Barriers to and Facilitators of Integrated Primary Mental Health Care in South Africa

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Abstract

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South Africa faces a staggering burden of syndemic HIV and chronic disease compounded by untreated mental illness. However, only one quarter of South Africans experiencing mental disorder have access to mental health treatment. Integration of mental health treatment into primary care may be an effective way to deliver essential services and improve health outcomes. Primary integration has been shown to cost-effectively improve health outcomes in high-resource settings, though in lower-resource settings the barriers to mental health integration remain largely undefined. Our objective was to identify determinants and potential cost-savings of successful integrated mental health service delivery in South Africa.

The first study used data from patients with at least moderate depressive symptoms receiving care for chronic disease at primary health care facilities in Amajuba District, KwaZulu-Natal, South Africa. We observed whether nurses successfully detected the depressive symptoms and whether they made appropriate referrals. Nurses successfully detected depressive symptoms about half the time and referred under half of patients whose depression they detected. More depressed patients were more likely to be detected but not more likely to be referred once detected.

The second study was guided by the Consolidated Framework for Implementation Research and combined data from interviews and questionnaires with professional nurses at primary health care facilities in Amajuba District, KwaZulu-Natal, South Africa. We used crisp set qualitative comparative analysis to determine whether factors like training and competency were necessary for successful service delivery. Nurses face significant staff shortages, demanding targets, and the expansion of PHC services. Competency was critical for appropriate care. We suggest several strategies to improve service delivery.

The third study analyzed data from a trial of an integrated care model in North West Province, South Africa. Participants were adult patients living with HIV and at least moderate depression. We estimated health care use and expenditure over one year. We found that depressive symptom severity may drive use and cost in this context, and that patients with HIV and depression may be especially likely to suffer catastrophic out-of-pocket medical expense. Integrated care may eventually save health system and patient costs in this setting.

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DEDICATION

For Emily and Ezra.

Chapter 1. Introduction

Mental disorders are the leading causes of disability globally [1], yet in low- and middle-income countries (LMICs) and other low-resource settings, three-quarters of those in need of treatment for mental disorder never receive care [2,3]. To overcome this treatment gap, we need to identify, test, and scale effective mental health services [4,5]. Such services must account for financial resource and workforce shortages and cannot rely exclusively on specialists to deliver mental health interventions [6]. Few LMICs prioritize mental health or have the financial or political capital to develop mental health programs in parallel to other services [7]. Many are also confronted with the growing syndemics of chronic and infectious disease, especially among their most vulnerable populations [8]. In such settings, it will be critical to leverage available resources and the infrastructure of existing community-based and clinical environments to deliver mental health services at scale. Evidence suggests that integration of mental health into routine primary and specialist care services can be cost-effective and equitable, even for low-income patients or patients with co-morbid illness [9]. Integrated care – defined by the World Health Organization as "health services that are managed and delivered so that people receive a continuum of health promotion, disease prevention, diagnosis, treatment, disease-management, rehabilitation and palliative care services, coordinated across the different levels and sites of care within and beyond the health sector, and according to their needs throughout the life course" – may be a promising strategy to increase access to effective mental health services globally [10].

South Africa faces a staggering burden of HIV, chronic disease, and co-morbid mental illness [11-13]. Mental and substance use disorders are the leading causes of disability in South Africa [1]. Rates of common mental disorders (CMDs) like depression, anxiety, and alcohol abuse

are elevated among South Africans living with HIV and other chronic diseases [12-14]; untreated co-morbid CMDs limit the effectiveness of treatments for HIV and other chronic diseases by reducing retention and medication adherence [15,16]. However, only one quarter of people in South Africa experiencing mental disorder receive mental health treatment [17]. Given the paucity of financial and human resources for mental health, most South Africans seek mental health treatment from general medical providers rather than mental health specialists [17]. Integration of effective mental health care into the primary health care (PHC) platform – in line with the South African National Mental Health Policy Framework and Action Plan (2013-2020) [18] – has the potential to reduce the treatment gap and improve associated health outcomes [19].

Preliminary evidence from South Africa suggested that implementation of an integrated care model led to improved PHC provider detection of CMDs and subsequent reductions in depressive symptoms among patients with chronic disease [20]. Professional nurses are at the core of this integrated model [21]. They are responsible for detecting CMDs during routine chronic disease care, offering brief psycho-education, referring patients into appropriate treatment, and managing ongoing care [22,23]. However, even once trained in integrated care, PHC nurses were still able to positively identify only about 16% of patients with depression and 14% of patients with alcohol use disorder [20]. With at least three-quarters of probable CMD cases going undetected, the overall effectiveness of integrated care is threatened.

Nurses and other PHC providers face many barriers to integrating mental health into their activities [24]. In South Africa, such determinants remain critically undefined. Identification and exploration of these barriers to implementation – and any facilitators - will enable targeted refinements to the integrated care model and its implementation strategy [25,26]. Moreover, little is known about the patterns of health service use and expenditure among patients with co-morbid

HIV and depression in this setting, and the potential cost savings associated with integrating care and reducing depression severity have never been estimated. The objectives of this dissertation were threefold. First, we identified patient-level factors that predicted successful detection of depression and referral for depression-related treatment, by PHC-based professional nurses, as part of integrated mental health service delivery in South Africa. Second, we identified barriers to and facilitators of primary depression care at the level of the professional nurses. Third, we characterized health service use and expenditure, and estimated the effects of depression severity on use and expenditure, among patients with co-morbid HIV and depression in South Africa.

Chapter 2. Patient-Level Predictors

2.1 ABSTRACT

Objective: Integration of mental health care into chronic disease services at the primary care level has the potential to reduce the mental health treatment gap and improve associated patient outcomes in low-resource settings. Nurse detection and referral of patients with depression is a key bottleneck limiting the overall effectiveness of integrated care. This study identified patient-level factors that predicted successful detection of depressive symptoms and referral for depression-related treatment, by professional nurses, as part of integrated primary mental health care in KwaZulu-Natal, South Africa.

Design: Cross-sectional analysis of prospective cohort baseline data.

Methods: Participants were adult patients with at least moderate depressive symptoms attending chronic disease services at ten different primary health care facilities. Participants were screened for depressive symptoms and completed a baseline questionnaire prior to undergoing routine assessment and care by a professional nurse. Fieldworkers tracked subsequent service delivery outcomes. Generalized linear mixed effects models were used to estimate associations between patient sociodemographic and clinical characteristics and symptom detection and referral.

Results: Data from 446 participants were analyzed. Nurses successfully detected depressive symptoms in 218 (48.9%, 95% confidence interval [CI]: 44.1, 53.6) participants; of these, they referred 81 (37.2%, 95% CI: 30.7, 43.9) for depression treatment. Depressive symptom severity, alcohol use severity, and perceived stress were all independently associated with detection. The same factors did not predict referral for depression treatment.

Conclusions: Nurses detected and referred patients with depressive symptoms at rates comparable to providers in primary care settings around the world, though substantial gaps persist. Nurses were more likely to detect depressive symptoms among patients in more severe mental distress. Implementation strategies for integrated primary mental health care in low-resource settings may need to incorporate targeted approaches to improve rates of detection and referral.

2.2 INTRODUCTION

An estimated 75% of South Africans experiencing mental disorder never receive any kind of mental health treatment [17]. Common mental disorders (CMDs) like depression, anxiety, and alcohol abuse frequently coexist with the growing syndemics of HIV and other chronic diseases [12-14], and limit the effectiveness of therapies for these physical diseases by reducing medication adherence and retention in care [15,16]. The limited percentage of South Africans with common mental disorders that receive help for their condition are over three times more likely to do so from a general medical provider than from a mental health specialist [17]. Integration of evidence-based mental health care into routine chronic disease services at the primary health care (PHC) level has been advanced by the South African National Mental Health Policy Framework and Action Plan (2013-2020) as an important strategy to reduce the treatment gap and improve associated mental and physical health outcomes [18,19].

Evidence from high-income countries suggests that collaborative models for the integration of mental health care into the PHC platform can be cost-effective and equitable for patients with co-morbid chronic illness [9]. Integrated care models have also demonstrated promising effectiveness in South Africa [21]. PHC-based professional nurses are at the core of the South African model for integrated care: they are responsible for detecting patients with co-morbid

CMDs during routine care for chronic diseases like HIV and hypertension, providing brief psycho-education, referring patients into appropriate mental health treatment, and managing their ongoing care [22,23]. Implementation strategies for this model include nurse training in the use of a national standard clinical decision support tool, outreach and change management workshops with clinic staff, and the addition of in-facility counselling by trained lay counsellors. However, early evidence from this model suggested that, once trained, PHC nurses were able to positively detect only about 16% of patients with depression [20]. Nurse detection and referral of patients with depression and other CMDs is therefore a critical bottleneck threatening the overall effectiveness of integrated care in this context. Professional nurses face unique, multi-level barriers to detecting and referring patients with depression and other CMDs [24]; identification of these barriers will enable targeted refinements to the integrated care model and its implementation strategy [25].

Patient-level predictors to nurse detection and referral are particularly relevant given that integrated care models expect providers to holistically meet the diverse needs of patients with multiple co-morbidities [27]. It is therefore important to understand whether variation in patient sociodemographic characteristics, clinical presentation, and medical history predicts whether PHC nurses are able to successfully detect co-morbid CMDs and make appropriate referrals. Our objective was to identify patient-level factors that predicted successful detection of depressive symptoms and referral for depression-related treatment, by PHC-based professional nurses, as part of integrated mental health service delivery in KwaZulu-Natal, South Africa.

2.3 METHODS

2.3.1 *Conceptual Model*

Our approach was informed by the idea of the depression treatment cascade, that is, among patients in primary care with co-morbid chronic disease and depression, a proportion will be detected as having probable depression by providers; a proportion of those will be referred into appropriate depression treatment; a proportion of those will take up treatment; and a proportion of those will experience remission [28]. Patient losses are thus anticipated at each level of the cascade. By targeting steps with large losses – and modifiable factors that predicted those losses – it is expected that overall rates of depression remission can be improved. This study investigates the first two steps: detection and referral.

2.3.2 *Data Source*

We analyzed baseline data from the prospective cohort of the Southern African Research Consortium for Mental health INTegration (S-MhINT), an implementation study of integrated primary mental health service delivery in South Africa. S-MhINT study methods are described in detail elsewhere, as are the specifics of the integrated care model [22,23]. From April to October 2018, patients attending chronic disease services at ten different PHC facilities in Amajuba District, KwaZulu-Natal, South Africa, were invited to participate in the cohort study. These facilities had been implementing the integrated primary mental health care model since late 2017. Interested patients were given a brief screening tool including assessments of depressive symptoms (PHQ-9) and alcohol use (AUDIT). Both have been validated for use in this setting and population [12,14]. Patients were eligible for enrollment in the cohort if they were at least 18 years old; had the time and ability to complete the baseline interview; and scored ≥ 9 on the PHQ-9 or ≥ 8 on the

AUDIT. Patients were excluded from enrollment if they were unable to provide informed consent (e.g., in case of severe intellectual disability, acute medical issue, or lack of private space). Fieldworkers were trained to make this assessment. Most patients were recruited from the chronic care waiting room, prior to routine assessment and care by the nursing staff. In an effort to increase the sample size of patients who had received a referral for depression treatment, some were recruited post-referral. Patients were only eligible for the current analysis if they scored ≥ 9 on the PHQ-9 and were enrolled in the study prior to the routine assessment by the nurse (that is, their enrollment was not conditional on detection or referral).

Following written informed consent, participants completed a baseline questionnaire in their choice of English or isiZulu. Questionnaire data were collected using tablets. Screening results, cohort enrollment, and questionnaire data were not disclosed to nurses, who assessed and cared for patients as usual. Fieldworkers tracked the mental health-related service delivery outcomes of enrolled patients, including nurse detection of depressive symptoms and referral for depression-related treatment, using nurse-completed checklists and patient records. All study procedures were approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BF190/17) and by the Department of Health of the Province of KwaZulu-Natal.

2.3.3 *Outcomes*

We assessed two outcomes of interest (Table 2.1). The first was detection of depressive symptoms by the nurse, defined as the PHC-based professional nurse noting the depressive symptoms in the patient record or indicating on the checklist that the patient had a probable case of depression. The second was referral for depression-related treatment by the nurse, defined as the nurse completing a referral form for treatment and/or confirmation of diagnosis by a PHC-based physician, district hospital-based psychologist, or PHC-based counsellor. The second

outcome was conditional on the first, as a depression referral could not be made without first detecting the depressive symptoms.

Table 2.1. Questionnaire Measures

Variable	Measure
Predictors:	
Socio-demographics	Self-reported
Healthcare use	Self-reported
Prior chronic disease diagnoses	Self-reported
Assessment of chronic illness care	PACIC [29]
Perceived stress	PSS [30]
Social support	Oslo 3-item [31]
General disability	WHODAS [32]
Depressive symptom severity	PHQ-9 [33]
Alcohol use	AUDIT [34]
Outcomes:	
Detection of depressive symptoms by professional nurse	Checklists and patient records
Referral for depression-related treatment	

Abbreviations: PACIC: Patient Assessment of Care for Chronic Conditions scale. PSS: perceived stress scale. WHODAS: WHO Disability Assessment Schedule. PHQ-9: Patient Health Questionnaire-9. AUDIT: Alcohol Use Disorders Identification Test.

