-4	91%	44%		
Spies et al.[108]	429 PLHIV	K-10	MINI	67%	77%	0.29	0.94
Rochat et al.[123]	109 antenatal women (50% HIV +)	EPDS	SCID	60.78%	89.66%	83.78%	72.22%
Myer et al.[61]	465 PLHIV	CES-D	MINI	79% (95% CI 76-83%)	61% (95 % CI 56-85%)		

PPV: Positive predictive value, NPV: Negative predictive value, PHLIV: People living with HIV, 95% CI: 95 % Confidence interval, ART: Antiretroviral treatment, SAMISS: Substance abuse and mental illness symptoms screener, MINI: Mini international neuropsychiatric interview, BDI: Beck depression Inventory, SCID: Structured clinical interview for DSM, CES-D: Center for epidemiological studies-depression, DSM-4: Diagnostic and statistical manual of mental disorders, EPDS: Edinburgh postnatal depression scale

Part 2. Process of care for PLHIV and comorbid depression in South Africa

The process of care has to do with how care is delivered and the interaction of services with patients.

Medication types and amounts

In guidelines for HIV-clinicians in Southern Africa, recommendations are given for treatment of depressive disorder. Fluoxetine, amitriptyline and citalopram are antipsychotics described on the essential drug list (EDL) and are often used as treatment.[23,127] Also psychotherapy is recommended if it is available. In the WHO AIMS report on SA it is reported that most healthcare services in SA have access to psychotropic medication (88 % of outpatient clinics, 96 % of inpatient community clinics and 100% of mental hospitals).[128] No guidelines are in place for intensive counselling techniques for MDD in PHC.[129]

In one study it is mentioned that due to a lack of personnel often treatment with medication is given instead of psychotherapy.[130]

In the South African Stress and Health Study it was found that 28% of adults with severe psychiatric disorder received treatment.[28]

Integrated care

South Africa is changing its mental healthcare system and tries to shift mental healthcare to communities and PHC. In addition, they try to improve the PHC system and develop integrated care models for PHC. One of the approaches to shift mental healthcare to communities and to improve PHC, is the Ideal Clinic Programme.[50,117,118] In this programme they stimulate PHC centres to become Ideal clinics. In theory an Ideal clinic is a clinic that offers high quality care with enough staff and resources, good infrastructure and adequate collaboration with stakeholders.[29,118]

Searching for integrated care models specifically for HIV care and mental health care one study was found that described a full integrated care model for PLHIV and MHD's, including depression (see box 1).[131] Next to that five studies were found that presented data on healthcare providers perceptions on working in integrated care models for HIV and mental health.[96,120,125,132,133] No studies were found on patient's perceptions of integrated care models for mental health and HIV.

Dos Santos et al. did study health care beliefs on MHD's among staff working in five different HIV clinics in Gauteng. The interviewees described that there was a lack of guidelines, screening tools and mental health workers to screen, diagnose and treat MHD's in PLHIV attending the clinics. The researchers also noted that staff often lacked good counselling skills for treating psychosocial conditions.

Data collection was done for patients in the clinics, but no mental health data was collected. Furthermore, while doing a situational assessment in the region, the authors concluded that there was a lack of specialized psychiatric units for treatment of HIV and psychiatric disorders in the province. The authors also note that health care providers sometimes were unaware of the presence of NGO's providing mental healthcare or had doubts on the sustainability of NGO services. Although the interviewees thought it was important to provide information on services providing mental healthcare at ART clinics. In one of the ART clinics described, they made use of "courtesy managers" who showed people where to find mental health services. In the study one of the problems in the process of care that was mentioned was the lack of privacy in the clinics for PLHIV with MDD.[96]

This lack of privacy is also mentioned in another study by Burgess et al.[125]

Burgess et al. studied the understandings of mental health problems in women affected by HIV among 14 healthcare workers (5 doctors, 3 nurses, 2 physiotherapists, 2 occupational therapists, 1 voluntary counsellor, 1 social worker) working in PHC clinics in Kwazulu-Natal. One study participant mentioned the lack of privacy in the following phrase: *''At general clinics often there's no privacy, there's someone sitting beside you screaming, they can hear everything, people screaming..."* The study also mentions the support that some clinics receive by collaborations with NGO's and the potential of NGO's to fill service gaps. Although they also describe a lack of continuity.[125]

Mall et al. did study mental health literacy among 66 HIV healthcare providers (nurses, counsellors, physicians) working in public health facilities. 89% had ever heard of MHD and 51% was able to correctly identify depressive symptoms. The respondents mainly believed that depression was caused by psychosocial stress. Biological factors for depression were mentioned less.[133] In another study by Mall et al. among 22 HIV service providers in three PHC clinics similar findings were described. Service providers did not feel confident in providing mental health care screening and had poor knowledge of MHD.[132]

Task shifting ART treatment to nurses and evaluating nurses ability to integrate HIV treatment and to screen for MHD's was studied by Modula et al.[120] 24 nurses trained in HIV care and working at PHC centres were interviewed. All nurses mentioned that mental health screening was important, and nurses were aware of the interactions between HIV and MHD's. One of the findings was that screening for mental health was not routinely done. One nurse mentioned: "*We are to monitor patients for ARVs adverse effects such as fatigue, depression and anxiety, I do the general physical assessments and just note if*

there was anything suggesting mental illness." An important conclusion was the lack of a standard screening tool for MHD's and the lack of nurses trained in psychiatry. Another result of the study was inadequate service provision of psychiatrists, psychologists and social workers. This was highlighted in the following phrase by one of the participants: *"Psychologist and social workers do outreach at our clinic. The periodic visits are not adequate, we need frequent visits to support us identify mental health problems early especially when patients do not show any obvious signs."* The authors conclude that nurses working in HIV care need further training in mental health and be provided with better screening opportunities. The HIV/AIDS guidelines do mention to screen for MHD, but do not provide the tools. [120]

Box 3: Jonsson et al. [131]

The Luthando clinic

Jonsson et al. describe a successful integration model for HIV and neuropsychiatric care. In their Luthando clinic in Soweto, a team of psychiatrists started a program to treat HIV in mentally ill patients. The Luthando clinic serves as an outpatient clinic for patients with HIV and mental illness and is linked to the Chris Hani Baragwanath Academic Hospital (CBAH) in Soweto.

While the psychiatrists in CBAH noted a high unmet need for HIV care in their mentally ill patients they started to follow HIV training and became certified to provide ART. The psychiatrists were able to consult infectious disease specialists and HIV clinicians from the CBAH hospital.

While working closely together with the psychiatry unit, HIV programs, laboratory and the pharmacy in the CBAH hospital, the Luthando team has access to specialist care, testing and medication. The authors note that while HIV providers are often too busy to take care of mental illnesses the mental health team can take over these patients while having enough knowledge about HIV.

After a first successful integration of HIV and mental health care the patient population started to grow, and the medical team also received more patients affected by Tuberculosis. They were able to also integrate the care for TB with TB-testing and treatment.

The Luthando clinics provides integrated care for mental illnesses, HIV and TB and mental health workers are trained in all three diseases. As the authors note providing care for all three diseases in the same building makes it much easier for patients to come to appointments and therefore to adhere to therapy. Also, they can provide the different medication in the same pharmacy, which makes it easier for patients.

Next to medical therapy the clinic also gives psychosocial support. They started with a support group but recognized that this was not according to the patients' needs. Many patients were poor, and patients and providers missed a social activity with the support group. Therefore, they started two groups where patients learned skills such as beading, and gardening and patients were able to sell some of their products and grow food in their communities. These groups are led by trained occupational therapists.

At last the Luthando clinic teaches patients and home visitors in adherence to therapy. As they note that adherence to ART is three times less in depressed patients, they want to increase their attention to these groups in the future.

The Luthando clinic offers care for around 600 patients and is open three days a week. The most common mental illnesses were major depressive disorder and bipolar mood disorder.

Part 3. Outcomes of care for PLHIV and comorbid depression in South Africa

While looking at outcomes of care for PLHIV with comorbid depressive disorder articles were screened on outcomes for quality of life, improved functioning and reduction of symptoms and adherence to therapy.

Quality of life

Four out of 79 studies mentioned health related quality of life (HRQoL) and depression in PLHIV.

Thomas et al. did study health related quality of life outcomes among 18 941 people in South Africa of whom 4012 (22%) were HIV positive. 2026 people out of 4012 (50%) were unaware of their HIV status. Thirty-one percent of HIV patients was on ART. Almost 9% of the respondents was aware of their HIV positive status, but not yet in care. Main findings were that HRQoL did not differ between HIV negative patients and patients with HIV unaware of their status or on ART for more than five years. HIV positive patients not receiving care or treatment were more likely to report to be depressed. The authors estimate that starting ART treatment in HIV positive patients would gain around 26.24 Quality Adjusted Life Year (QALY) for each patient. In their conclusion the researchers note that although the differences found are small on an individual level, the results become more important when seen from a population level. Benefits for the whole population would be substantial when at least 90% of all HIV positive patients would be on treatment.[134]

In a study among 903 HIV positive patients (468 patients on ART), Nglazi et al. found that HRQoL was significantly higher in the group on ART treatment compared with HIV positive patients not on ART treatment. Furthermore depressive symptoms were higher in ART naïve patients than patients on treatment (22.4% vs 8.8%).[57]
A third study (134 HIV positive adolescents on ART) did find that having symptoms suggestive for MDE in screening was associated with poor QoL.[51] At last, Hughes et al. did research on HRQoL in patients with stage 3 or 4 HIV (N=123) who were not yet on treatment and compared these patients with a sample (N=108) from the general population. HRQoL was lower in the HIV positive group as expected. The authors found high prevalence of depression in both groups (33.4% and 24.2%) and therefore note the important role counselling services have in general in detecting depressive symptoms.[73]

Reduction of symptoms and improved functioning

Five studies were found that investigated outcomes of psychotherapy (1 cognitive behavioural therapy (CBT), 3 on interpersonal psychotherapy (IPT), 1 art psychotherapy) for depressive symptoms in PLHIV in SA. Although study groups were small and groups were heterogenous, results in most studies were promising for reduction of depressive symptoms (Table 4).[76,129,135–137] One study by Thurman et al. did not find significant changes in intervention and control groups in depressive scores in youth affected by HIV after IPT.[137]
In a meta-analysis on interventions for depression in PLHIV in SSA countries, the authors found that pharmacological interventions had significant greater effect on depressive scores than psychological interventions.[138]
Next to treatment of depressive disorder the effect of social support and support groups were also investigated. Seven studies looked at the effects of family support and social support.[56,66,88,91,126,139,140] Stein et al. stress the importance of family support for promoting child development in families affected by HIV/AIDS. HIV/AIDS and MHD both have adverse effects on child development. Supporting families socially and economically improves child development.[126] Two studies were found that did look at support groups.[141,142] As studied by Dageid, PLHIV joining their support group had higher levels of stress and depressive scores. Reasons for joining were to deal with stress, get support

and gain information.[142] As found by Mundell et al. joining a support group did not lower depressive scores in PLHIV.[141] Thurman et al. did study psychological health outcomes for families affected by HIV. They studied psychological outcomes for 1487 children and 918 caregivers over a two-year time period who received psychosocial support. The use of voluntary lay health workers with limited training was compared with the use of paraprofessionals who received salary and official training to offer psychosocial support. Psychological health outcomes in the families investigated did not improve after two years follow up and there was no difference between the groups.[143]

Table 4 – Outcomes for different psychotherapy interventions in PLHIV with comorbid MDD in SA

Study	Study group	Intervention	Before intervention	After intervention
Andersen [135]	14 PLHIV +MDD	Nurse delivered CBT Weekly session 6-8 sessions 3 months follow up	CES-D (m=40.9, SD 8.45) HAM-D (M=26.4, SD 5.5)	CES-D (M=6.58, SD 7.61) HAM-D (M=5.8, SD 5.8)
Moosa[76]	32 PLHIV +MDD	Citalopram 20 mg/day start dose (N=19) IPT (N=13) 5-12 session 8 weeks follow up	Citalopram HAMD 25.7 IPT HAMD 22.5	Citalopram HAMD 6.2 IPT HAMD 8.2
Petersen [129]	34 PLHIV +MDD	Group based IPT, Lay health counsellors (N=17) Control (standard care) (N=17) Weekly session for 8 weeks 3 months follow up	IPT PHQ-9 (M=15.47, SD 4.46) Control PHQ-9 (M=15.18, SE 5.46)	IPT PHQ-9 (M=6.94, SD 4.14) Control PHQ-9 (M=11.06, SD 4.58)
Thurman [137]	236 adolescents LHIV + MDD	Group based IPT N=134 Control (standard care) N=102 Weekly session 16 total 1 year follow up	IPT CES-D (M=23.60, 22.31-24.88) Control CES-D (M=23.65, 22.34-24.96)	IPT CES-D (M=19.27, 16.66-21.87) Control CES-D (M=18.91, 16.75- 21.07)
Field[136]	18 women LHIV +MDD	ART psychotherapy (N=9) Control Video entertainment viewing activity (N=9) Follow up 1 session	BDI-II Scores not mentioned	BDI-II (M = -0.5291, SD = 0.167) control group (M=-0.1376, SD = 0.231).

PLHIV: People living with HIV, MDD: Major depressive disorder, CBT: Cognitive behavioural therapy, IPT: Interpersonal psychotherapy, CES-D: Center for epidemiological studies depression, HAM-D: Hamilton depression rating scale, BDI: Beck Depression Inventory
N= Number of patients, M= Mean, SD: Standard deviation

Adherence to therapy

Three studies were found that studied adherence to ART therapy in PLHIV with depression in SA and one study was found studying adherence to antidepressant therapy in PLHIV and MDD.

Nel et al. did study rates of depression among PLHIV and looked at associations with compliance to therapy. In 101 PLHIV, 40.4% of patients scored positive for depression. Patients not adherent to ART were more likely to be depressed (OR 2.73 95% CI 1.09-6.82).[78]

Moosa et al. studied ART adherence among 32 PLHIV with depression who either received IPT or medication (Citalopram 10-20mg). Adherence to therapy at the start of the study was 92.1%. Adherence improved in both groups significantly; patients receiving 5 sessions of IPT (91.1% to 99.6%) and patients on medication (92.8% to 99.5%). Depression rates in both groups also declined with at least 7 points (Hamilton depression scale (HAMD)) in both groups.[144] In a sample of 146 PLHIV of whom 91 scored positive for depression on the CES-D checklist, Kitshoff et al. did not find significant differences in adherence to ART therapy between depressed and non-depressed patients. Non-adherence in their study was mainly linked to unemployment. Adherence to therapy in the whole study was low.[82]

In 127 PLHIV and MDD who were studied by Slabbert et al. compliance to antidepressant therapy was less than in patients with MDD not positive for HIV (N=12 270); (74.43% ± 32.03, 95% CI: 71.51-77.34) vs. (80.94% ± 29.44, 95% CI: 80.56-81.33).[86] The authors note that the clinical relevance was low, as non -compliant patients only missed approximately 2 doses in a 30-day treatment period. Looking at different antidepressants, compliance to tricyclic antidepressants (TCA) (26.83%) was lower than that for serotonin reuptake inhibitors (SSRI's) (44.93%). Patients using serotonin noradrenalin reuptake inhibitors (SNRI's) were the most compliant (58.57%).[86]

Discussion

Research studying mental health issues and quality of care in PLHIV is scarce. South Africa, the country where the most people with HIV live, therefore forms a good opportunity to study these topics. In this thesis an overview is given for the prevalence of MDD in PLHIV in SA, combined with a description of the major determinants involved. Furthermore, an assessment of the quality of mental healthcare for PLHIV with comorbid depressive disorder is performed. To my knowledge this is the first appraisal on quality of mental healthcare in this population using consistently Donabedian's framework on structure, process and outcomes of care.

An extensive search was performed to find all relevant research involved on mental healthcare in PLHIV with comorbid depressive disorder in SA. This resulted in 79 articles that directly involved research on PLHIV with comorbid MDD or depressive symptoms suggestive for MDD in SA. For the purpose of this thesis, general reports and articles on mental healthcare in SA, SSA and international mental healthcare were investigated as well. Next to that, international guidelines on quality of mental healthcare and integrated care in PLHIV were assessed. Although efforts have been made to include all relevant research it still can be that research is missed that indirectly or directly studied depressive disorder in PLHIV in South Africa. As will be discussed the quality of found articles was mixed. In general study groups tended to be heterogenous and often the use of a control group was lacking.

No studies were found that directly studied the quality of care in PLHIV with depression in SA according to Donabedian's SPO framework. Results sometimes were taken from studies that had other primary endpoints or described only components of quality of care measurements. Results on the quality of care in those cases were taken from general descriptions or suggestions made by the authors in the different studies. Although, not less relevant, results in general therefore have higher risks to be biased. Linking study results from different studies together gives a good and complete overview of the problems described and, in this scenario, seems to be the best available option.

Not many studies were found that included recent data. Most studies were done before the year 2016. Only two studies included data from 2016 and in two studies published in 2018 no information was found on when data was collected.[51,58,62,63] One of the main publications on the prevalence of MDD in South Africa was the South African Stress and Health study with data up to the year 2004. Prevalence numbers from this study are still mainly used in recent reports.[28] As SA and the South African health care system have changed and also HIV treatment has significantly been improved in the last years, it is likely that results might not be the same any more. It shows the need for continuous studies on mental health, HIV and quality of care.