2.3.4 *Predictors*

We examined predictors related to patient socio-demographic characteristics, healthcare use, prior chronic disease diagnoses, assessment of chronic illness care, perceived stress, social support, general disability, and clinical characteristics (Table 2.1). Socio-demographic characteristics were age, sex, race, educational attainment, employment status, income, and self-reported household food insecurity. Healthcare use was measured by self-report of the number of PHC visits and number of hospitalizations in the previous three months. Prior diagnoses were measured by self-report and included depression, HIV, asthma, chronic obstructive pulmonary disease, hypertension, heart disease, stroke, tuberculosis, diabetes, high cholesterol, arthritis, epilepsy, and other chronic and mental disorders. Assessment of prior chronic illness care was measured using the Patient Assessment of Chronic Illness Care (PACIC), which evaluates quality

of care and alignment with the chronic care model (CCM) [29]. Perceived stress was measured using the perceived stress scale (PSS), which assesses the extent to which situations in a person's life are appraised as stressful [30]. Social support was measured using the Oslo 3-items social support scale [31]. General disability was measured with the 12-item interviewer-administered version of the WHO Disability Assessment Schedule (WHODAS), which is a generic assessment instrument for disability for diseases including mental disorders [32]. Clinical characteristics included depressive symptom and alcohol use severity. Depressive symptoms were measured with the PHQ-9, which is aligned with the Diagnostic and Statistical Manual (DSM-IV-TR) diagnostic criteria for major depressive disorder [33]. Scores between 9 and 14 therefore indicated moderate depression, between 15 and 19 indicated moderately severe depression, and between 20 and 27 indicated severe depression. Alcohol use was measured with the AUDIT [34]. All measures have been previously used and found to be valid in South Africa [12,14,35-37].

2.3.5 *Statistical analysis*

Descriptive analyses, including t tests and $\chi 2$ tests, were conducted to summarize and compare participant characteristics stratified by service delivery outcome: not detected vs. detected, and not referred vs. referred. We then used generalized linear mixed effects models to estimate associations between the predictors of interest and the nested service delivery outcomes. Both models used the binomial family and logit link, and included a random facility-specific intercept to adjust for clustering. As a sensitivity test for type II error, parsimonious models with only covariates with adjusted *p*-values < 0.1 were included. Finally, we used the model estimates to calculate and plot the predicted probabilities of detection and referral over the range of PHQ-9 scores observed at screening, with all other covariates at their means [38].

All analyses were performed in Stata and R [39,40].

2.4 RESULTS

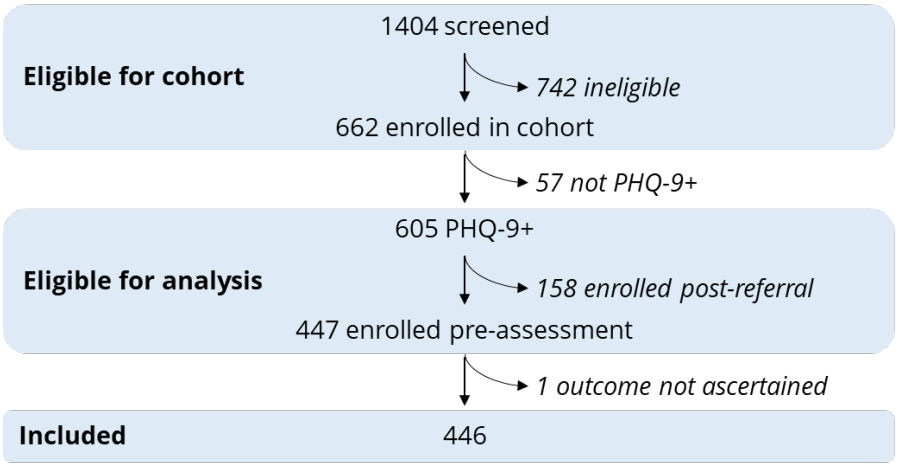


Figure 2.1. Cohort recruitment flow diagram

We screened 1404 patients for study eligibility; 662 patients were eligible for enrollment and recruited into the cohort (Figure 2.1). Six hundred and five participants had PHQ-9 scores ≥ 9, of whom 447 were enrolled prior to nurse assessment and were eligible for this analysis. Service delivery outcomes were ascertained for 446 participants who formed our sample. Overall, nurses detected depressive symptoms in 218 (48.9%, 95% confidence interval [CI]: 44.1, 53.6) participants; of these, they referred 81 (37.2%, 95% CI: 30.7, 43.9) for depression treatment. 18.2% (95% CI: 14.7, 22.1) of all participants were referred for depression treatment. Participants with moderately severe (57.4%, 95% CI: 47.8, 66.6) or severe depressive symptoms (78.0%, 95% CI: 65.3, 87.7) were more likely to be detected compared to participants with moderate depressive symptoms (39.0%, 95% CI: 33.2, 45.0) (Figure 2.2, $p < 0.001$). Among detected participants, participants with moderate (40.6%, 95% CI: 31.1, 50.5), moderately severe (31.8%, 95% CI: 20.9, 44.4) and severe depressive symptoms (37.0%, 95% CI: 23.2, 52.5) were equally likely to be referred for treatment ($p = 0.513$).

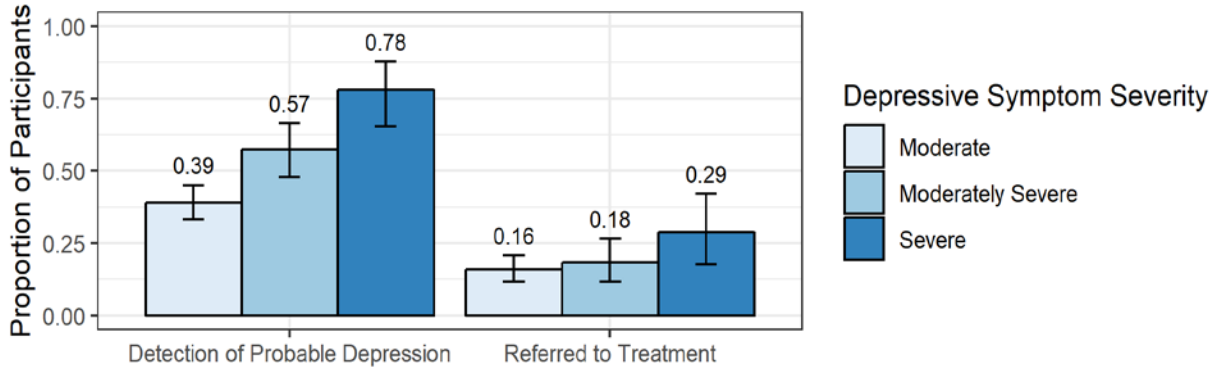


Figure 2.2. Depression care cascade stratified by depressive symptom severity

The mean participant age was 44.6 years (standard deviation [SD]: 13.2) (Table 2.2). The majority were female (80.0%), almost all were Black (99.6%), and few (21.3%) had matriculated from high school. Overall, nearly two-thirds (272, 61.0%) had moderate depressive symptoms, and most (360, 80.7%) had low risk alcohol use. Participants detected as having depression had slightly lower incomes than undetected participants ($p = 0.039$). Few (5.2%) had been hospitalized in the previous three months. The majority had an HIV diagnosis prior to study enrollment (77.5%); detected participants were slightly more likely to have an HIV diagnosis (80.7% vs. 74.3%, $p = 0.035$) and to have reported a prior diagnosis of depression compared to undetected participants (7.3% vs. 3.1%, $p = 0.018$). Participants receiving a referral for depression treatment were less likely than those detected but not referred to have reported a prior diagnosis for a chronic disease other than HIV, hypertension, or diabetes (24.7% vs. 43.1%, $p = 0.002$). Over one-third (39.1%) of all participants reported prior diagnoses of two or more chronic diseases. Almost none were currently taking anti-depressant medication (3, 0.7%). Detected participants detected were more likely than undetected participants to have reported high stress (29.0% vs. 15.6%, $p < 0.001$) and to have reported higher disability (WHODAS score of 0.27 vs 0.22, $p = 0.16$. They also more likely to have severe depressive symptoms (21.1% vs. 5.7%, $p = 0.007$) and to have high-risk and dependent alcohol use (12.4% vs. 2.6%, $p < 0.001$). Participants receiving a referral for depression

treatment were less likely than those detected but not referred to report high social support (8.6% vs. 17.6%, $p < 0.001$).

Regression models suggested that depressive symptom severity, alcohol use severity, and perceived stress were all independently associated with detection by the chronic care nurse (Table 2.3). Specifically, each additional point in PHQ-9 score was associated with a 15% increase in odds of detection (adjusted odds ratio [aOR]: 1.15, 95% CI: 1.08, 1.22), each additional point in AUDIT score was associated with a 4% increase in odds of detection (aOR: 1.04, 95% CI: 1.00, 1.08), and additional point in PSS score was associated with an 10% increase in odds of detection (aOR: 1.10, 95% CI: 1.05, 1.16). No other predictors were independently, statistically significantly associated with detection. In contrast, prior diagnosis of a chronic disease other than HIV or depression was the only predictor significantly associated with referral for depression treatment, conditional on detection (aOR: 0.43, 95% CI: 0.20, 0.94). No other predictors were independently, statistically significantly associated with referral for depression treatment.

Table 2.2. Participant characteristics stratified by detection and referral (n=446)

	Detection			**Referral** (given Detection)			
Factor	Not Detected	Detected	p^1	Not Referred	Referred	p^1	Total
N	228	218		137	81		446
Age, mean (SD)	45.0 (13.7)	44.2 (12.6)	0.57	44.6 (12.6)	43.5 (12.7)	0.47	44.6 (13.2)
Female	188 (82.5%)	169 (77.5%)	0.14	107 (78.1%)	62 (76.5%)	0.79	357 (80.0%)
Black	226 (99.1%)	218 (100.0%)		137 (100.0%)	81 (100.0%)		444 (99.6%)
Matriculated	48 (21.1%)	47 (21.6%)	0.86	32 (23.4%)	15 (18.5%)	0.36	95 (21.3%)
Employed	69 (30.3%)	56 (25.7%)	0.33	38 (27.7%)	18 (22.2%)	0.16	125 (28.0%)
Income > 2000 ZAR/month	79 (34.6%)	60 (27.5%)	**0.039**	40 (29.2%)	20 (24.7%)	0.19	139 (31.2%)
Household food insecurity	93 (41.0%)	102 (46.8%)	0.21	61 (44.5%)	41 (50.6%)	0.38	195 (43.8%)
Healthcare use in previous 3 months							
Other PHC visit	147 (64.5%)	134 (61.5%)	0.71	86 (62.8%)	48 (59.3%)	0.76	281 (63.0%)
Hospitalized	13 (5.7%)	10 (4.6%)	0.36	6 (4.4%)	4 (4.9%)	0.87	23 (5.2%)
Prior diagnoses							
HIV	168 (74.3%)	176 (80.7%)	**0.035**	108 (78.8%)	68 (84.0%)	0.35	344 (77.5%)
Depression	7 (3.1%)	16 (7.3%)	**0.018**	8 (5.8%)	8 (9.9%)	0.48	23 (5.2%)
Hypertension	65 (28.8%)	57 (26.1%)	0.48	41 (29.9%)	16 (19.8%)	0.071	122 (27.5%)
Diabetes	19 (8.4%)	19 (8.7%)	0.86	14 (10.2%)	5 (6.2%)	0.34	38 (8.5%)
Other chronic disease	65 (28.8%)	79 (36.2%)	0.087	59 (43.1%)	20 (24.7%)	**0.002**	144 (32.4%)
Number of chronic disease diagnoses			**0.021**			**0.045**	
0	2 (0.9%)	1 (0.5%)		1 (0.7%)	0 (0.0%)		3 (0.7%)
1	147 (64.8%)	121 (55.5%)		70 (51.1%)	51 (63.0%)		268 (60.2%)
≥2	78 (34.4%)	96 (44.0%)		66 (48.2%)	30 (37.0%)		174 (39.1%)
On depression medication	2 (0.9%)	1 (0.5%)	0.58	0 (0.0%)	1 (1.2%)		3 (0.7%)
PACIC, range: 0-3, mean (SD)	0.43 (0.46)	0.43 (0.48)	0.99	0.41 (0.45)	0.47 (0.53)	0.60	0.43 (0.47)
PSS			**<0.001**			0.80	
Low stress	27 (12.0%)	5 (2.3%)		4 (2.9%)	1 (1.2%)		32 (7.2%)
Moderate stress	163 (72.4%)	149 (68.7%)		92 (67.6%)	57 (70.4%)		312 (70.6%)
High stress	35 (15.6%)	63 (29.0%)		40 (29.4%)	23 (28.4%)		98 (22.2%)