Discussion: The burden of depressive disorder in PLHIV in South Africa

Prevalence of major depressive disorder in PLHIV in South Africa

Depressive disorder is one of the leading causes for disability worldwide. Global point prevalence estimate is that 4.4% (4.1-4.7%) of the global population experiences MDD. Estimate for SSA is 5.5% and in SA 4.9%.[19,28] In a systematic review among PLHIV in SSA pooled prevalence estimate was 31.2% (95 %CI 25.5 – 38.2).[145]

In this thesis 33 studies were found that reported prevalence numbers of depressive disorder in PLHIV in SA. Prevalence numbers were between 5.2% and 78.2%.[51,52] Results are similar to other findings in SSA countries.[145]

Strengths of the findings are that most studies included many patients (*see: Appendix 2).* More people included makes results more reliable and chances for possible selection bias less. In ten studies with more than 500 PLHIV included, prevalence was between 11% - 33% (excluding 2 studies among pregnant women with prevalence of 45.1 - 48.7%).[25,56,57,59,65,68,70,74,79,80] Only in two studies also a control group of HIV negative patients were included.[67,73] In these studies significant differences for MDE between PLHIV and people not infected with HIV were described, respectively; 22% vs. 13% and 33% vs. 24.2%.[67,73]

Looking at the different prevalence outcomes in the different studies give some interesting findings.
Over one third of all studies reported prevalence numbers between 20-40% and 22 out of 33 studies had prevalence numbers higher than 20%. Comparing the three studies with the lowest prevalence rates of depression in PLHIV with the three studies with the highest rates give some insight in the differences reported.
In two studies with low MDD prevalence (5.2% and 7%) the authors describe that study results might be influenced by the high adherence rates to ART in their study groups.[51,54] Also unemployment rates were low in the samples and most patients were higher educated. Furthermore, patients had access to well-resourced HIV clinics in urban settings. All these factors might have resulted in lower depressive scores.
In a study by Govender et al. high MDD prevalence numbers were found with prevalence of 82.8% within 72 hours after positive HIV testing and 78.2% after 6 weeks.[52] Screening shortly after HIV diagnosis might explain the study results. Although in four other studies in patients with recent diagnosis of HIV prevalence of MDD were lower (22%, 25.4% and 34.8%).[25,64,67]
In a different study with high prevalence of depressive disorder it can be that the used screening tool influenced study results. Bongongo et al. used the Zung self-rating scale. Prevalence of mild, moderate and severe depression were 69.2%, 1.7% and 0.9%, respectively. In the study no cut-off points were given for the different classifications, but it might be that the tool used, or the cut-off points used where not suitable for the investigated population.[81]

In four studies among HIV positive pregnant women and one study in postnatal HIV positive women prevalence rates for depression were between 11% and 48.7%.[56,59,71,79,80] Common risk factors for depression in these studies were stigma, poverty and experienced violence.
Four studies in adolescents showed prevalence numbers between 5.2% and 30.3%.[51,60,62,63] Overall access to ART therapy in the study groups was high and adherence to ART therapy was good.
In this thesis no studies were included, researching mental health in gay people and prisoners. It is obvious that these populations also face difficulties on their own and it is

probable that MDD also is prevalent in these populations. In one study in Tanzania, MDD prevalence was 68.2% in 44 HIV-positive men having sex with men (MSM).[146]

In the 33 studies 12 different tools were used for screening and two for diagnosis (MINI, CIDI) of depressive disorder. First, the abundance of tests used shows that there is no clear agreement among researchers and healthcare providers which test should be used. As found in a systematic review among PLHIV in SSA pooled estimates for MDE for the studies with the diagnostic tests was 18% and in the screening tests pooled estimates for significant depressive symptoms was 31%. Results show that there can almost be a two times difference in outcomes when different tests are used.[145] In this thesis no clear pattern was discovered comparing tests that resulted in higher or lower prevalence rates. The MINI and CIDI diagnostic tests were used in 6 studies. The three most used screening tools were the BDI (4 studies), CES-D (4 studies) and the PHQ-9 (3 studies). In table 3 an oversight was given for studies that assessed the validity of different screening tools for MDD in PLHIV in the South African context. No studies were found that investigated the reliability of the PHQ-9, although this test is recommended by the Southern HIV Clinicians Society.[23] Sensitivity of the CES-D was high, but specificity was low.

Tsai et al. did a systematic review on the reliability and validity of screening for depression in PLHIV in SSA.[147] They found that the CES-D was the most studied screening test with a pooled sensitivity of 82% (95% CI 73% - 87%). Overall, they found that there are high rates of false positives in screening for depressive disorder. As resources are limited it is important that screening tools are easy to use and short, but also that over detection of depressive symptoms is limited.[147] Patients who score positive should receive additional testing for confirmation of the screening results. To make optimal use of the screening tools it is important that the test is adapted to the local context and that interviewers understand local synonyms and descriptions for depressive symptoms.[20,145,147]

In conclusion, the MINI and CIDI are well validated, if performed by a trained person, to diagnose depressive disorder. Limitations of these tests are that they are not easy to use, and questionnaires are long. The CES-D and PHQ-9 are studied most in SSA and recommended by the South African HIV Clinicians Society and other researchers. Using these screening tools give chances for an overestimation of people with depressive symptoms.[23,145,147] Moreover it is important that tools are adjusted to the local setting.[20]

Studies were done in six out of nine provinces with most studies done in Western Cape province (11 studies from which nine were done in Cape Town).
Interestingly ten out of 12 studies reporting prevalence numbers below 20%, were done in the biggest cities of the country ((Cape Town, 7 studies) and Johannesburg (3 studies)). It can be that the difference between rural and urban areas explains that most studies with lower prevalence rates were done in urban settings. As previously described (chapter on structure of care) it can be that access to healthcare was higher in urban areas and that socioeconomic status is higher, which reduces the chances for depressive disorder. If access to care is better it makes it easier for patients to follow up in care, adhere to HIV therapy, which can reduce chances for depressive disorder. Although in one study rates of depressive symptoms were higher in an urban setting compared to a rural setting.[98] No other clear differences were found for the prevalence estimates in the different provinces.
In all studies, but one[72] more women than men were included. As was found, female gender is often a risk factor for depressive disorder. This could result in higher prevalence rates reported, but could also indicate that women are more willingly to participate in research and men are underrepresented. Often study participants are included at HIV clinics, it could also mean that men are seen less in HIV care.

Major determinants associated with major depressive disorder in PLHIV in South Africa

The determinants involved in the risks for depression in PLHIV were structured according to the Lalonde model. Looking at determinants associated with human biology and lifestyle, female gender[54,60,64,66,74,75,86–88] and younger age[54,56,59,61,62,88,93] were associated with higher rates of depression in HIV affected populations in SA.

This is according to what is also found in the international literature. In different studies it is found that there are often no specialized centres available for these populations. The high prevalence of HIV has a great impact on society in SA. Many family structures are disrupted and the loss of family members and orphan hood caused by HIV can be important factors in the development of depression.[87,102] Next to that people affected by HIV often experience stigma in the communities and the workplace. This can be either caused by a lack of knowledge in the public or coping styles and internalized stigma by the patient.

It seems that increased efforts to educate people on depression and HIV can help to reduce stigma and positively affect the health seeking behaviour of patients. Moreover, training of health workers in recognizing depression appears to be recommended. As is discussed in other chapters in this thesis knowledge in healthcare workers is often low. As symptoms of depression are not recognized it can be expected that treatment will be less. Furthermore, it seems important that healthcare workers are aware of the social determinants associated. As it might be difficult for healthcare workers to solve problems as poverty, unemployment and family dynamics, good interaction and collaboration with the social welfare system is important. The treatment of depression in PLHIV needs a multidisciplinary approach in which the healthcare sector, the social welfare sector, the economic sector and employers, schools and institutions and communities need to be involved.

At last the biological factors of HIV should not be underestimated. Lower CD4 counts are related to higher rates of depression.[54,81,96,98,148,149] Treating PLHIV can still be improved as studies show that many PLHIV still do not receive treatment in SA. Improved treatment improves HIV outcomes, reduces chances for depression and in the end the whole population and economy can benefit.

Discussion: Looking at the quality of care

This thesis provides a first assessment of the quality of mental healthcare in PLHIV with comorbid depression in SA. The quality of care was evaluated according to the Donabedian SPO framework. Donabedian's framework forms the backbone of many assessments of quality of care and was considered suitable for the objective of this thesis.[34,150,151] As quality of care can be described in many ways this framework forms a broad and inclusive model and gives the opportunity to include many different aspects that play a role in quality of care. The items that were evaluated in this thesis, were based on items mentioned in the WHO package for quality improvement in mental health.[34] The results give important insight in the general quality of mental healthcare in PLHIV with MDD in SA and can be used to give recommendations on how to improve care in the future.

Hence, although the intention was to give a complete oversight, probably not all aspects that are involved in quality of care are included in this thesis. For instance, human rights are important in mental health, but was not assessed in this thesis.

While looking at the quality of care it is important to include all stakeholders involved (e.g. healthcare providers, patients, social workers, policy makers). In this thesis I found 79 studies that studied depression in PLHIV in SA, but research that studied patients' perceptions on the quality of healthcare received were lacking. Four studies were found that did research healthcare providers perceptions on mental healthcare. For that reason, it is possible to say something on the quality of care as perceived by healthcare providers, but less for patients. Furthermore, evaluation of the private healthcare sector was not part of this thesis.