Oslo Social Support			0.23			**<0.001**	
Poor support	95 (42.2%)	109 (50.2%)		60 (44.1%)	49 (60.5%)		204 (46.2%)
Moderate support	84 (37.3%)	77 (35.5%)		52 (38.2%)	25 (30.9%)		161 (36.4%)
Strong support	46 (20.4%)	31 (14.3%)		24 (17.6%)	7 (8.6%)		77 (17.4%)
WHODAS, range: 0-1, mean (SD)	0.22 (0.18)	0.27 (0.19)	**0.016**	0.27 (0.18)	0.28 (0.19)	0.90	0.24 (0.18)
PHQ-9			**0.007**			0.42	
Moderate Depression	166 (72.8%)	106 (48.6%)		63 (46.0%)	43 (53.1%)		272 (61.0%)
Moderately Severe Depression	49 (21.5%)	66 (30.3%)		45 (32.8%)	21 (25.9%)		115 (25.8%)
Severe Depression	13 (5.7%)	46 (21.1%)		29 (21.2%)	17 (21.0%)		59 (13.2%)
AUDIT			**<0.001**			0.074	
Low risk	192 (84.2%)	168 (77.1%)		102 (74.5%)	66 (81.5%)		360 (80.7%)
Risky or hazardous	25 (11.0%)	15 (6.9%)		10 (7.3%)	5 (6.2%)		40 (9.0%)
High-risk or harmful	5 (2.2%)	8 (3.7%)		7 (5.1%)	1 (1.2%)		13 (2.9%)
High-risk and dependent	6 (2.6%)	27 (12.4%)		18 (13.1%)	9 (11.1%)		33 (7.4%)

[1]p-values adjusted for clustering by health facility

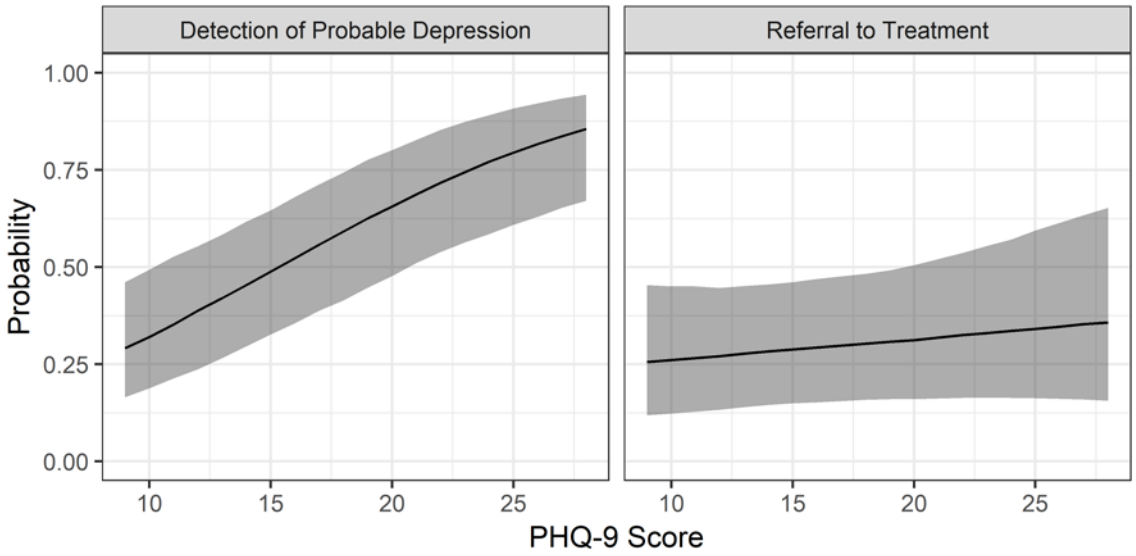
Abbreviations: SD: standard deviation. ZAR: South African Rand. PHC: primary healthcare. PACIC: Patient Assessment of Care for Chronic Conditions scale. PSS: perceived stress scale. WHODAS: WHO Disability Assessment Schedule. PHQ-9: Patient Health Questionnaire-9. AUDIT: Alcohol Use Disorders Identification Test.

Table 2.3. Generalized linear mixed effects model estimates of predictors of detection and referral

	Detected (vs. Not Detected)						**Referred** (vs. Not Referred)					
	Full			*Parsimonious*			*Full*			*Parsimonious*		
Predictors	*aOR*	*95% CI*	*p*	*aOR*	*CI*	*p*	*aOR*	*95% CI*	*p*	*aOR*	*CI*	*p*
(Intercept)	0.01	0.00 – 0.08	**<0.001**	0.01	0.00 – 0.05	**<0.001**	0.09	0.00 – 2.74	0.168	0.54	0.23 – 1.29	0.165
Age, years	1.01	0.98 – 1.03	0.635				1	0.97 – 1.03	0.89			
Female	0.64	0.35 – 1.15	0.136				0.81	0.34 – 1.91	0.626			
Matriculated	1.17	0.65 – 2.12	0.595				1.04	0.44 – 2.46	0.935			
Employed	1.18	0.60 – 2.32	0.641				0.89	0.33 – 2.43	0.827			
Income > 2000 ZAR/month	1.02	0.54 – 1.95	0.945				1.22	0.48 – 3.12	0.678			
Household food insecurity	1.25	0.77 – 2.04	0.361				1.38	0.68 – 2.83	0.375			
Healthcare use in last 3 months												
Other PHC Use	1.08	0.62 – 1.88	0.78				0.84	0.39 – 1.82	0.658			
Hospitalized	0.52	0.19 – 1.43	0.204				0.69	0.15 – 3.18	0.638			
Prior diagnoses												
HIV	1.66	0.82 – 3.36	0.159				0.99	0.37 – 2.70	0.991			
Depression	1.18	0.41 – 3.45	0.758				3.25	0.85 – 12.43	0.084	2.64	0.81 – 8.62	0.107
Other chronic disease	1.53	0.87 – 2.72	0.143				0.43	0.20 – 0.95	**0.036**	0.43	0.23 – 0.81	**0.009**
PACIC Score	1.12	0.62 – 2.00	0.711				1.05	0.44 – 2.49	0.913			
PSS Score	1.10	1.05 – 1.16	**<0.001**	1.10	1.05 – 1.14	**<0.001**	1.04	0.96 – 1.12	0.36			
Oslo Score	0.98	0.88 – 1.08	0.653				1.05	0.90 – 1.23	0.527			
WHODAS Score	0.52	0.08 – 3.35	0.495				1.5	0.10 – 22.75	0.77			
PHQ-9 Score	1.15	1.08 – 1.22	**<0.001**	1.14	1.08 – 1.22	**<0.001**	1.01	0.93 – 1.10	0.776			
AUDIT Score	1.04	1.00 – 1.08	**0.039**	1.05	1.02 – 1.09	**0.002**	1.01	0.97 – 1.05	0.786			
Random Effects												
σ^2			3.29			3.29			3.29			3.29
τ_{00}			0.98 $_{\text{facility}}$			0.90 $_{\text{facilitycode}}$			1.91 $_{\text{facility}}$			1.31 $_{\text{facilitycode}}$
ICC			0.23 $_{\text{facility}}$			0.22 $_{\text{facilitycode}}$			0.37 $_{\text{facility}}$			0.29 $_{\text{facilitycode}}$
Observations			436			442			214			218
Marginal R^2 / Conditional R^2			0.235 / 0.411			0.221 / 0.389			0.073 / 0.414			0.050 / 0.321

Abbreviations: aOR: adjusted odds ratio. CI: confidence interval. ZAR: South African Rand. PHQ-9: Patient Health Questionnaire-9. AUDIT: Alcohol Use Disorders Identification Test. PHC: primary healthcare. PSS: perceived stress scale. WHODAS: WHO Disability Assessment Schedule. ICC: intraclass correlation.

The predicted probability of depressive symptom detection rose from 29.7% (95% CI: 16.6% - 45.0%) at the lowest level of observed depressive symptoms to 84.9% (95% CI: 67.6% - 94.5%) at the highest level, holding all other covariates at their means (Figure 2.3). In contrast, the predicted probability of treatment referral rose from 25.5% (95% CI: 12.1% - 46.6%) at the lowest level of observed depressive symptoms to 35.9% (95% CI: 15.0% - 65.8%) at the highest level, holding all other covariates at their means.



Shaded areas represent 95% prediction intervals.

Figure 2.3. Predicted probability of depression detection and treatment referral by depressive symptom severity

2.5 Discussion

This study is among the first to characterize disparities in depressive symptom detection and referral for treatment, by PHC professional nurses, across patient sociodemographic and clinical characteristics in an LMIC setting. Patients in the sample were mostly Black, low-income women living with HIV experiencing moderate depressive symptoms. Many had two or more chronic disease diagnoses, though few had a prior diagnosis of depression. Nurses successfully

detected depressive symptoms in nearly half of the sample; among those they detected, they referred just over one-third into treatment. Nurses were more likely to detect depressive symptoms in patients with greater depressive symptom severity, alcohol use severity, and perceived stress, independent of other patient-level clinical and socio-demographic characteristics. However, these same factors did not drive referral into treatment.

These results reflect a substantial improvement in the rate of successful nurse detection compared to the rate found by the PRIME evaluation of this model in North West province [20]; indeed, this rate of detection closely matches global findings suggesting that, on average, PHC-based providers correctly detect depression about half of the time [41]. The rate of referral seen in this study also closely matches rates of treatment initiation proximal to mood disorder onset seen in other high- and middle-income settings [42,43]. Still, many patients with depressive symptoms were missed. The overall probability of treatment referral was low even among patients with severe depressive symptoms, suggesting that there may be opportunities to strengthen or hasten implementation of the integrated care model in this setting. Interestingly, though studies in the United States have identified significant disparities across the depression treatment cascade by sex and race [44,45], we found no evidence that sociodemographic characteristics were associated with the likelihood of detection or referral in this context. Nurses in our study appeared to be more focused on clinical characteristics. For example, we found that alcohol use symptoms were positively associated with referral, in contrast with prior findings from other settings [46]. Mental distress was a key predictor of detection but not referral, suggesting that factors other than patient level characteristics may be preventing the referral of patients in need. Future research will need to assess nurse- and facility-level predictors of referral in this context, especially related to the availability and perceived efficacy of evidence-based mental health treatment modalities.

This study had several limitations. First, our small sample size limited our ability to identify statistically significant predictors of referral conditional on detection. Second, our data did not distinguish between referrals to facility-based psychosocial counsellors, physicians, or psychologists. Further investigation is necessary to assess whether depressive symptom severity and other forms of mental distress predict referral to appropriate treatment modalities under a stepped care model [47]. Finally, this analysis did not assess predictors of patient treatment uptake or subsequent remission from depression. There was a limited sample size remaining among patients referred for treatment, and our focus was on nurses as the core of the integrated care model, rather than the accessibility and effectiveness of mental health treatment subsequent to referral. Almost none of the participants in our sample were currently taking anti-depressant medications; this is consistent with other findings from South Africa [48].

Nonetheless, our findings have significant implications for the implementation of integrated, PHC-based mental health care in rural South Africa and other low-resource health systems implementing similar models, including those in Ethiopia, Zimbabwe, Uganda, and Haiti [49-52]. Though rates of detection and referral closely matched those seen in higher-resource settings, the effects of drop-offs in the depression treatment cascade are likely more egregious in this context. Given the paucity of alternative pathways to effective mental health care in this and similar settings [17], patients with undetected or untreated co-morbid depression will likely remain undetected and untreated. Therefore, targeted implementation strategies may be warranted to increase detection and referral rates. For example, brief educational interventions have been shown to improve rates of appropriate nurse detection of and care for depressed patients [53]. Validated screening tools for depression and other CMDs should also be considered for use at patient intake [54]; such tools are widely recommended in systems with appropriate systems for subsequent

diagnosis, treatment, and follow-up [55], and are increasingly available and validated for use in South Africa and other contexts [56].

2.6 CONCLUSION

We assessed the patient-level predictors of nurse detection and referral of patients with co-morbid chronic disease and depressive symptoms in KwaZulu-Natal, South Africa. Results suggest that the establishment of the integrated care model in this health system has led to nurses detecting and referring patients at rates comparable to PHC settings around the world, though substantial gaps persist. Nurses may be specifically targeting patients in more severe mental distress. To ensure that integrated mental health care reaches those who need it, strategies for implementation in low-resource settings may need to incorporate targeted efforts to improve detection and referral rates.

Chapter 3. Nurse-Level Barriers and Facilitators

3.1 Abstract

Objective: Integration of mental health and chronic disease services in primary care could reduce the treatment gap and improve associated health outcomes in low-resource settings. Low rates of nurse identification and referral of patients with depression limit the effectiveness of integrated care; the barriers and facilitators of primary depression care by nurses remain undefined. This study explored barriers to and facilitators of primary depression care, by PHC-based professional nurses, as part of integrated mental health service delivery in KwaZulu-Natal, South Africa.

Design: Mixed methods study incorporating qualitative and quantitative data.

Methods: Data collection, analysis, and interpretation were guided by the Consolidated Framework for Implementation Research (CFIR). Participants were professional nurses at ten different primary health care facilities in Amajuba, KwaZulu-Natal, South Africa. Qualitative data collection involved semi-structured interviews with high- and low-referring nurses targeting specific CFIR constructs. Deductive and inductive coding were used to derive primary themes related to barriers and facilitators. Quantitative data collection involved a structured questionnaire assessing determinants explored in the interviews. Qualitative comparative analysis was used to identify the necessary or sufficient conditions for high and low nurse referral.

Results: Twenty-two nurses were interviewed. Primary themes related to insufficient training, supervision, and competency; low mental health stigma and high emotional burden; limited human and physical resources; high perceived patient need for integrated services; and high intervention acceptability. Sixty-three nurses completed questionnaires. Quantitative results confirmed and

expanded upon the qualitative findings. Competency appeared to be common across nurses appropriately referring patients for depression care.

Conclusions: To promote the success of integrated care in a context of severe staff shortage and over-burdened providers, implementation strategies including direct training, structured supervision, and routine behavioral health screening tools are warranted.

3.2 INTRODUCTION

Mental and substance use disorders are the leading causes of disability in South Africa [1]. Rates of common mental disorders (CMDs) like depression, anxiety, and alcohol abuse are elevated among South Africans living with HIV and other chronic diseases [12-14]; untreated co-morbid CMDs limit the effectiveness of treatments for HIV and other chronic diseases by reducing retention and medication adherence [15,16]. However, only one quarter of people in South Africa experiencing mental disorder receive mental health treatment [17]. Given the paucity of financial and human resources for mental health, the few South Africans seeking mental health treatment visit general medical providers rather than mental health specialists [17]. Integration of effective mental health care into the primary health care (PHC) platform has the potential to reduce the treatment gap and improve associated health outcomes [19]. South Africa has adopted an Integrated Clinical Services Management (ICSM) model to strengthen care for chronic disease – including care for CMDs – through the use of a standardized clinical decision support tool, with the goal of serving the majority of patients at the PHC delivery point [57].

Integration of mental health and chronic disease care at the PHC level has repeatedly been shown to be cost-effective and equitable in high-income settings [9]. Preliminary evidence from South Africa suggested that real-world implementation of an integrated care model led to improved

PHC provider detection of CMDs and subsequent reductions in depressive symptoms among patients with chronic disease [20]. Professional nurses are at the core of this South African model [21]. They function as case managers and are responsible for detecting CMDs during routine chronic disease care, offering brief psycho-education, referring patients into appropriate treatment, and managing ongoing care [22,23]. However, even once trained in this integrated model, PHC nurses were still able to positively identify only about 16% of patients with depression and 14% of patients with alcohol use disorder [20]. With at least three-quarters of probable CMD cases going undetected, the overall effectiveness of the integrated care model is limited.

Nurses and other PHC providers face many barriers to integrating mental services into their activities [24]. Identification and exploration of these barriers will enable targeted refinements to the integrated care model and its implementation strategy [25,26]. In the case of integrated mental health services in South Africa, such provider-level determinants remain critically undefined. There is therefore an urgent need to identify these barriers and facilitators and refine implementation strategies accordingly. Our primary objective was to explore barriers to and facilitators of primary depression care, by PHC-based professional nurses, as part of integrated mental health service delivery in KwaZulu-Natal, South Africa. Our secondary objective was to identify the particular combinations of nurse-level barriers and facilitators that were necessary or sufficient for appropriate referral.

3.3 METHODS

3.3.1 *Theoretical Framework*

Data collection, analysis, and interpretation were guided by the Consolidated Framework for Implementation Research (CFIR), which is a meta-theoretical framework synthesizing the

spectrum of terminologies, definitions, and constructs related to implementation into a set of multi-level determinants of implementation outcomes [58]. The CFIR can be adapted and applied flexibly to identify contextual factors that predict implementation success, with the goal of refining intervention components and implementation strategies [59]. It comprises thirty-nine constructs sorted under five domains: intervention characteristics, outer setting, inner setting, characteristics of individuals, and process.

3.3.2 *Setting*

This was part of the Southern African Research Consortium for Mental health INTegration (S-MhINT), an observational implementation research study aiming to strengthen integrated primary mental health service delivery in South Africa. S-MhINT study methods are described in detail elsewhere, as are the specifics of the integrated care model [22,23]. Most relevant to this study, however, is the idea that professional nurses receive supplemental training in clinical communication skills and enhanced training in the mental health components of the standardized clinical decision support tool [60], and are subsequently responsible for identifying patients with CMDs, assessing severity, making referrals, and managing care. Appropriate referral pathways depend on symptom severity and include PHC physicians and district-level psychologists for severe or complex cases, or newly introduced PHC-based counsellors, who are trained and supervised to deliver individual and group-based counselling in mild and moderate cases [61]. Professional nurses at ten different PHC facilities in Amajuba District, KwaZulu-Natal, South Africa, were invited to participate in the study components outlined below. These facilities had been implementing the integrated care model since late 2017.

3.3.3 *Qualitative Data Collection*

We conducted in-depth, semi-structured interviews with professional nurses. Nurses were sampled purposively. We used routine program data to create a sampling frame of all professional nurses at ten PHC facilities implementing the integrated care model, and counted the chronic care patients referred for depression counselling by each nurse in the previous three months. We stratified nurses as high or low referring, defined as above or below their facility's median volume of depression referrals, and sampled from the high and low referrers within each facility.

Potential participants were recruited at each health facility with approval of their respective facility managers. Interviews were conducted in private rooms once written informed consent was obtained. One to three members of the study team (CK, NM, and DS) conducted each interview following a guide that explicitly drew from CFIR constructs in the Intervention, Individual, Inner Setting, domains and additionally covered: exposure to training and supervision related to integrated mental health care, experience of service delivery, perceived barriers and facilitators to implementation and service delivery, perceived benefits of implementation, and suggestions for modifications to the implementation strategy. Only constructs hypothesized to be relevant were included to limit interview duration [62]. Interviews lasted up to fifty minutes and were digitally audio-recorded with participant permission. Interviews were conducted in English, though participants occasionally switched to isiZulu. All study team members were proficient in isiZulu. Interviews occurred in September 2018.

3.3.4 *Qualitative Data Analysis*

Recorded interviews were transcribed verbatim. Transcripts were analyzed using qualitative content analysis [63]. We started with a publically available codebook containing the

CFIR domains and constructs and their associated definitions [64]. The first author read all transcripts several times to allow for full immersion of the data, and examined the transcripts for patterns, connections, similarities, and points of difference, blinded to the referral outcome. Speech content was coded deductively into specific CFIR constructs where possible. Where speech content did not map to existing CFIR constructs, new codes were created inductively as central concepts emerged and key terms and phrases were identified. Inductive codes and CFIR constructs were grouped into broader themes through a process of constant comparison and axial coding [65,66]. Qualitative analysis was performed using QSR International NVivo 12 [67].

3.3.5 *Quantitative Data Collection*

We then invited professional nurses to completed brief structured questionnaires. All professional nurses at ten PHCs were invited to participate with facility manager approval. S-MhINT fieldworkers conducted questionnaires on tablets in private rooms once written informed consent was obtained. Questionnaires were designed to assess the multi-level barriers and facilitators that had been explored in the qualitative portion of our study. Measures included the 16-item Mental Illness: Clinicians' Attitudes (MICA) scale of mental health-related stigma [68], the 6-item measure of role overload [69], the 4-item Acceptability of Intervention Measure (AIM) [70], and the 12-item Organizational Readiness for Implementing Change (ORIC) [71]. Questionnaires also measured nurse self-reported exposure to in-service training and competency related to the screening, assessment, treatment, and referral of patients with depression, their self-reported rates of depression service delivery, and their perceived barriers to implementation of the integrated model and providing depression care. Table 3.1 summarizes questionnaire measures. Questionnaires lasted up to thirty minutes and were conducted in English. Data collection occurred between January and April 2019.

Table 3.1. Questionnaire Measures

Variable	Measure
Barriers and Facilitators:	
Socio-demographics	Self-reported
Exposure to in-service training related to depression care	Self-reported
Competency related to depression care	Self-reported
Barriers to implementation and service delivery	Self-reported
Mental health stigma	MICA [68]
Role overload	Role Overload Scale [69]
Intervention acceptability	AIM [70]
Facility readiness to implement change	ORIC [71]
Outcome:	
Proportion of patients with depressive symptoms appropriately referred	Self-reported

Abbreviations: MICA: Mental Illness: Clinicians' Attitudes scale. AIM: Acceptability of Intervention Measure. ORIC: Organizational Readiness for Implementing Change.

3.3.6 *Quantitative Data Analysis*

Self-competency, AIM, ORIC, and role overload summary scores were created by averaging respective item responses. Training exposure and MICA scores were created by summing responses, using reverse scoring where necessary. An outcome variable of proportion of patients appropriately referred was created by multiplying self-reported proportions of patients with depressive symptoms screened, then assessed, then referred. Descriptive analyses, including t tests and $\chi 2$ tests, were conducted to summarize and compare participant characteristics stratified by self-reported referral rate (fewer than 100% appropriately referred vs. 100% appropriately referred).

We then used crisp set qualitative comparative analysis (csQCA) to identify the conditions that were necessary or sufficient for self-reported 100% referral, as well as the conditions that were necessary or sufficient for ≤100% referral [72]. csQCA is ideal for the analysis of medium-N sample sizes where the goal is to understand the multiple ways in which explanatory variables come together to reach a given outcome [73]. The first step was to identify the relevant conditions

for the analysis: these were the k=4 factors that were found to vary significantly between 100% and ≤100% referrers (training exposure, competency, intervention acceptability, and organizational readiness), and an additional factor that we hypothesized would interact with the others (role overload). Given high correlation between the two ORIC sub-scales (r = 0.81), these were combined into an overall ORIC score for the csQCA. With k=5 conditions, or 2^5=32 possible condition combinations, we maximized the number of conditions given the risk of limited diversity (i.e. many unpopulated condition combinations, also called logical remainders). The second step was to calibrate the condition and outcome sets by dichotomizing the continuous condition variables as *high* or *low*. Calibration thresholds were set by reviewing response distributions for clear cut-offs or in relation to Likert scale options. For the training exposure score, *high* was defined as complete training exposure and *low* was incomplete exposure. For competency, AIM, and ORIC summary scores, *high* was defined as mean scores indicating overall responses of 'Agree' or 'Strongly Agree' (>4) while *low* was defined as mean scores indicating overall responses of 'Strongly Disagree,' 'Disagree,' or 'Neither' (≤4). Role overload had a bimodal response distribution and the threshold was set between the two peaks. Role overload was then inverted so that *high* role overload was positive, in alignment with the other scores. As a sensitivity analysis, we calibrated conditions above vs. below their median values. The third step was to test for necessity, assessing whether any condition or combination of conditions was a superset of the positive 100% referral or negative ≤100% referral outcomes. Conditions exceeding a minimum consistency threshold of 0.90, coverage threshold of 0.50, and relevance threshold of 0.60 were considered necessary [72]. The fourth step was to construct truth tables listing all possible condition combinations, the numbers of participant cases populating each combination, and the consistency (i.e., proportion of each combination that are 100%-referring). Truth tables were

created for both the positive and negative outcomes. Combinations exceeding a minimum consistency threshold of 0.75 were considered productive of each outcome. Finally, we used Boolean minimization to derive parsimonious solutions incorporating logical remainders (i.e., condition combinations with no populating cases) but excluding contradictory simplifying assumptions (i.e., logical remainders which may be incorporated into parsimonious solutions for both positive and negative outcomes) [74]. These analyses were performed in Stata and R [39,40].

3.3.7 *Ethics*

All study procedures were approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BF190/17), by the Department of Health of the Province of KwaZulu-Natal, and by the Human Subjects Divisions of the University of Washington (STUDY00002331).

3.4 RESULTS

3.4.1 *Qualitative Results*

Table 3.2. Interview participant characteristics (n=22)

	Low Referring	**High Referring**	**Total**
N	12	10	22
Female	12 (100.0%)	9 (90.0%)	21 (95.5%)
Facility Trainer	2 (16.7%)	2 (20.0%)	4 (18.2%)

We interviewed 22 nurses (**Error! Reference source not found.**). This sample was sufficient to achieve data saturation given purposive sampling by referral volume [75]. Almost half of the participants were classified as high referrers (10, 45.5%). Most were female (21, 95.5%), and few were the assigned trainers for their respective facilities (4, 18.2%).

We identified five broad themes. Quotations are cited using the scheme [sex/facility trainer vs. not/high vs. low referring].