Assessing the quality of care for PLHIV and comorbid MDD is important as the burden of both diseases is high in SA. It is important for all stakeholders that are involved in the care for these patients to be aware of quality, because only then improvements can be made. The SPO model is a suitable and well-known framework to evaluate this quality and is inclusive for the different domains that can influence the quality of care.

Structure of care

Most results on the structure of care were based on data provided by Lund et al.[111,112,152] The data shows that human resources for treating MHD's are lacking in SA. For instance, as modelled in one study, SA need at least five times more psychiatrists to provide mental healthcare.[112] And compared to high income countries, high income countries have almost 30-times higher amounts of psychiatrists available for the population.[44] Interesting finding was that almost one in five psychiatrists in SA move to another country. It is important that the factors that drive psychiatrists out of SA are identified. Described factors so far are the economic situation and high crime rates, which shows that it is important that SA needs not only to improve its healthcare system.[111] In the interview with dr. Ebuenyi *(see: Appendix 1)* it was also mentioned that working in mental healthcare is for several reasons often less attractive to medical doctors. Not only for SA it is important to improve the image of mental healthcare, but also in other countries this can be improved. One study that did look at why psychiatry is less attractive to work in, shows that factors that play a role are a lack of funding, lack of collaboration with other medical disciplines and that not enough students are made enthusiastic to work in psychiatry.[153] These factors can be taken in to consideration, especially in LMIC's, such as SA.

As was found in different studies in SA and the international literature task shifting of the basic treatment of depressive disorder in PLHIV could be a resolution for the lack of resources.[43,120,122,129,132,154,155] Task shifting approaches can increase the workload to

lower healthcare professionals who already must deal with many other medical conditions in patients. Next to that there is a risk that diagnosis or treatment of depressive disorders is not done appropriately and the quality of care that patients receive is lower. With more mental health treatment facilities and mental healthcare providers situated in urban areas there is also inequity in service delivery for people living in rural areas.[111,156] At last as also was shown in a study by Thurman et al. the effects of the use of lay health workers should be adequately measured. Thurman et al. showed that psychological outcomes after two-year follow up did not differ between HIV-affected families receiving home based care from lay health workers with limited training and paraprofessionals who received more training.[143] This example shows that only providing additional training might not be sufficient and that there is a clear need for continuous evaluation of programs that use a task shifting approach. At last, as was also studied by Webb-Robbins et al., caregivers of people affected by HIV also suffer from psychosocial stress and have increased risks for MHD. While this group is of great importance in the care of PLHIV it is important to provide support for caregivers, but moreover to also look in possibilities in training caregivers to give psychosocial support to PLHIV.[155]

A successful intervention for task shifting mental health to lay health workers was described in Zimbabwe. In a high prevalent HIV setting lay health workers were trained in problem solving treatment (PST) for CMD's. A new project was set up called "friendship bench" were patients attending primary care and who were suspected for CMD's were referred to. The "friendship bench" is a place (bench) where patients can talk to lay health workers about their mental health problems. Lay health workers were trained in screening, PST and were supervised by professional mental health workers. Study outcomes show high success rates for treatment of common mental disorders (CMD's) and that the intervention was well accepted by patients and health workers.[157] It can be interesting to implement a similar intervention in PHC clinics in SA adapted to local norms.

In two districts data was available on the amount of training that doctors and nurses receive on mental health. For nurses this was much higher than for doctors (21% vs 5.5%). As mental health issues are complex it is important that doctors are trained well enough to support their staff. Especially with the integration of HIV care in PHC care in South Africa and increasing numbers of NCD's with high numbers of comorbid MHD's it is important that healthcare providers are aware of mental health problems and can give support to patients, but also to less educated staff. Next to that, in this regard, the quantity of training does not seem to say much, as in different studies it was found that general knowledge in healthcare workers on depressive disorder was low. [96,120,125,132,133]

The financial resources available for MHD's are not clearly known in SA. Budget allocation was only available for three provinces. There seem to be big differences between provinces in the budget allocated for mental health. On top of this it seems that most budget is allocated to mental health hospitals.[111] As SA is trying to improve its PHC system and to deinstitutionalize mental healthcare it seems to be important that provinces define clearly the budget available for mental health and distribute this equally among services. As an example, in one study it was found that the indirect costs involved for society in SA when a person has a depression was estimated 4798 US dollar per year per person.[158] The most cost-effective method was to integrate mental health into PHC to lay health workers. [158]

Within the costs that society faces when people suffer from depression, also the costs for the individual and families need to be taken in to account. Poverty is an important determinant in the risks for depressive disorder in PLHIV and instrumental support and generating-income programmes were found important in reduction of depressive symptoms.[56,66,94,102,125]

The South African Government provides grants for poor people who have disabilities, including mental diseases, which make people unfit to work for at least six months. Some people with HIV loose these grants while they are on treatment.[115] South Africa needs to

find a way to give continuous support to people, even if their conditions improve. While it might not be feasible to continue with giving grants it might be important to include social services from the first instance a person enters care. If people learn skills to earn their own income or to grow food, they are less depended on state services and can be more productive for the community. Next to that, to include people in social activities, is also beneficial for their mental health.[131]

In addition to costs and low resources it is important to correctly identify the people that need care. As was shown in this thesis many studies use different screening tools. Screening tools have the risk to falsely classify patients as being depressed. This could increase the workload and costs. There is a need for screening, but moreover also for the right screening tool.

Process of care

As is shown in this thesis treatment of depressive disorder often is done with medicine, rather than psychotherapy. This is often due to of a lack of resources of trained personnel who can provide psychotherapy.[130] In existing guidelines for PHC workers no tools are given on how to perform psychotherapy.[129] Most clinics seem to have access to psychotropic medication.[128] In a review on treatment of depression in SSA it was discussed that therapy with medication might be more effective than psychotherapy on depressive scores.[138] Psychotherapy, such as CBT and IPT are proven effective for treatment of depression in PLHIV. As psychotherapy does not have the risks and disadvantages involved when compared with treatment with antipsychotics, such as side effects and interactions it can be an effective tool used by lay health workers. Especially less severe patients can already benefit. Probably a combination of both psychotherapy, psychosocial support, and psychotropic medication will provide the best outcomes.

South Africa is changing its mental healthcare system and tries to shift mental healthcare to communities and PHC. In addition, they try to improve the PHC system and develop integrated care models for primary healthcare. One of the approaches is the Ideal Clinic Programme.[50,117,118] The guidelines in place for this programme are very inclusive and looking specifically at depression and HIV, the guidelines definitely address to look at depressive symptoms in PLHIV and provide tools on how to diagnose depression and treat this.[118] Within their shift to improve the PHC system there is also a strong emphasis on quality improvement. As was found, a strong point is that quality improvement manuals are in place. It stimulates facilities to improve the healthcare provided and sets goals to improve in the future.[29] While this programme is still being developed future analysis and studies are needed to look at the outcomes of this programme and where improvements can be made. It should be advised that in this evaluation also patients' perspectives are considered.

As was shown in the different studies found in this thesis on depression and HIV: one of the problems mentioned is the interaction with the social welfare system.[56,75,90,94,125,126] The social problems (e.g. unemployment, housing issues, money problems) are mentioned in the guidelines for treatment of depression in PHC and guidelines advise to refer depressed patients to social workers.[118] While in theory this is good advice, in practice studies show that interaction with the social welfare system is not working well.[125] No studies were found that looked at perspectives from social workers on the care that they provide. It might be interesting to look at the difficulties that social workers face in daily work and to include their perspectives on best practices to improve health outcomes for PLHIV and depression. This can maybe help to identify barriers that currently exist for PLHIV with depression that need social services. In the end it might improve the infrastructure between the healthcare system and the social welfare system.

Fully integrated services for PLHIV and depression were found in the Luthando clinic.[131] The training of mental health personnel in the treatment of HIV and TB helped to relieve the workload for professionals less experienced in mental healthcare and to improve the

healthcare provided for people with MHD's. A strong point in their service provision seems to be to include social activities and to learn patients how to earn some income. Although this is a good example of good integrated care it might be difficult to upscale this program as there is already a lack of mental health workers in the country. Which can be used from this program is that the healthcare workers in the Luthando program have access to consult specialist clinicians and make use of pharmacies and laboratories nearby. In the country this would also work if clinicians have the possibility to consult mental health workers. Having a system to ask for expert advice could strengthen healthcare workers. This can be done either in person or at a distance. Also herein lie possibilities for distant consultation with telepsychiatry.[159]

At last, process indicators do not solely depend on the healthcare system, but often is also dependent on patients. If for instance a patient is advised to join a support group, but refuses to participate, then the process is depended on patients' attitudes. Sorsdahl et al. also mention that while knowledge of MHD in the public is lacking many people do not seek help.[104]
In analysis of the quality of care it is therefore also important to look at patient characteristics and behaviours to say something about the quality of care.[160]

Outcomes of care

Treatment of HIV is associated with improved quality of life and less depression in PLHIV. As was shown by Thomas et al. the benefits on population level in the amount of QALY's gained can be substantial when ART treatment is started in PLHIV. Important finding in their study was that in their study population (18 941 people) almost 50% was not aware of their HIV status and only 31% of all people with HIV in the study received ART. This shows that there is still an enormous treatment gap for HIV. To improve the mental health of the population it might already be very effective to first improve screening and treatment for HIV in the population to improve quality of life and to reduce the chances for depression.[134]

Studies investigating psychotherapy (CBT, IPT, art psychotherapy) for depression in PLHIV showed reduction of depressive symptoms and seem to be effective. As was previously mentioned the lack of skilled personnel in a resource constrained setting is probably the biggest limitation in the potential effects for treatment of depressive disorder.