3.4.1.1 Training, Supervision, and Competency

This theme aligns with the Access to Knowledge and Information construct under the Inner Setting domain of the CFIR, as well as with the Knowledge and Beliefs about the Intervention, Self-efficacy, and Individual Stage of Change constructs under the Characteristics of Individuals domain. Participants felt that in-service training was an important first step to professional nurses providing appropriate, effective services for patients with depression. High-referring participants were more likely to report high exposure to mental health-related training. However, even high-referrers questioned the reliance on the cascade model of training, wherein facility trainers were expected to train and mentor their peers at the clinic during the workday. Some facility trainers advocated for comprehensive, direct training in skills related to mental health service delivery, noting that they had insufficient time to adequately train their peers:

> I think all the professional nurses… must go through the trainings because it is not so easy to do the trainings at [the] workplace, because we, you know have targets that you have to do and what what… I was suggesting that each and every professional nurse to attend the course.
>
> [F/Master Trainer/High Referring]

Though participants were aware of the mental health-specific training that they had received, most were vague about or unaware of any specific supervision or mentorship they had been offered related to mental health. Some indicated that there had been once-off or occasional visits by district or project-related staff to their facilities in relation to depression care, though few could describe what had been discussed during those visits. Several participants, including both

high- and low-referrers, recommended that mental health-related supervision should be strengthened and made routine in order to promote appropriate service delivery:

> This thing is an ongoing process for somebody who's like, clued in on what is supposed to be done. You need to mentor the other people. You train them, you mentor them at the same time. But now the mentoring part, sort of lacks… So that at least now they come to grips with what is expected.
>
> [F/Master Trainer/Low Referring]

Regardless of the limitations of prior approaches to in-service training and supervision, most participants reported feeling competent and capable of identifying depression in their patients, assessing its severity, making an appropriate referral, and managing care over time. Even low-referring nurses generally stated that they had the necessary skills, referencing pre-service training in primary health care and psychiatric nursing, the utility of the structured decision support tool, and the visibility of depressive symptoms in their patients:

> Using the skills of a psychiatric… we used to manage, we used to manage.
>
> [F/Not Trainer/Low Referring]

3.4.1.2 Mental Health Stigma and Emotional Burden

This theme was inductive, though it aligns with the Other Personal Attributes construct under the Characteristics of Individuals domain of the CFIR. Participants exhibited few stigmatizing attitudes towards patients with depression and other mental disorders, and there were no apparent differences between high- and low-referrers. Instead, many participants emphasized that their goal was to treat their patients in a holistic manner, referencing their role as primary care providers:

> When a patient comes, he or she must be assessed in totality. Spiritually, psychologically, physically… you must nurse the patient as a whole. [F/Not Trainer/Low Referring]

Indeed, rather than stigmatize patients with depression, participants often discussed how closely they empathized with patients in emotional distress, indicating that working with those patients resulted in the surfacing of some of their own personal issues. This made engaging with patients with depression difficult, though in some cases it was also highly motivating. Several participants suggested that for the integrated care model to be successful, nurses in need must first be offered counselling and support:

> But sometimes it's also difficult to me, because the person's problems stay with me, and there's no-one I can talk to, so sometimes I myself have got a headache because of other people's problems. But then I have to help them, no one's helping me, though." [F/Facility Trainer/High Referring]

3.4.1.3 Human and Physical Resources

This theme aligns with the Readiness for Implementation construct and Available Resources sub-construct under the Inner Setting domain of the CFIR, as well as with the External Policies and Incentives construct under the Outer Setting domain. All participants stressed repeatedly that they were working at maximum capacity and that they did not have enough time to see all their patients, meet their service delivery targets, and fill out the necessary paperwork – much less to carefully screen all patients for depression and perform in-depth mental health assessments. High- and low-referrers were equally likely to describe their workload as overwhelming. Several felt that the integration of new services at the PHC level had resulted in them becoming increasingly burdened with tasks, all while they faced a severe staff shortage:

> We're short staffed, we've got to do our targets, we've got to treat our clients, we've got a long queue outside, and the clients complain that someone's in with you for a long time, and you actually have to do everything, everything's got a target. And there's a lot of paperwork that comes with it too.
>
> [F/Facility Trainer/Low Referring]

Even high-referring participants reported struggling to offer appropriate depression care given their workload. Several stated that this was a significant stressor, leading to low self-esteem and symptoms of depression, as they felt they were failing to provide their patients with adequate attention. Participants suspected that they were missing a significant proportion of their clients with depressive symptoms and other mental disorders:

> When will I see that depression that you are talking about? Because I'm rushing, I'm rushing… we must look at the actual workload of each individual, if you need to have the complete, give holistic care… Because we want to, but the pressure of the work, we end up pushing the bench.
>
> [F/Not Trainer/High Referring]

Beyond the nursing staff shortage, participants reported barriers related to the availability of other human and physical resources. Though physicians visited PHC facilities with increasing frequency, district-level psychologists were facing their own staff shortage and did not visit the PHC level. Meanwhile, only one lay psychosocial counsellor had been trained per facility implementing integrated care; when a lay counsellor was sick or was asked to perform other duties in the facility (e.g., driving), as was often the case, participants reported that it became difficult to make appropriate referrals. Limited access to telephones restricted provider ability to follow up

with patients and link them to care. Finally, several participants noted that they were unable to make appropriate referrals when the mental health referral forms ran out.

3.4.1.4 Patient Needs, Barriers, and Facilitators

This theme aligns with the Patient Needs and Resources construct under the Outer Setting domain of the CFIR. Most participants believed that there was a significant burden of untreated depression and other mental disorders in their communities, with some noting that, "stress is everywhere," [F/Not Trainer/Low Referring] or that, "there's a lot of patients that we are missing out there," [F/Facility Trainer/High Referring] and that there was a clear need for integrated mental health care at the PHC level. Participants reported that, given their time constraints, they were more likely to identify depression in patients in obvious distress, rather than those patients requiring careful assessment:

> I can identify the client with depression, especially those who seem to have different moods like mood swings, maybe crying, many of them cries when they have some problems which may need me and finally, says maybe, she or he has depression.
>
> [F/Not Trainer/High Referring]

On the other hand, participants frequently suggested that they were less able to identify depression among patients with low mental health literacy, or among patients who hide their emotional distress, as considerably more consultation time is required to identify such cases:

> For the patients who have got depression, the problem we are getting is from the patient themselves. Because are patients sometimes are not honest, they cannot reveal the whole thing, even if you can see that the person has got a

problem, you need to probe, and probe, and probe.

[F/Not Trainer/Low Referring]

3.4.1.5 Intervention Acceptability and Relative Advantage

This theme aligns with the Relative Advantage, Complexity, and Cost constructs under the Intervention Characteristics Domain. Overall, participants were pleased with the integrated care model. They felt it was improving patient health and that it made sense to deliver services for depression and other CMDs at the PHC level, given that PHC facilities were numerous and accessible at the community level:

> I am satisfied because it is… within the community where the patient lives. It is accessible. There is no transport that is needed to the patient, if the patient feels like coming, the patient has a problem, she needs to come, walking, and find the person to assist the patient.
>
> [F/Not Trainer/Low Referring]

High-referring participants tended to be more expressive and specific in describing the aspects of the integrated care model that they appreciated. For example, some believed that the introduction of mental health services at the PHC level – especially the delivery of so-called "morning talks," or mental health-focused vignettes delivered by lay counsellors to waiting rooms full of patients – had the potential to improve overall patient mental health literacy:

> And another thing that helps us a lot, is the reading of the story. When they hear those stories, you find a lot of them saying hmm I think I've also got this…then they start telling you about their problems.
>
> [F/Not Trainer/High Referring]

Several participants acknowledged that the implementation of the integrated care model came with added cost. In particular, they worried about the additional time required to identify depressive symptoms and other disorders, to assess severity, and to make appropriate referrals. Some recalled initially having a negative attitude towards the model given their full workload. However, several high-referring participants suggested that if implemented well, integrated care could actually save them time and effort in the long run, as they found they were able to treat the underlying problems of patients presenting repeatedly with diffuse symptoms and minimize future patient visits:

> I was so confused that it can help, I just saw an extra, what? An extra work that we were given here in the clinic, on top of this heavy load we are having. But it helps a lot, it helps a lot, now I don't want to lie, it helps.
>
> [F/Not Trainer/High Referring]

3.4.2 *Quantitative Results*

Sixty-three participants completed the questionnaire (Table 3.3). Twenty-four (38.1%) reported that they routinely referred all eligible patients for depression treatment. Most (58, 92.1%) were female and almost all (61, 96.8%) were Black. On average participants had been working as nurses for 21.8 years (standard deviation [SD]: 9.8), and had been at their respective health facilities for 7.7 years (SD: 6.4). Exposure to in-service training related to depression care was high overall (mean: 3.1, SD: 1.3), as was self-reported competency (mean: 4.2, SD: 0.5); 100%-referring nurses had somewhat higher training exposure ($p = 0.066$) and higher competency ($p < 0.001$) than ≤100%-referring nurses. Mental health stigmatization was low to moderate (mean: 40.9, SD: 12.3) and equal across groups. Intervention acceptability (mean: 4.3, SD: 0.6), organizational commitment (mean: 4.1, SD: 0.8), and organizational efficacy (mean: 4.0, SD: 0.8)

were high overall, and higher in the 100%-referring group (p = 0.003, 0.009, and 0.004, respectively). Role overload was moderately high (mean: 3.5, SD: 1.0) and equal across groups. The most frequently reported barriers to providing depression care included insufficient time (39, 61.9%), insufficient training (19, 30.2%), insufficient practice (16, 25.4%), inability to prescribe appropriate medication (15, 23.8%), and insufficient supervision (12, 19.0%).

No conditions or combination of conditions met the minimum thresholds for necessity for the positive 100%-referring or negative ≤100%-referring outcomes. Table 3.4 presents the truth table for the positive, 100%-referring outcome, representing all thirty-two possible combinations of five dichotomized conditions. All but six possible combinations were populated by at least one case; three of the unpopulated logical remainders (9, 11, and 26) were identified as contradictory simplifying assumption and were excluded from subsequent minimization. Four combinations resulted in the 100%-referral outcome among at least 75% of cases. Boolean minimization reduced these four to two parsimonious solutions: 1) incomplete in-service training * high competency * high acceptability * high role overload, and 2) complete in-service training * high competency * high organizational readiness * low role overload (overall coverage = 0.458). High competency related to depression care was therefore observed in both solutions. A supplemental file presents truth tables and results for the negative outcome and alternative calibration sensitivity analyses (Supplemental File: Truth Tables). In the negative outcome truth table, all but eight combinations were populated by at least one case; all eight were considered contradictory simplifying assumptions and were excluded from minimization. Boolean minimization reduced these to six solutions (overall coverage = 0.692); low competency was a factor in four of these. Sensitivity analyses testing the median-value calibration confirmed that high competency was common among solutions leading to high referral.

Table 3.3. Questionnaire participant characteristics stratified by self-reported referral rate (n=63)

Factor	**≤100% Referring**	**100% Referring**	***p***	**Total**
N	39	24		63
Female	34 (87.2%)	24 (100.0%)	0.068	58 (92.1%)
Black	37 (94.9%)	24 (100.0%)	0.26	61 (96.8%)
Married	18 (46.2%)	14 (58.3%)	0.35	32 (50.8%)
Diploma in Nursing	30 (76.9%)	22 (91.7%)	0.13	52 (82.5%)
Years as nurse, mean (SD)	20.2 (9.9)	24.4 (9.2)	0.11	21.8 (9.8)
Years at facility, mean (SD)	7.0 (5.5)	8.8 (7.6)	0.28	7.7 (6.4)
Training summary score, range: 0-4, mean (SD)	2.9 (1.4)	3.5 (0.8)	0.066	3.1 (1.3)
Competency summary score, range: 1-5, mean (SD)	4.0 (0.5)	4.5 (0.4)	<0.001	4.2 (0.5)
MICA, range: 16-96, Cronbach's alpha: 0.76, mean (SD)	41.0 (12.5)	40.6 (12.2)	0.91	40.9 (12.3)
AIM, range: 1-5, Cronbach's alpha: 0.82, mean (SD)	4.1 (0.5)	4.6 (0.5)	0.003	4.3 (0.6)
ORIC				
Commitment, range: 1-5, Cronbach's alpha: 0.86, mean (SD)	3.9 (0.8)	4.4 (0.7)	0.009	4.1 (0.8)
Efficacy, range: 1-5, Cronbach's alpha: 0.95, mean (SD)	3.7 (0.8)	4.3 (0.6)	0.004	4.0 (0.8)
Role Overload, range: 1-5, Cronbach's alpha: 0.83, mean (SD)	3.6 (0.9)	3.5 (1.2)	0.71	3.5 (1.0)

Abbreviations: SD: standard deviation. MICA: Mental Illness: Clinicians' Attitudes scale. AIM: Acceptability of Intervention Measure. ORIC: Organizational Readiness for Implementing Change.

Table 3.4. Truth table for 2^5=32 possible condition combinations, including logical remainders

Combination	Training	Competency	AIM	ORIC	Role Overload	Cases	Consistency	Outcome
1	0	0	0	0	0	5	0	0
2	0	0	0	0	1	4	0	0
3	0	0	0	1	0	1	0	0
4	0	0	0	1	1	3	0.33	0
5	0	0	1	0	0	1	0	0
6	0	0	1	0	1	0	-	?
7	0	0	1	1	0	0	-	?
8	0	0	1	1	1	2	0	0
9	0	1	0	0	0	0	-	?
10	0	1	0	0	1	0	-	?
11	0	1	0	1	0	0	-	?
12	0	1	0	1	1	3	0.33	0
13	0	1	1	0	0	1	1	1
14	0	1	1	0	1	1	0	0
15	0	1	1	1	0	3	1	1
16	0	1	1	1	1	3	0.67	0
17	1	0	0	0	0	1	0	0
18	1	0	0	0	1	2	0	0
19	1	0	0	1	0	3	0.67	0
20	1	0	0	1	1	2	0	0
21	1	0	1	0	0	2	0	0
22	1	0	1	0	1	0	-	?
23	1	0	1	1	0	0	-	?
24	1	0	1	1	1	5	0.2	0
25	1	1	0	0	0	1	0	0
26	1	1	0	0	1	0	-	?
27	1	1	0	1	0	1	0	0
28	1	1	0	1	1	1	1	1
29	1	1	1	0	0	3	0.67	0
30	1	1	1	0	1	1	1	1
31	1	1	1	1	0	8	0.5	0
32	1	1	1	1	1	9	0.56	0

Abbreviations: AIM: Acceptability of Intervention Measure. ORIC: Organizational Readiness for Implementing Change.