In a vicious cycle adherence to ART therapy and antidepressant therapy is interacting with outcomes for immune status in HIV and depressive scores in patients. Improvement in adherence reduces depressive rates and give better outcomes for immune status in PLHIV. Adherence to therapy might also be dependent on other social determinants. If, for instance, a person is unemployed and does not have the money to go to a clinic for follow up, adherence can be low.[82] As was mentioned in the example of integrated mental healthcare for PLHIV by Jonsson et al. the possibility for the clinic to have direct access to a well-equipped pharmacy and laboratory makes it easier for patients to adhere to therapy.[131]

While treating patients with medication, healthcare workers should be alert on the possible psychological side effects of Efavirenz in treatment of HIV. Although a recent study did show that Efavirenz can be used safely and did not increase chances for psychological side effects.[99] Slabbert et al found that in the treatment for depression SSRI's and SNRI's seem to have the best results in PLHIV.[86] The authors discuss that compliance in their study group was less for antidepressants who also have more non-specific binding to muscarinic, histaminic and alpha-1-adrenoreceptors and that this might be related to increased cholinergic drive in PLHIV. SSRI's are prescribed the most frequent, but in this study compliance with SNRI's was higher. SNRI's are second line treatment for MDD in HIV patients and the authors discuss if this should be changed.

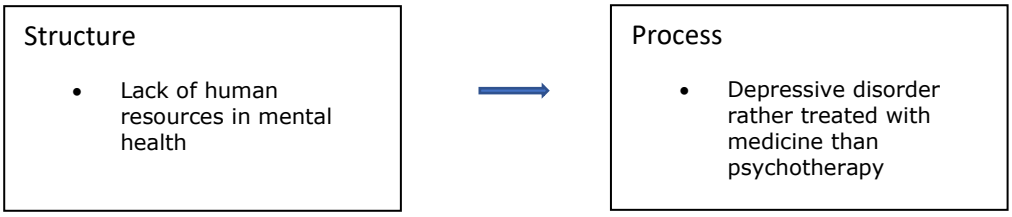
Outcome measurements can be used as indicators for the quality of care provided by healthcare professionals. Sometimes these measurements are used as incentives for professionals to improve care. One of the risks is that healthcare professionals will treat patients in who better outcomes are more easily achieved. Or in other words, there is a risk that "difficult" patients face more challenges to find healthcare.[160]

Discussion: The SPO framework and linking the results

To assess the quality of care a look at all components in the SPO framework is needed. Linking results on structure, process and outcomes of care can help to better understand what influences quality. By giving some examples of the items found in this thesis it becomes clear how these interact.

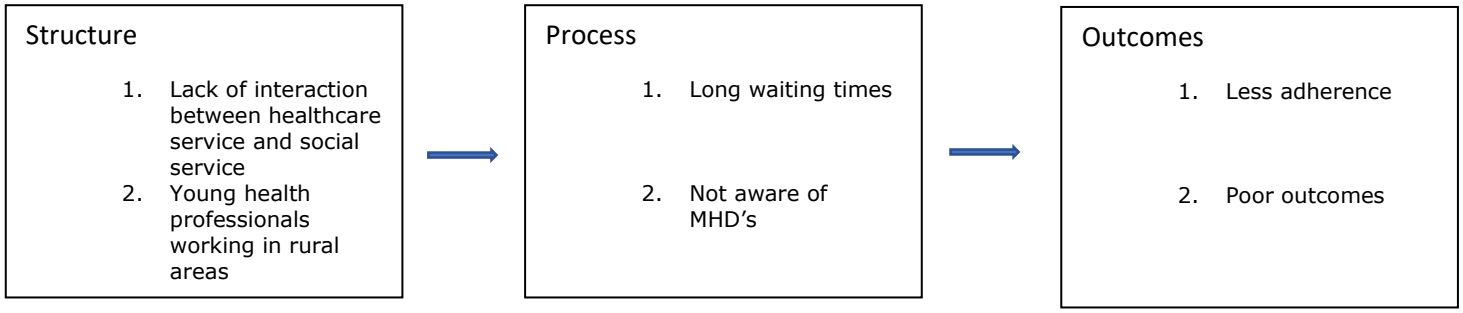
Sometimes components in the structure of care, influence the process of care. A clear example of this unidirectional pathway is the following:

Figure 6a – Example of Donabedian's SPO framework and quality of care for PLHIV with MDD in SA



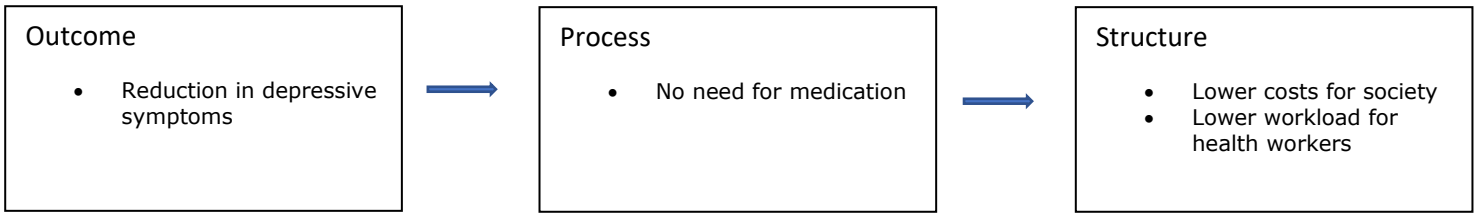
Other examples were all three components of the SPO framework are involved are the following:

Figure 6b – Example of Donabedian's SPO framework and quality of care for PLHIV with MDD in SA



If one would start to look at outcomes, the framework could look as follows:

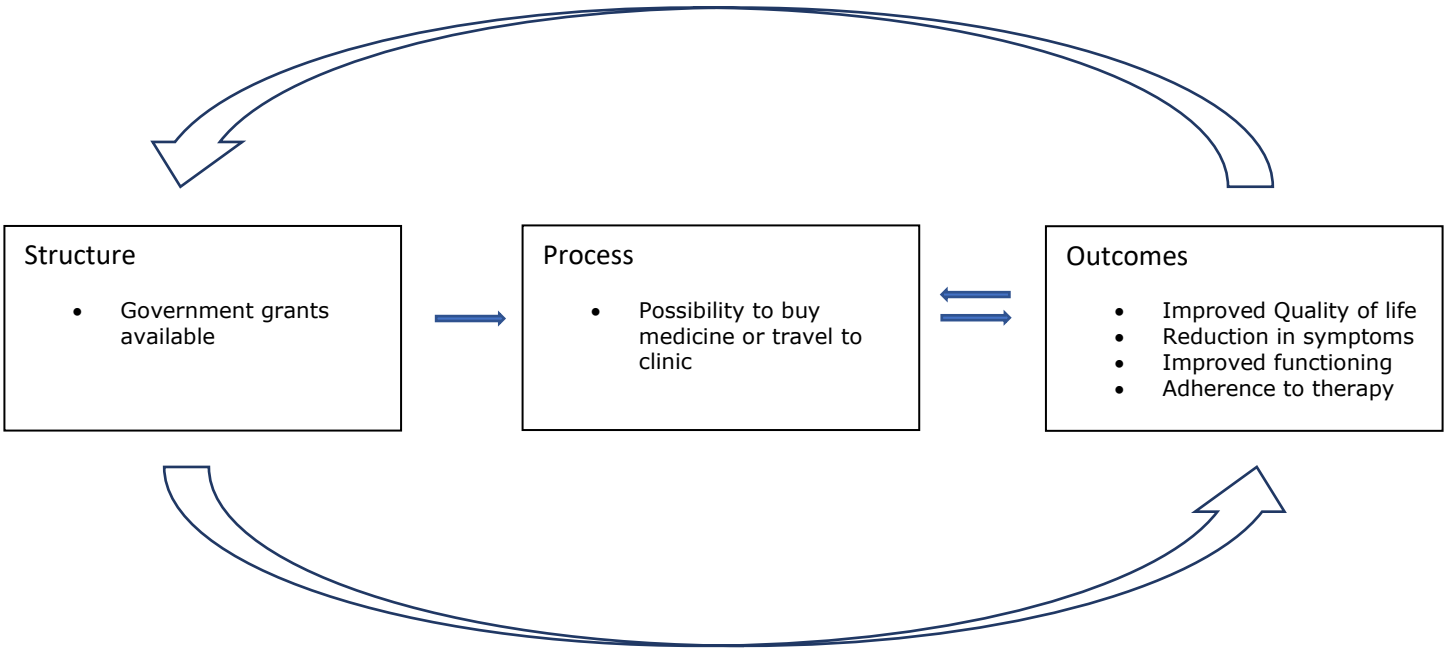
Figure 6c – Example of Donabedian's SPO framework and quality of care for PLHIV with MDD in SA



The complexities that can arise when looking at quality of care is shown in the following example where outcomes influences the structure of care.

Financial grants can improve quality of life in patients, with better adherence to therapy and reduction of symptoms. With reduction of symptoms and improved functioning, patients can lose their rights for government assistance, which in the end can give worse outcomes.

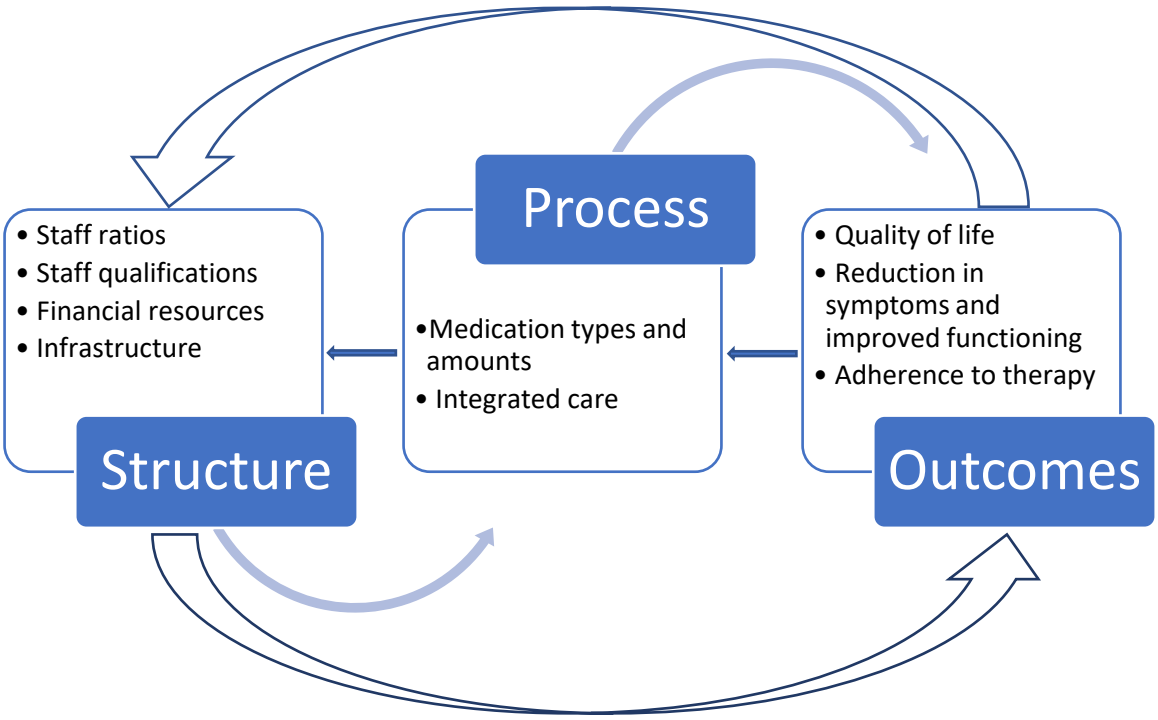
Figure 6d – Example of Donabedian's SPO framework and quality of care for PLHIV with MDD in SA



The Donabedian SPO framework is often explained as a linear model where the structure of care influences the process of care and the structure and process of care influence outcomes. The examples given actually show that quality often includes all three items in the SPO framework and that all items are interacting with each other.

A simplified version of the SPO framework for factors described in this thesis on depressive disorder in PLHIV in SA therefore would look like the following:

Figure 7 – Comprehensive model for Donabedian's SPO framework on quality of care



The interaction of these components needs to be recognized by policymakers and health workers.

Conclusion

In conclusion, depression has been observed to be common in PLHIV in SA. Studies show that the prevalence is at least almost twice as high as in the normal population, but more studies show that prevalence would be around 8-times as high with prevalence numbers of around 30%.

Results for prevalence numbers of MHD in SA seem to be outdated with one of the most cited studies on MHD prevalence in SA presenting data from 2004.

There seem to be many studies that studied depression in PLHIV in SA, but the different screening methods used makes it difficult to compare results. It should be advised that researchers align their study methods and that on the national level clear guidance is given which tools should be used. Aligning study methods will make results more reliable and valuable for this resource constraint setting. Research is needed to look if screening tools can easily be used by lay health workers and if they need to be adapted to the local setting. At this moment, the PHQ-9 and CES-D seem to be the most recommended. The MINI and CIDI are reliable diagnostic tests if performed by a trained person.

Common determinants involved in the risks for MDD in PLHIV are female gender, younger age, poverty, coping styles, associated stigma and lack of support. A lack of support seems to be influenced by family structures and a lack of knowledge on depression in the public. Disease specific determinants in PLHIV are low CD4-count and not being on ART. It is important that healthcare workers are aware of the common determinants involved that increase the risks for depression in this population. Moreover, awareness campaigns in the public should be held to improve the knowledge on depression and MHD. As depression in PLHIV is often influenced by social determinants it is especially important that the health sector and social services work closely together. It is important that studies are performed that include patients and social workers perspectives on quality of care. It is important for policy makers in the provinces to create multidisciplinary teams that involve all stakeholders, including at least healthcare workers, patients, social workers and representatives of employers' organizations. Special attention needs to be given to women and adolescents.

Looking at the quality of care there is a lack of human and financial resources for the care of depression in PLHIV. It is important to create pull factors to involve people in mental healthcare in SA and to prevent mental health workers from leaving the country. Clear budget allocation for mental healthcare provision at the provincial level would be a first step. All provinces should start to collect a minimum set of data on MHD's in their province and use this data for adequate budget allocation. It can be advised to make rural areas more attractive to work as distribution of services now seem to be unequal. Although efforts are made to shift from institutional care to community care this still needs improvement. Financial resources need to be more equally divided between community services and mental health hospitals.

The use of lay health workers is promising, but results show that with the lack of continuous supervision, care provided does not always improve outcomes. Programs using lay health workers therefore need ongoing evaluation and monitoring. One key issue is to train lay health workers in the provision of psychotherapy. Examples from other SSA countries, such as the friendship bench are interesting, and it is recommended that this program is evaluated in the South African context.

More severely affected patients need to be consulted by trained health workers and if psychotropics are considered depression is best treated with SSRI's and SNRI's. Training of nurses and primary care physicians should include treatment of CMD's. Next to that these services should have the availability of consulting more specialised mental health workers. Mapping of mental health institutions and providers in an area can help to find

adequate supervision and possible referral options. Telepsychiatry can be an interesting tool to investigate in areas where resources are scarce.

South Africa is making good progress in integrated care models. A good example is the development of the Ideal clinics where primary healthcare services are provided with tools to integrate care and develop the right infrastructure. Future studies need to be done to look at outcomes and service providers and patients' perspectives. While looking at the care for depression in PLHIV it is important that clinics have enough privacy for clients and that adequate supervision is available. As was shown in an example from the Luthando clinic it is important that mental health workers are trained in non-mental health issues and furthermore that social activities and income generating programmes are available for patients. As treatment of multiple disorders can be complex it is important that lower educated staff feel safe to provide care and that supervision, either on distance, is available.

With the use of integrated care models, it is possible to develop the right infrastructure for patients to treat multiple diseases. When the infrastructure is well developed it saves patients time and money and can improve adherence. Next to that it is important that the right treatment is available.

Recommendations

Policymakers

- Make a quality improvement plan for mental healthcare in PLHIV and depressive disorder The WHO package on Quality improvement for mental health can be used as an example
- Budget allocation for mental health should be clear in every province
- Strategies to shift from institutional care to community care should be improved
- Make sure that continuous evaluation and monitoring of implemented programs is done
- Develop a minimum set of mental health data to be collected by health services

Health workers

- Should be aware of the high burden of MDD in PLHIV
- Health facilities should collect a minimum set of data on mental health
- Continuous and adequate supervision for lay health workers that treat PLHIV and depressive disorder should be available
- Psychiatrists are recommended to look at possibilities for telepsychiatry and distance-based supervision of lay health workers
- Health workers working in HIV services need to be trained in basic mental health issues. Lay health workers need training in the basics of psychotherapy
- The PHQ-9 and CES-D are the most recommended screening tools for depressive disorder in PLHIV
- Map services that provide mental healthcare
- Collaborate with social services and include social activities in the treatment of MDD in PLHIV

Researchers

- More research on quality of mental healthcare is needed
- More research on the evaluation of integrated care models is needed
- Research investigating patients' perceptions on quality of mental healthcare for MDD in PLHIV is needed
- Research investigating social workers perceptions on quality of mental healthcare for MDD in PLHIV are needed
- Align mental health research programs in the country with other researchers
- Create sustainable research programs, meaning; to provide continuous supervision and training for lay health workers that were trained in research programs