3.5 DISCUSSION

We used a novel, theory-driven mixed methods approach to explore the barriers and facilitators of primary depression care as part of real-world implementation of an integrated care model in KwaZulu-Natal, South Africa. Participants were professional nurses at the PHC level; many had over twenty years of nursing experience. Interviewed nurses felt the cascade model of training and the limited approach to supervision were insufficient to build and maintain their competence. Mental health stigma appeared to be uncommon, and untreated emotional issues among nurses may be a barrier to service delivery. Nurses faced significant staff shortages, demanding targets, and the expansion of PHC services; few felt they had the necessary time or resources to appropriately assess patients with depression. However, most recognized the unmet need for mental health services and felt the model had the potential to be effective. Quantitative results confirmed and expanded upon the qualitative findings. Competency appeared to be a critical condition for nurses to appropriately care for patients with depression. Mental health stigma was low to moderate and role overload was moderately high, and neither were associated with self-reported referral rate. Common self-reported barriers to providing depression care, including insufficient time, training, and practice, aligned closely with qualitative findings.

Our results agree with previous studies emphasizing that generalist providers require adequate training, supervision, mentorship, and emotional support to adopt evidence-based mental health services and deliver them with fidelity [76-78]. Though important, initial trainings are not enough [79]: competence only comes from a cycle of learning, doing, and reflecting, guided by supervision and mentorship [80-83]. Without robust supervision, programs risk low intervention fidelity, low clinician competency, and reductions in rates of service delivery [84,85]. Supervision is also an important source of emotional support and burnout prevention; our findings agree with

previous studies suggesting that stress management and debriefing sessions for PHC staff are much needed in this context [86-88]. Programs that train generalists to offer mental health services without first considering their workload and skillset, and without reinforcing their competence through supervision, risk exposing patients to inappropriate treatment [89]. Task-sharing cannot be effective if generalists are overwhelmed with services they cannot provide [90]. Interestingly, though previous studies suggest that South African healthcare providers do perpetuate stigma related to mental disorder [91], we found no relationship between stigmatizing attitudes and reduced referral volume in this sample.

This study had several limitations. First, we recruited a convenience sample of nurses at PHC facilities implementing the integrated care model who were available during data collection periods. We were unable to sample nurses on night duty or nurses on leave. We attempted to minimize this bias by stratifying interview recruitment by referral volume in order to maximize the diversity of our sample, and by sampling sequentially from high and low referrers at each facility. We also invited all available professional nurses to complete the questionnaire. Second, we relied on routine program data to estimate referral volumes for interview sampling stratification. These data allowed us to count depression referrals to in-facility counsellors, though we could not estimate numbers of referrals to physicians and psychologists, nor could we adjust referral volumes for the underlying number of patients with depression seen by each nurse. Third, questionnaire data were de-identified and we could not link questionnaires to observed referral rates; we relied on self-reported referral rates in our quantitative analysis. Nonetheless, our mixed methods approach minimized this limitation by triangulating findings across observed and self-reported data. Moreover, our use of the CFIR to guide data collection and analysis promoted the rigor, replicability, and comparability of the study.

Despite these limitations, our results have substantive implications for the future implementation of integrated care in South Africa and comparable low-resource settings. Direct in-service training and structured, supportive supervision of PHC providers are warranted over a reliance on the cascade model of training and unstructured supervision. Though there is broad recognition that specialist mental health providers can supervise PHC providers to deliver mental health care, these supervisory roles will have to be clearly delineated and compensated [92,93], and there may be insufficient numbers of specialist providers to offer sustained supervision [94,95]. Indeed, integrated care and specialized mental health services face many of the same challenges in low-resource settings, namely: staff shortages, under-spending, and a lack of essential governance, policy, and regulations to support and enforce the provision of high-quality care [6,7]. Given this, additions to nurse workload should be minimized wherever possible. For example, mental health referral forms should be harmonized with the patient file and other routine clinic forms to reduce the burden of new paperwork. Deployment of electronic medical record systems would be a further improvement, and would facilitate measurement-based care by giving providers access to real-time, longitudinal data on patient care and health outcomes. Validated CMD screening tools should be considered for use at patient intake to reduce the burden of nurse case detection and assessment [54]; validated tools are increasingly available in South Africa and other settings [56].

3.6 CONCLUSION

We sampled professional nurses to assess the barriers and facilitators of primary depression care as part of an integrated model in KwaZulu-Natal, South Africa. Results suggest that nurses are motivated to meet the needs of patients with depression and other mental disorders, believing

that integrated services could be effective. However, gaps in training, supervision, and competence persist, and nurses are under-staffed and over-worked. To promote the success of integrated care in this context, implementation strategies including direct training, structured supervision, and routine screening tools are warranted.

Chapter 4. Health Service Use and Expenditure

4.1 ABSTRACT

Objective: Integration of depression and HIV-related care has the potential to reduce the mental health treatment gap and improve associated mental and physical health outcomes, especially in high burden settings like South Africa. Appropriate depression treatment may lower health system costs by reducing service use and expenditure. Our objectives were to characterize health service and medication use and health service expenditure, and estimate the effects of depressive symptom severity on use and expenditure, among patients on anti-retroviral therapy with depressive symptoms in North West Province, South Africa.

Design: Econometric analysis of data from a pragmatic, cluster randomized controlled trial.

Methods: Participants were adult HIV-infected patients on anti-retroviral therapy with at least moderate depressive symptoms attending primary health care (PHC) facilities. Participants were interviewed at baseline, six months, and twelve months post-baseline. Health care use and expenditure were estimated over the twelve months post-baseline using self-report and administrative records. Generalized linear models were used to estimate associations between depressive symptom severity, health service use, and expenditure, adjusting for potential confounders.

Results: Data from 2,002 participants were analyzed. Participants visited PHC/outpatient facilities nearly monthly. Few (95, 4.7%) were hospitalized, and almost none were on second-line anti-retroviral therapy or anti-depressant medication. Almost one-fifth (363, 18.2%) had catastrophic health care expenditure. PHC/outpatient costs were responsible for the greatest proportion of overall expenditure. Higher depressive symptom severity was associated with higher inpatient use

and expenditure, higher medication use and expenditure, and higher total payer and societal expenditures.

Conclusions: Depression severity was associated with health service use and expenditure in this population. This population may be especially vulnerable to catastrophic out-of-pocket spending.

4.2 INTRODUCTION

South Africa faces a staggering burden of HIV and co-morbid depression: 19% percent of South Africans live with HIV [11], and South Africans living with HIV are disproportionately at risk of depression and other common mental disorders [12,13]. Untreated co-morbid depression limits the effectiveness of antiretroviral therapy (ART) by reducing retention and medication adherence [15,16]. Treatment of depression among patients on ART may improve adherence and subsequent HIV-related health outcomes [96], though few in South Africa are able to access and receive mental health treatment, and those that do tend to seek it from primary care providers rather than mental health specialists [17]. Integration of effective depression treatment and other mental health services into primary health care (PHC) therefore has the potential to reduce the treatment gap, improve mental and physical health outcomes, and protect investments in HIV treatment programs [19].

Depression has been repeatedly found to be associated with greater health care use and expenditure among patients with chronic disease in high-income settings, including among patients living with HIV [97], diabetes [98], and congestive heart failure [99]. In low-resource settings, depression may be particularly associated with risk of catastrophic out-of-pocket expenditure [100,101]; out-of-pocket expenditure, including fees for private providers and transport costs, remains a significant barrier to accessing health care in rural South Africa [102].

Integration of effective treatment could therefore lower overall rates of health service use and expenditure, including catastrophic out-of-pocket expenditure, among patients with co-morbid HIV and depression in South Africa and other low- and middle-income countries (LMICs) by reducing depression severity. Such effects have been seen in high-income settings [103].

However, little is known about the patterns of health service use and expenditure among patients with co-morbid HIV and depression in LMIC settings, and the cost savings associated with reducing depression severity have not been estimated. To better understand the potential effects of integrated services for mental health, HIV, and other chronic diseases at the PHC level in South Africa and other LMIC settings, it is important to understand whether integration could save costs to patients and to the health system. Our study objectives were to characterize health service use and expenditure, and to estimate the effects of depressive symptom severity on use and expenditure, among patients with depressive symptoms on ART in North West Province, South Africa.

4.3 METHODS

We analyzed data from the Comorbid Affective Disorders, AIDS/HIV, and Long Term Health (CobALT) study, which was a pragmatic cluster randomized controlled trial that evaluated the effectiveness of a collaborative care model for the detection and management of depression among patients on ART with depressive symptoms attending primary care (PHC) facilities in North West Province, South Africa [23]. Trial and intervention methods are described in detail elsewhere [22,23]. Participants were recruited from PHC waiting rooms in Dr. Kenneth Kaunda District Municipality and Bojanala Platinum District Municipality from April 2015 until December 2016. PHC facilities were public sector clinics providing ART in the two districts. The twenty

largest eligible clinics in each district (40 total) were enrolled and randomized to receive either the collaborative care model or care as usual.

Patients were eligible for the study if they were at least 18 years of age, receiving ART, had at least moderate depressive symptoms (≥9) as indicated the Patient Health Questionnaire-9 (PHQ-9), and gave informed consent. The PHQ-9 has been validated for use with chronic care patients in South Africa [14]. Patients were excluded if they planned to relocate away from the clinic in the next year or were unable to provide informed consent because of illness or psychosis. Patients with suicidal ideation were not excluded but were referred for clinical review. Participants consented to being interviewed at enrollment and at six- and twelve-months post-enrollment, to viral load testing, to abstraction of routine viral load data from the national laboratory database, and to review of clinic and hospital records. Dates of any participant deaths were identified using a national population register. Interviews were conducted in the participant preference of Setswana, English, or Afrikaans.

All study procedures were approved by the University of Cape Town Human Research Ethics Committee (reference number 211/2013), King's College London Research Ethics Office (reference number PNM/12/13-159), the University of Kwazulu-Natal Biomedical Research Ethics Committee (reference 211/2013), and the North West Provincial Department of Health. CobALT was registered under Clinicaltrials.gov number NCT02407691.

4.3.1 *Outcomes*

Two types of outcomes were examined for this analysis. The first related to health service and medication use; these outcomes were derived from interview data collected at baseline, six months, and twelve months post-baseline, and through review of clinical and hospital records. The second related to health services expenditure; these outcomes were derived by combining the

health services and medication use outcomes with relevant unit cost estimates, and by summing to create category-specific and total expenditure estimates. All outcomes were estimated over a standardized twelve-month period post-baseline. All outcomes are defined in Table 4.1.

Table 4.1. Summary of outcome measures

Type	**Outcome**	**Definition**	**Data Sources**	**Notes**
Health service and medication use	PHC/outpatient use	Estimated total number of PHC/outpatient visits over 12 months post-baseline.	Participant self-report at baseline and 12 months.	Includes visits to index PHC, other PHCs, and outpatient facilities. Includes one visit per study interview completed.
	Inpatient use	Estimated total number of nights hospitalized over 12 months post-baseline.	Hospital records.	
	Private provider use	Estimated total number of private provider visits over 12 months post-baseline.	Participant self-report at baseline and 12 months.	Includes visits to GP, private pharmacy, traditional healer, and other health facilities.
	Second-line ART use	Any second-line ART use over 12 months post-baseline.	Participant self-report at baseline and 12 months.	Includes use of Aluvia.
	Anti-depressant use	Any anti-depressant use over 12 months post-baseline.	Participant self-report at baseline, 6 months, and 12 months.	Includes use of Amitryptiline, Fluoxetine, Citalopram, Imipramine, Clomipramine, Dothiepin, Mianserin, or Venlafaxine.
Health service expenditure	PHC/outpatient expenditure	Estimated total payer expenditures related to PHC/outpatient visits over 12 months post-baseline.	Participant self-report at baseline and 12 months, viral load records, unit costs.	Includes costs associated with PHC/outpatient visits, ambulance rides to PHC/outpatient facilities, and viral loads.

Inpatient expenditure	Estimated total payer expenditures related to hospitalization over 12 months post-baseline.	Hospital records, unit costs.	Includes costs associated with nights hospitalized and ambulance rides to hospital.
Medication expenditure	Estimated total payer expenditures related to medication (ART and anti-depressant) use over 12 months post-baseline.	Participant self-report at baseline, 6 months, and 12 months, unit costs.	Includes costs associated with estimated days on ART and days on anti-depressants.
Out-of-pocket expenditure	Estimated total out-of-pocket health care expenditures over 12 months post-baseline.	Participant self-report at baseline, 6 months, and 12 months, unit costs.	Includes costs associated with fees, travel fare, and/or private vehicle use to all estimated health care visits.
Catastrophic health care expenditure	Estimated out-of-pocket expenditure ≥40% of estimated annual household income.	Participant self-report at baseline.	Includes income from employment and social grants.
Payer expenditure	Estimated total payer health care expenditures over 12 months post-baseline.	As above.	Sum of PHC/outpatient, inpatient, and medication expenditures.
Societal expenditure	Estimated total societal health care expenditures over 12 months post-baseline.	As above.	Sum of out-of-pocket and payer expenditures.

4.3.1.1 Health Service and Medication Use

Health service use outcomes included the estimated number of visits to a PHC or outpatient facility over the twelve months post-baseline, the number of nights hospitalized, and the number of visits to a private provider (e.g., general practitioner [GP], private pharmacy, or traditional healer). Medication use outcomes included whether participants reported using a second-line ART

at any point over the twelve months post-baseline and whether they reported using anti-depressant medications at any point over the twelve months post-baseline.