Media

- Be involved in campaigns for mental health and depressive disorder

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Appendix 1. Meeting dr. Ebuenyi 06-12-18

"You cannot treat poverty"

On the 6th of December 2018 I had a very interesting meeting with dr. Ikenna Ebuenyi, who is a researcher on mental health at the faculty of Science, Vrije Universiteit Amsterdam, Athena Institute for Research on Innovation and Communication in Health and Life Sciences. His specialisation is on mental health in Sub Saharan Africa and he is author and co-author of several important research papers and reviews on mental health and HIV care. Important recent reviews are:

Ebuenyi I, Taylor C, O'Flynn D, Matthew Prina A, Passchier R, Mayston R. The Impact of co-morbid severe mental illness and HIV upon mental and physical health and social outcomes: a systematic review. AIDS Care. 2018;1–9.[161]

Passchier RV, Abas MA, Ebuenyi ID, Pariante CM. Effectiveness of depression interventions for people living with HIV in Sub-Saharan Africa: A systematic review & meta-analysis of psychological & immunological outcomes. Brain Behav Immun. 2018;73:261–73.[138]

Goal of the meeting was to get expert advice on mental healthcare in Sub Saharan Africa in relation to HIV. We had an informal meeting where we discussed different health issues within mental health care and HIV and dr. Ebuenyi own experiences. Below is a non-structured representation of our conversation.

Question: *How did your interest in mental health start?*
After medical school I started working in the south of Nigeria in a teaching hospital. HIV is very prevalent in this region and I started to work with PLHIV. The first intention was to work for one year in this place, but it became five years. Next to HIV there were also a lot of people with MHD's and there was a lot of data not being used. So, I started working on this. Mental health problems interested me and after my clinical work I did a master in Mental Health in London and started to collaborate with different people.
There are not many people who want to work with HIV and/or mental health. Often the HIV clinics are very crowded and there a lot of people in a small space. That there are a lot of patients means that there is a lot of work to do and people are afraid of being infected with TB as there are many people in a small room. There are not many doctors who want to work with MHD's. It does not pay much, such as obstetrics & gynaecology or surgery. Psychiatrists don't earn much money. There is also a lot of stigma around mental health by doctors and health care providers as well. Doctors and mental health workers often do not know the differences between intellectual disability or MHD's
Next to a lot of people with HIV in the clinic we only had two beds for people with MHD's. And we were a tertiary hospital. This meant we had to send people back home or tell them to look for another clinic, while there is none. This was very difficult and sad.
A problem with the HIV clinic was that all people knew that our building was the HIV clinic and could see the people waiting outside our clinic.

Other signs of stigma?
There are many forms of stigma. If you look at the socio-ecological models. Sometimes there is a lot of stigma from the family or community. A good support from family can really help, but often there is also a lack of support, which is of course difficult.

Do you think that stigma is reduced over the years?
Definitely not. We did a study where we rated stigma or perceived stigma. And within the results (shows preliminary results from a not yet published research paper) you can see that there is still a lot of stigma. People find difficulties in finding a job for instance. As in a lot of countries there is still a man hierarchy a lot of women don't dare to go to a

hospital to seek care for HIV or MHD's, as people might judge them, and it would be hard to find a husband.
For men there are other problems. A lot of times people think about MHD's as a women's disease and if a man has depressive disorder, people would say "man up".
Other signs of stigma are that people with drugs abuse often have psychiatric symptoms and people would say that it is their own fault if they have these symptoms or HIV. This is not right.

Another story is that I was trying to talk with an important organization in Nairobi to talk about mental health for employees. First, they did not want to talk to me and were more interested in cardiovascular disease and diabetes. Until one of the important men in the company committed suicide. Within two weeks they called me to talk about mental health and they were aware of the importance.

Other problems?
Sometimes it is not about the environment or stigma, but it can also be that people do not seek treatment. "The willingness to accept care" is something that is hard to describe, but interesting to investigate. I had a case where I was treating a younger man with HIV. He was doing well, he took his medicine, he had a job, was working and was making something off his life. The older brother of this man, with the same background, did not do so well and was having more issues and was not so adherent. This is interesting to investigate.

What about medication?
For patient's treatment for HIV in Nigeria and in a lot of African countries is for free. But in Africa we often do not have the same or newer medication as you have here. Some of these pharmaceuticals have a lot of side effects. This leads to retention in care or worse outcomes.
For psychiatric medication you often see that not all the medication from the essential drug lists are available or only the cheaper medication like haloperidol are bought. But as this is not used so much a lot of these medicines will expire and are not useful anymore.
We did a meta- analysis on different kinds of therapy and what we concluded is that pharmacological therapy has better effects on depression than psychological therapies. If a person is very sick in the beginning, talking is not so much effective. These people need medicine. Depressive disorder also influences the immune system, but it is sometimes hard to investigate this as often it is only possible to check for the CD4 count and not the viral load. I had one patient with postpartum psychiatric problems. The family did not understand and wanted to take the patient away from the clinic. I convinced the family to try medication for two days and if this did not help, they could take her. I gave antipsychotics and some diazepam. In these first days she slept better and was calmer. When the family saw this, they were more convinced that she could be alright. If I did not start medicine but had provided psychological therapy the family had taken her away.
In Zimbabwe you have support groups, called friendship bench. Here, lay health workers provide support and problem-solving treatment. Peer groups can help, but you often also need medication.
You also see that a lot of the HIV, vertical programmes, will give money for HIV treatment. But if people need extra care, for example, if you need treatment for diabetes, people need to pay. And often people do not have enough money to pay for these medications. Sometimes you also see that drugs, like marihuana, are cheaper than these medicine and people, like younger people, take these drugs more easily. There is a report on how people smoke antiretrovirals to get hallucinating effects.

Do you think lay health workers have enough training to treat mental health problems?
The training is not a problem, but it is often a problem of motivation or how to keep people motivated. Community health workers are taken care of by the district. And often

the reimbursement is very little. Therefore, it is hard to keep them motivated. The training only costs two or three weeks, which is easy, but then it becomes more difficult.

What are your thoughts on how NGO's work together with public hospitals or clinics?
I think this goes well and is not a problem. Sometimes you see that the hospitals wait for donors to give them extra testing material. For instance, with Gene Expert in TB, if the cartridges are out of stock, they wait until they receive new ones from the donors.

Access to care?
Universal health coverage is important. Often you see that mental health is not insured as it is not seen as a disease. Only very little money from the total health budget in countries is spent on mental health care.

Do you think that western countries can also learn something from African countries on mental health?
Often you see that communities take care when there is no health care available. But in the end, it is important that everybody anywhere is treated the same.

What do you think are important needs for PLHIV with comorbid depressive disorder?

PLHIV and comorbid depressive disorder have important social and health needs. The health needs would entail an inclusive/integrated health care that ensures that none of their disease conditions are treated in isolation. This may only be possible in centres/settings where there is universal health coverage.

What would you say are knowledge gaps when reviewing HIV and depressive disorder in Sub Saharan Africa?

The knowledge gaps are dependent on the part of Africa and the specific needs of the individuals. Sub-Saharan Africa is composed of about 54 different countries and about 6 regions. Country and regional differences apply in available knowledge and resources. It is important to consider specific country differences and their health system. There are countries that have made some strides in updating their health system and delivering needed care. These countries are likely to offer better health care experiences for persons with HIV and depressive disorder. Hence, they are likely to have better knowledge and evidence base on the subject compared to countries with deficient health systems.

What kind of recommendation would you give to a government or clinic on how to treat depressive disorder in PLHIV?

The generic recommendation would be for government/clinics to deliver integrated and comprehensive health care for all in need of care. Again, that may be difficult unless there is health care coverage for all. Depending on where the individuals with HIV/depressive disorder exist, the recommendations may also include strategies to improve on socio-economic inclusion.