4.3.1.2 Health Service Expenditures

Health service expenditure outcomes included the estimated total cost to provide PHC/outpatient care over the twelve months post-baseline, the estimated total cost to provide inpatient care, the estimated total cost of medication use, and the estimated total patient out-of-pocket expenditure. Catastrophic expenditure was defined as total out-of-pocket expenditure ≥ 40% of the estimated household annual income [104]. Estimated total payer (i.e., South African DOH) expenditure was calculated by summing the total PHC/outpatient, inpatient, and medication expenditures. Estimated total societal (i.e., DOH and patient) expenditure was calculated by summing total payer and out-of-pocket expenditures.

4.3.2 *Outcome Variable Estimation*

Total visits to PHC/outpatient facilities and private providers over the twelve months post-baseline were estimated using participant self-reported number of visits to respective facilities and providers over the three months pre-baseline and three months pre-endline. For participants who completed interviews at baseline and endline, total visits were mean-imputed using the baseline and endline self-report data. For participants who were lost-to-follow-up, total visits were forward-imputed using baseline data over the twelve-month period. For deceased participants, total visits were forward-imputed over the period until death. Total days on each medication were similarly estimated using participant self-reported medication use at baseline, six months (anti-depressants only), and twelve months post-baseline. Total days on each medication were mean imputed over

study periods with complete data, and forward-imputed over relevant time periods in cases of loss-to-follow-up or death.

Category-specific health expenditures were estimated by multiplying the estimated use of each service, calculated above, by unit costs derived from the literature (Supplemental File: Unit Costs), and by summing over the relevant health services. For example, out-of-pocket expenditure for private GP visits was estimated by taking the sum of each participant's estimated total number of GP visits and multiplying by the self-reported fee per visit, the self-reported round-trip travel fare per visit, and/or the estimated cost to drive a private vehicle to those visits. Cost to drive a private vehicle was estimated by multiplying the self-reported total round-trip distance, in kilometers, by the mean unit cost to drive a private vehicle, per kilometer, in South Africa. Cost estimates came from South Africa's database of medicine prices, the South African Revenue Service, the National Health Laboratory Service price list, and other sources. All unit costs were inflation-adjusted to 2017 and are represented in South African Rand.

4.3.3 *Predictor*

The predictor of interest was depressive symptom severity at baseline, measured using the PHQ-9 [105]. The Setswana version of the PHQ-9 has been validated for use in this context [14]. PHQ-9 items were summed assuming equal weighting to yield a score ranging from 0 to 27. Higher scores indicated greater depressive symptom severity. Validation data indicated that a threshold of 9, rather than the common threshold of 10, was appropriate for detecting moderate depression in this population. Scores between 9 and 14 therefore indicated moderate depression, between 15 and 19 indicated moderately severe depression, and between 20 and 27 indicated severe depression.

4.3.4 *Covariates*

Covariates were chosen to account for potential observed confounding and as exploratory predictors of health service use and expenditure. These included viral suppression at baseline (<400 HIV-1 RNA copies/mL), index PHC facility CobALT study arm (binary), sex (female or male, binary), ethnicity (Black or non-Black, binary), at least high school-educated (binary), employed at baseline (binary), and total estimated household income at baseline (continuous).

4.3.5 *Analysis*

Descriptive analyses, including univariate multinomial logit regression models adjusting for clustering by health facility, were conducted to summarize and compare participant characteristics and outcomes, stratified by depressive symptom severity at baseline. We then used generalized linear mixed effects models to estimate adjusted associations between the predictor and covariates of interest and the health service use and expenditure outcomes. For binary outcomes (e.g., second-line ART use, anti-depressant use, catastrophic expenditure), models used the binomial family and logit link. However, most health service use and expenditure outcomes were severely right-skewed, and several outcomes (e.g., inpatient use and expenditure) had large fractions of zeroes; both issues are common with health service use and expenditure data [106]. We used negative binomial regression for health service use count outcomes without zeroes, given over-dispersion. For expenditure outcomes without zeroes, we used the Modified Park test to assess the relationship between the sample mean and variance and establish the preferred probability distribution; we then used the Pregibon Link and Modified Hosmer-Lemeshow tests to assess link function fit [107]. The gamma distribution and log link were preferred for all expenditure outcomes. For both service use and expenditure outcomes with large fractions of

zeroes, we used two-part models, first estimating the probability of any use or cost using binomial/logit models, and then proceeding to estimate the actual, non-zero use or cost using negative binomial or gamma/log models as above. All models included a random facility-specific intercept to adjust for clustering. Lastly, we used the model estimates to calculate and plot the predicted PHC/outpatient, inpatient, medication, and out-of-pocket expenditures over the range of PHQ-9 scores observed at screening, among virally suppressed and non-suppressed participants, with all other covariates held at their means [38]. Two-part model estimates were combined by multiplying predicted probabilities of any use/expenditure by predicted mean non-zero use/expenditure.

All analyses were performed in Stata and R [39,40].

4.4 RESULTS

Two-thousand and two participants were enrolled in CobALT. Table 4.2 summarizes participant characteristics, health service use, and estimated expenditure, stratified by depressive symptom severity at baseline. Mean age was 41.9 years (SD: 10.8). Most participants (1637, 81.8%) were women, and almost all (1948, 97.8%) were Black. Educational attainment and employment were low: 55.2% had attended any high school and 26.7% were employed. Participants with more severe depression were slightly less likely to report being employed (p = 0.005). Most participants were virally suppressed (1519, 81.0%); more severely depressed patients were not significantly less likely to be suppressed (p = 0.093). Forty-six (2.3%) participants died over the twelve months post-baseline.

On average, participants visited a PHC or outpatient facility 10.9 (standard deviation [SD]: 5.4) times over the twelve months post-baseline. Few participants (95, 4.7%) were hospitalized;

among those who were hospitalized, median inpatient use was 7 nights (inter-quartile range [IQR]: 3-15). Few sought out any private care (250, 12.5%). Almost no participants were on second-line ART (27, 1.3%) or anti-depressant medication (33, 1.6%); more depressed participants were more likely to be on anti-depressants than less depressed participants ($p < 0.001$). Inpatient expenditure, though rare, tended to be much greater (mean: 17,514.50 South African Rand [ZAR], SD: 23,181.40, given >0 expenditure) than PHC/outpatient, medication, or out-of-pocket expenditure. Though being on ART was a criteria for trial enrollment, 67 (3.3%) participants reported no ART or anti-depressant use and therefore had no estimated medication expenditure. More depressed participants had higher probability of any medication expenditure ($p = 0.004$). Just over half of all participants had any out-of-pocket expenditure (1024, 51.1%). Almost one-fifth (363, 18.2%) of participants were estimated to have had catastrophic health care expenditure over the twelve months post-baseline. More depressed participants had slightly higher payer and societal expenditures than less depressed participants, though these differences were not statistically significant ($p = 0.061$ and 0.071, respectively).

Table 4.2. Participant characteristics, service and medication use, and expenditure, stratified by depressive symptom severity (n=2002)

			Depressive Symptom Severity				
		Missing	**Moderate**	**Moderately Severe**	**Severe**	***p*[2]**	**Overall**
	N		1302	497	203		2002
Socio-demographic and clinical	Intervention Arm	0	667 (51.2%)	254 (51.1%)	87 (42.9%)	0.36	1008 (50.3%)
	Dr. Kenneth Kaunda District	0	630 (48.4%)	264 (53.1%)	112 (55.2%)	0.59	1006 (50.2%)
	Age, mean (SD)	0	41.6 (10.8)	42.4 (10.5)	42.5 (11.3)	0.54	41.9 (10.8)
	Female	0	1047 (80.4%)	419 (84.3%)	171 (84.2%)	0.13	1637 (81.8%)
	Black	11	1263 (97.7%)	486 (98.2%)	199 (98.0%)	0.77	1948 (97.8%)
	High school-educated	11	735 (56.8%)	266 (53.7%)	99 (48.8%)	0.25	1100 (55.2%)
	Employed	11	369 (28.5%)	118 (23.8%)	44 (21.7%)	0.005	531 (26.7%)
	Household annual income (ZAR), mean (SD)	11	13300.3 (21994.1)	11389.0 (17529.6)	10740.9 (17620.1)	0.21	12564.2 (20564.5)
	Virally suppressed (< 400 copies/mL)	126	1007 (82.2%)	365 (79.0%)	147 (77.8%)	0.093	1519 (81.0%)
	Died	0	32 (2.5%)	9 (1.8%)	5 (2.5%)	0.70	46 (2.3%)
Health service and medication use	Total PHC/outpatient visits, mean (SD)	0	10.7 (5.4)	10.9 (5.3)	11.7 (5.1)	0.29	10.9 (5.4)
	Any nights hospitalized	0	50 (3.8%)	32 (6.4%)	13 (6.4%)	0.028	95 (4.7%)
	Total nights hospitalized, mean (SD)[1]	0	13.0 (13.8)	18.3 (53.2)	15.0 (20.6)	0.71	15.1 (33.1)
	Any private provider visits	0	151 (11.6%)	72 (14.5%)	27 (13.3%)	0.41	250 (12.5%)
	Total private provider visits, mean (SD)[1]	0	3.1 (2.2)	3.1 (2.2)	2.9 (1.2)	0.48	3.1 (2.1)
	Second-line ART use	0	13 (1.0%)	10 (2.0%)	4 (2.0%)	0.030	27 (1.3%)
	Anti-depressant use	0	11 (0.8%)	11 (2.2%)	11 (5.4%)	0.002	33 (1.6%)
Health service expenditure	Total PHC/outpatient expenditure, mean (SD)	0	2119.8 (763.5)	2170.2 (817.2)	2232.6 (721.8)	0.18	2143.8 (773.6)
	Any inpatient expenditure	0	66 (5.1%)	39 (7.8%)	14 (6.9%)	0.040	119 (5.9%)
	Total inpatient expenditure, mean (SD)[1]	0	17354.4 (21990.8)	15666.6 (21710.5)	23417.4 (32156.9)	0.66	17514.5 (23181.4)

Any medication expenditure	0	1248 (95.9%)	489 (98.4%)	198 (97.5%)	0.004	1935 (96.7%)
Total medication expenditure, mean (SD)[1]	0	807.5 (1499.5)	995.8 (1885.6)	1045.2 (1917.2)	0.096	879.4 (1652.5)
Any out-of-pocket expenditure	0	682 (52.4%)	242 (48.7%)	100 (49.3%)	0.60	1024 (51.1%)
Total out-of-pocket expenditure, mean (SD)[1]	0	376.9 (632.8)	426.3 (574.0)	390.9 (604.8)	0.44	390.0 (616.4)
Catastrophic health care expenditure	11	235 (18.2%)	90 (18.2%)	38 (18.7%)	0.97	363 (18.2%)
Total payer expenditure, mean (SD)	0	3773.5 (6455.2)	4379.4 (7800.9)	4867.0 (10324.6)	0.061	4034.8 (7285.7)
Total societal expenditure, mean (SD)	0	3971.0 (6496.1)	4586.9 (7824.3)	5059.6 (10576.0)	0.071	4234.3 (7351.8)

[1]Statistics for these variables are presented for participants with >0 estimated use or expenditure.
[2]p-values adjusted for clustering by health facility
Note: all expenditures are presented in South African Rand (2017).
Abbreviations: SD: standard deviation. ZAR: South African Rand.

Figure 4.1 presents average proportions of overall societal health expenditure by expenditure type and category of depressive symptom severity. Costs due to PHC/outpatient visits made up the greatest proportion of overall expenditure, followed by inpatient costs, medication, and out-of-pocket costs. Inpatient visits drove a larger proportion of overall costs among more depressed patients (32% among participants with severe depressive symptom severity vs. 22% among participants with moderate severity), and PHC/outpatient costs were correspondingly a less of overall costs among more depressed patients (44% among participants with severe depressive symptom severity vs. 53% among participants with moderate severity).