Appendix 2. Prevalence of MDD in PLHIV in SA

Article	Study Group	%women	Tool	District	Year	Prevalence
Bongogo et al[81]	117 PLHIV	70.1	Zung Self rating	Rustenburg, North West district	2009	Mild 69.2% Moderate 1.7% Severe 0.9%
Breuer et al [55]	269 PLHIV	100	SAMISS	Cape Town, Western Cape		19%
Breuer et al[53]	356 PLHIV	71	MINI	Cape Town, Western Cape		Current Mood disorder 3.3% Past Mood disorder 9.3%
Brittain et al[56]	623 HIV infected pregnant women	100	EPDS	Cape Town, Western Cape	2013-2014	11 % (threshold EPDS 13) 19% (threshold EPDS 10)
Cichowitz et al [72]	136 PLHIV	49	HADS	Johannesburg, Gauteng	2013	33%
Earnshaw et al [63]	250 youth (13-24years) living with HIV	?	Beck Depression Inventory	Soweto, Gauteng	2015-2016	Moderate-Severe 30.3 % (BDI >20 score)
Els et al [69]	100 PLHIV	57	MINI	Bloemfontein, Free State	1999	35%
Freeman et al [68]	900 PLHIV	74	CIDI	5 provinces	Unknown	Minor 29.1% Major 11.1%
Govender et al [52]	156 PLHIV (recent diagnosis)	?	BDI	Durban, Kwazulu-Natal	Unknown	82.8% (within 72 hours after test +) 78.2% (After 6 weeks)
Hughes et al [73]	123 PLHIV (not yet on treatment) at MSF clinic	65	EQ-5D	Khayelitsha, Western Cape		33% of PLHIV prevalence of depression/anxiety
Kagee et al[51]	134 HIV positive adolescents (11-18years old)	58	RCADS	Western Cape	Unknown	5.2%
Kitshoff et al [82]	146 PLHIV	62	CES-D	KwaZulu Natal	2010	62% (CES-D >16)
Leickness et al [74]	1063 PLHIV	60	CES-D	Cape Town, Western Cape	Unknown	30% (CES-D >30)
Moosa et al [76]	62 PLHIV	80	HAMD	Johannesburg, Gauteng	Unknown	52%
Moosa et al [77]	41PLHIV	71	BDI	Johannesburg, Gauteng	Unknown	56% (BDI>10)
Myer et al [61]	465 PLHIV	75	MINI	Cape Town, Western Cape	2004-2005	14%
Nel et al [78]	107 PLHIV	82	BDI-II			40.4% (moderate - severe, BDI-II>20)
Nglazi et al [57]	435 PLHIV (not on ART) vs 468 PLHIV on ART	78	EQ-5D	Cape Town, Western Cape	2007	13.4 % depressive/anxiety (14.5 % ART - vs. 12.4 % ART+)

Nyirenda et al [75]	422 PLHIV (>50 years)	?	CIDI	KwaZulu Natal (rural)	2010	42.4% (22.7% major depressive episode and 19.7% brief depressive episode) in past 12 months
Olley et al [64]	65 PLHIV (recent diagnosis)	78.5	MINI	Cape Town, Western Cape	2002-2003	34.8 % at baseline, 26 % at 6 months follow up
Pappin et al [25]	716 PLHIV (recent diagnosis)	75.7	HADS	Free State	2007-2008	25.4 %
Peltzer et al [79]	607 postnatal HIV + women in 48 primary health care clinics	100	EPDS	Mpumalanga	2008-2009	45.1 % of women described a depressed mood in the postnatal period.
Peltzer et al [80]	663 HIV positive prenatal women (>18 years)	100	EPDS	Mpumalanga		48.7% [95% CI: 44.8, 52.6] of women experienced prenatal depressed mood.
Peltzer et al [67]	143 PLHIV (recently diagnosed)	62.6	CES-D	Mpumalanga	2009-2010	22%
Rane et al [70]	1482 PLHIV	59	PHQ-9	KwaZulu Natal	2013-2016	33% Severe 3 % (PHQ > 14)
Shearer et al [54]	97 PLHIV	61	PHQ-9	Johannesburg, Gauteng	2014	7 % (PHQ>10) Mild 4 % Moderate 3 % Severe 0 %
Spies et al [58]	68 women living with HIV	100	CES-D	Cape Town, Western Cape		19 % (CES-D > 16)
Tuthill et al [71]	58 women prenatal living with HIV	100	PHQ-9	KwaZulu Natal	unknown	moderate 25% (PHQ>10) moderate/ severe 7.4%(PHQ>15) Severe 1.5% (PHQ >20) Postpartum: Mild 32.4% Moderate 11.8% Moderate/Severe 2.9% Severe 0%
West et al [62]	278 adolescents living with HIV (9-19 years)	53.2	CDI	Johannesburg, Gauteng	2013-2016	8 % (17.8% in 16-19-year-old group)
Wong et al [59]	628 prenatal women living with HIV	100	EPDS	Cape Town, Western Cape	2013-2014	11%
Woollett et al [60]	343 adolescents living with HIV (13-19 years old)	52	CDI-S	Johannesburg, Gauteng	unknown (After 2012)	14 %
Wouters et al [65]	716 PLHIV (recent diagnosis)	76	HADS	Free State	unknown (before 2012)	Mild 15.3% Moderate8.8% Severe 1.3 %
Yeji [66]	272 PLHIV (>15 years on ART)	78.7	GHQ-12	KwaZulu Natal (rural)	2007-2008	Estimates from 33% to 38%,

SAMISS: Substance abuse and mental illness symptoms screener, MINI: Mini international neuropsychiatric interview, BDI: Beck depression Inventory, SCID: Structured clinical interview for DSM, CES-D: Center for epidemiological studies-depression, EPDS: Edinburgh postnatal depression scale, HADS: Hospital Anxiety and Depression scale, CIDI: Composite International Diagnostic Interview, RCADS: Revised Child Anxiety and Depression scale, HAMD: Hamilton Depression scale, PHQ-9: Patient health questionairre, CDI: Children's depression inventory, GHQ-12: General health questionnaire

Appendix 3. Factors related to depression in PLHIV in SA

Author	Study Group	District	Determinants associated	No associations found
Andersen 2015 [95]	14 PLHIV	Western Cape	HIV infection	
Bongongo [81]	117 PLHIV	North West	Stavudine, Lamivudine, Efavirenz regimen Not married Unemployment	Female gender Age
Brittain [56]	623 women LHIV	Western Cape	younger age Not married Unplanned pregnancy Stigma Lack of social support	
Burgess 2014 [94]	19 women LHIV	KwaZulu Natal	HIV infection Poverty Violence	
dos Santos [96]	55 health workers and 200 PLHIV	Gauteng	HIV infection Violence	
Earnshaw [63]	250 adolescents LHIV (perinatally infected)	Gauteng	Internalized stigma Stigma	Age Gender Being orphan
Kagee [51]	134 adolescents LHIV	Western Cape		Unemployment
Kitshoff [82]	146 PLHIV	KwaZulu Natal	Unemployment Lower education	Adherence
Leickness [74]	1063 PLHIV	Western Cape	female gender Internalized stigma Lack of social support	
Moosa [77]	41 PLHIV	Gauteng		Gender Age CD4 Count Married Unemployment Educational level
Myer 2009 [101]	4351 PLHIV	National	Bereavement	
Myer 2008 [61]	465 PLHIV	Western Cape	Younger age Adherence Afrikaans speaking	
Nydoo [93]	40 pregnant women LHIV	KwaZulu Natal	Younger age HIV infection (not significant) Unemployment (not significant)	CD 4 count Married Unplanned pregnancy Lower education

Nyirenda [75]	422 PLHIV (>50 years)	KwaZulu Natal	Female gender Receiving government grant Urban residency Bereavement	
Olley 2006 [97]	149 PLHIV	Western Cape	Low CD4 count Disability Negative life events	
Olley [64]	149 PLHIV	Western Cape	Female gender Disability Stigma negative life events *Joining a support group offered protection	Age CD 4 count
Pappin [25]	716 PLHIV (recent diagnosis)	Free State	HIV infection	
Peltzer 2011 [79]	607 postnatal women LHIV	Mpumalanga	Internalized stigma Discrimination Lack of social support	Age Married Unemployment Low education
Peltzer 2016 [80]	663 prenatal women LHIV	Mpumalanga	Unplanned pregnancy Internalized stigma low adherence Unemployment Higher education) Violence	Age Poverty
Petersen 2010 [102]	25 adolescents LHIV	Kwazulu Natal	Poverty Stigma Bereavement	
Ramirez Avilla [98]	1545 PLHIV	Kwazulu Natal	CD4 Count Urban residency	Gender Age Unplanned pregnancy Afrikaans speaking
Rochat 2013 [90]	109 pregnant women LHIV	KwaZulu Natal	HIV infection Unplanned pregnancy Internalized stigma Poverty	
Sharer [88]	1380 adolescents affected by HIV	Mpumalanga and Western Cape	Female gender Older adolescent Rural residency	
Shearer [54]	97 PLHIV	Gauteng	Female gender Younger age Low CD 4 count High viral load	Adherence
Sherr [87]	1024 adolescent LHIV	Eastern Cape	Female gender Being orphan	
Slabbert [86]	127 PLHIV		Female gender	

Sorsdahl [104]	400 PLHIV	Western Cape	Unaware of MDD Stigma	
Spies [108]	429 PLHIV	Western Cape	Afrikaans speaking	Gender Age Education level
Spies 2018 [58]	68 women LHIV	Western Cape	Childhood trauma	Gender Age Low CD4 Count High viral load ART regimen Unemployment Poverty Low education Married/ Not married
West [62]	278 adolescents LHIV	Gauteng	Older adolescent HIV infection Orphan hood Lack of social support	
Wong [59]	628 women LHIV	Western Cape	Younger age Not married Stigma Violence Lack of social support	
Woollett [60]	343 adolescent LHIV	Gauteng	Female gender Disability Violence	Protective to make plans
Wouters [91]	435 PLHIV	Free State	Internalized stigma Avoidant coping style Lower education Stigma Rigid family structure	
Yeji [66]	272 PLHIV	KwaZulu Natal	Female gender (not significant) Avoidant coping style	Age