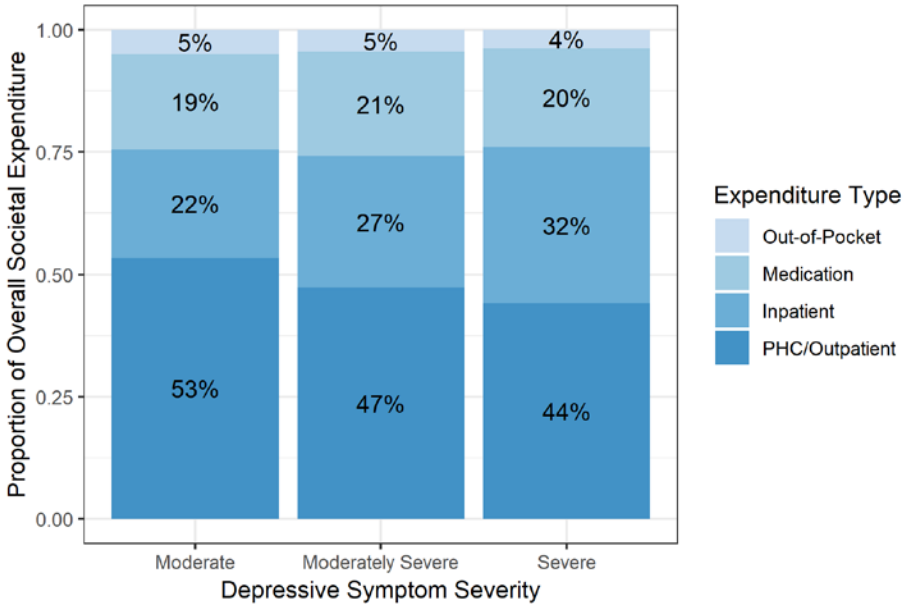


Figure 4.1. Proportion of overall health expenditure by type and depressive symptom severity

Table 4.3 presents summary estimates from generalized linear models assessing associations between depression symptom severity and health service use and expenditure, adjusting for viral suppression and other covariates listed above. Only associations between depressive symptom severity, viral suppression, and each outcome are presented in Table 4.3. Complete model estimates are presented in a supplemental file (Supplemental File: Use and

Expenditure Model Estimates). Among health service and medication use outcomes, these models suggested that increased depressive symptom severity was associated with increased probability of inpatient use (odds ratio [OR]: 1.06, 95% confidence interval [CI]: 1.01 – 1.12) and with increased probability of anti-depressant use (OR: 1.20, 95% CI: 1.11 – 1.29). Meanwhile, viral suppression was associated only with a decrease in probability of second-line ART use (OR: 0.15, 95% CI: 0.07 – 0.35). Among health service expenditure outcomes, the models suggested that increased depressive symptom severity was associated with increased total inpatient expenditure, given any inpatient expenditure (MR: 1.06, 95% CI: 1.00 – 1.13), with increased total medication expenditure, given any medication expenditure (MR: 1.02, 95% CI: 1.00 – 1.03), and with increased total payer (MR: 1.02, 95% CI: 1.00 – 1.03), and societal expenditures (MR: 1.02, 95% CI: 1.00 – 1.03). Meanwhile, viral suppression was associated with increased probability of any medication expenditure (OR: 2.02, 95% CI: 1.07-3.84) and with decreased total medication expenditure, given any medication expenditure (MR: 0.80, 95% CI: 0.69 – 0.92).

Table 4.3. Adjusted estimates of association between depression severity, viral suppression, and health service use and expenditure outcomes

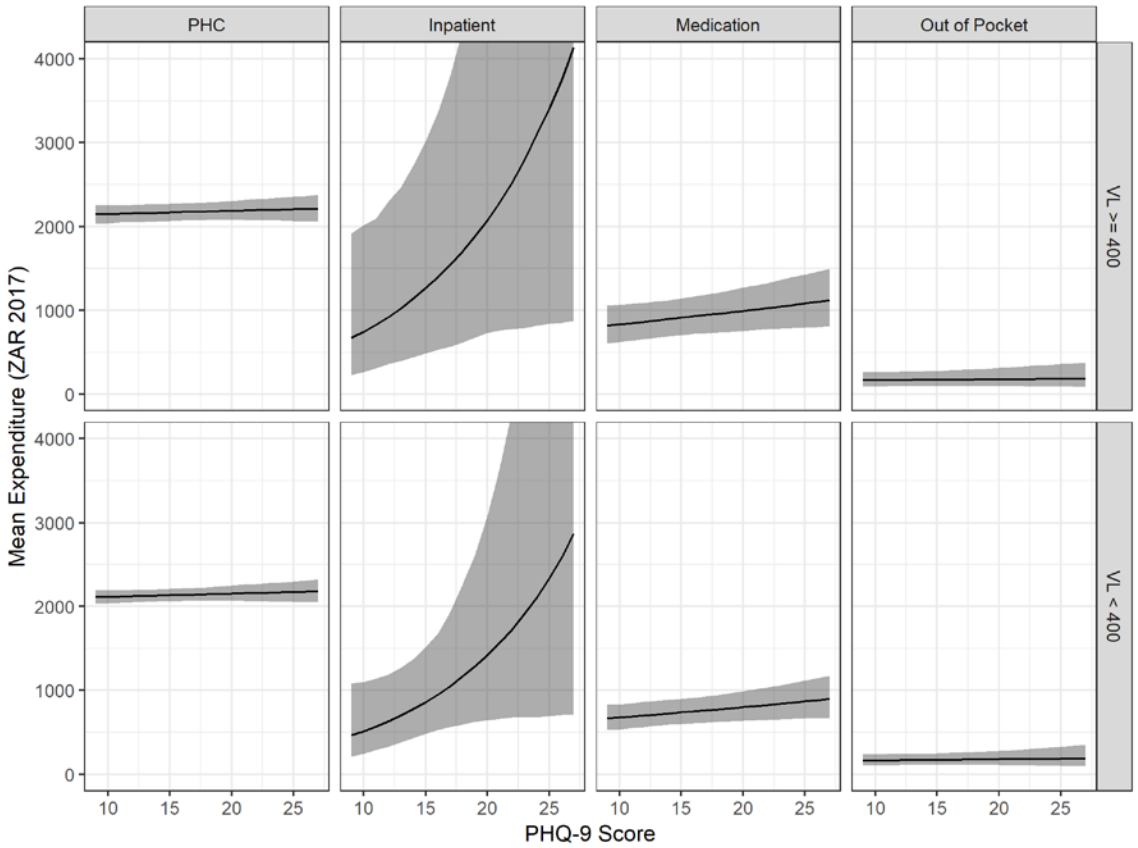
	Outcome		**Predictor**	
			PHQ-9	**VL < 400**
Health service and medication use	**PHC/outpatient use**	*MR*	1.00	1.03
		95% CI	1.00 – 1.01	0.98 – 1.08
		p	0.365	0.204
	Any inpatient use	*OR*	1.06	0.81
		95% CI	1.01 – 1.12	0.48 – 1.35
		p	**0.016**	0.422
	Total inpatient use (>0)	*MR*	1.05	1.16
		95% CI	1.00 – 1.11	0.68 – 1.99
		p	0.067	0.589
	Any private provider use	*OR*	1.04	1.34
		95% CI	1.00 – 1.07	0.90 – 2.00
		p	0.054	0.146
	Total private provider use (>0)	*MR*	1.00	1.18
		95% CI	0.98 – 1.02	0.92 – 1.52
		p	0.945	0.188

	Second-line ART use	*OR*	1.05	0.15
		95% CI	0.95 – 1.15	0.07 – 0.35
		p	0.332	**<0.001**
	Anti-depressant use	*OR*	1.20	1.61
		95% CI	1.11 – 1.29	0.54 – 4.75
		p	**<0.001**	0.392
Health service expenditure	**Total PHC/outpatient expenditure**	*MR*	1.00	0.99
		95% CI	1.00 – 1.01	0.95 – 1.02
		p	0.368	0.468
	Any inpatient expenditure	*OR*	1.04	0.74
		95% CI	1.00 – 1.09	0.47 – 1.17
		p	0.075	0.200
	Total inpatient expenditure (>0)	*MR*	1.06	0.92
		95% CI	1.00 – 1.13	0.51 – 1.66
		p	**0.048**	0.791
	Any medication expenditure	*OR*	1.08	2.02
		95% CI	0.99 – 1.17	1.07 – 3.84
		p	0.069	**0.031**
	Total medication expenditure (>0)	*MR*	1.02	0.80
		95% CI	1.00 – 1.03	0.69 – 0.92
		p	**0.036**	**0.002**
	Any out-of-pocket expenditure	*OR*	0.98	1.11
		95% CI	0.96 – 1.01	0.84 – 1.46
		p	0.244	0.465
	Total out-of-pocket expenditure (>0)	*MR*	1.02	0.94
		95% CI	0.99 – 1.04	0.75 – 1.19
		p	0.151	0.621
	Catastrophic expenditure	*OR*	0.98	1.31
		95% CI	0.93 – 1.02	0.85 – 2.03
		p	0.322	0.222
	Total payer expenditure	*MR*	1.02	0.91
		95% CI	1.00 – 1.03	0.78 – 1.05
		p	**0.012**	0.200
	Total social expenditure	*MR*	1.02	0.91
		95% CI	1.00 – 1.03	0.79 – 1.06
		p	**0.011**	0.221

Abbreviations: MR, mean ratio. OR, odds ratio. CI, confidence interval. PHC, primary health care.

Figure 4.2 presents predicted mean PHC/outpatient, inpatient, medication, and out-of-pocket health expenditures, with confidence intervals, given the observed range of depressive symptom severity and viral suppression vs. non-suppression. On average, severely depressed patients (PHQ-9 = 27) were predicted to have 64.10 ZAR (95% prediction interval [PI]: 17.89,

123.85) greater PHC/outpatient expenditure, 2546.59 ZAR (95% PI: 566.52, 10268.4) greater inpatient expenditure, 253.26 ZAR (95% PI: 146.20, 360.27) greater medication expenditure, and 26.23 ZAR (95% PI: -11.01, 103.49) greater out-of-pocket expenditure, compared to moderately depressed patients (PHQ-9 = 9). Virally suppressed patients (<400 copies/mL) were predicted to have 32.95 ZAR (95% PI: 0.77, 64.98) lower PHC/outpatient expenditure, 332.40 ZAR (95% PI: 3.75, 1337.10) lower inpatient expenditure, 253.26 ZAR (95% PI: 146.20, 360.27) lower medication expenditure, and 2.88 ZAR (95% PI: -10.37, 28.71) lower out-of-pocket expenditure, compared to non-virally suppressed patients.



Shaded regions represent 95% prediction intervals.
Abbreviations: PHC, primary healthcare. ZAR, South African Rand. VL, viral load.

Figure 4.2. Predicted mean total expenditures by type, depressive symptom severity, and viral suppression status, over twelve months post-baseline

4.5 DISCUSSION

We characterized health service use, medication use, and associated expenditure, and estimated the effects of depressive symptom severity on use and expenditure, among patients with depressive symptoms on ART in North West Province, South Africa. This study is among the first to assess health services use and expenditure among patients with co-morbid HIV and depression in an LMIC setting. Patients in the sample were mostly Black, low-income women who were virally suppressed. The majority were experiencing moderate depressive symptoms at enrollment. Patients received most of their healthcare from a public sector PHC or outpatient facility, visiting nearly monthly over the year post-enrollment. Hospitalization was rare but responsible for disproportionate expenditure. Private provider visits were also infrequent. Very few patients were on second-line ART or anti-depressant medication. A substantial proportion experienced catastrophic out-of-pocket expenditure. Depressive symptom severity may have driven small increases in inpatient and medication expenditures in this population, though it did not appear to have been independently associated with PHC/outpatient expenditure, out-of-pocket expenditure, or the risk of catastrophic expenditure.

Though the preponderance of global evidence suggests that depression leads to greater health service expenditure [108], our results indicate that among South African patients with co-morbid HIV and depression, depressive severity was not a strong independent driver of cost. One possible explanation is that most expenditures in this study were estimated to come from PHC/outpatient use, rather than inpatient or medication use. This is substantially different from previous studies of expenditure among patients with HIV in other settings, which have found far greater proportions of cost due to inpatient use [109] and medication [110,111]. Limited access to inpatient care and extremely low rates of anti-depressant prescription in this setting may therefore

help explain why depressive severity was not a strong cost driver. Another explanation relates to the detection of depression by PHC providers. Preliminary evidence from the South African collaborative care model suggested that once trained in integrated care, PHC nurses were still able to positively identify only about 16% of patients with depression [20]. With at least three-quarters of depression cases going undetected, few patients receive necessary treatment and incur the subsequent costs. Studies in other settings have similarly found that low rates of identification of mental disorder lead to reduced likelihood of mental health service delivery and subsequent cost [112]. Future research will need to compare patterns of service use and cost by depressive severity once treatment modalities are more widely available in this context.

This study had several limitations. First, data came from a trial-based sample of patients attending public sector PHC facilities for ART; given significant barriers to access and use of primary and specialist care in low-resource settings, participants likely differ substantially from the underlying population of people with co-morbid HIV and depression [113]. Further study of the predictors of health care use among a sample representative of the broader underlying population is warranted. Second, all participants had HIV and at least moderate depressive symptoms; we were therefore unable to estimate the differences in health service use and expenditure comparing patients with and without HIV or depression. Third, with the exception of hospitalizations and routine viral loads, our analysis relied on participant self-reported health care use. Self-report may underestimate the true number of health care visits [114], and deflate underlying variation in the data [115]. However, recall periods were restricted to three months to promote accuracy [116,117], and robust, pre-tested instruments were used [118]. Fourth, these three month recall periods left gaps of unmeasured health service use over the study period. We relied on imputation to estimate use over the whole period. Individual mean imputation has been

shown to produce valid estimates of health care use [119]; comparable studies have similarly used self-report and imputation to derive estimates of healthcare utilization [109]. Fifth, expenditure estimates were calculated by multiplying the volume of visits to health services by fixed costs per visit, rather than by examining medical claims data or other administrative sources of patient-level expenditure data. The variation in total expenditure may therefore have been underestimated. Sixth, out-of-pocket expenditure estimates were limited to service fees, travel fares, and private vehicle use. Food, childcare, and other potential out-of-pocket costs were not assessed. Finally, we analyzed outcomes with extreme skewness and heteroscedasticity. However, our use of generalized linear and two-part models was a strength of our approach; other approaches to analyzing highly skewed data, including ordinary least-squares regression with a logged outcome (log-OLS), may be severely imprecise and biased, especially for data with many zeroes [120].

Despite these limitations, our findings have significant implications for integrated depression and HIV care in South Africa and other health systems implementing similar models, including those in Ethiopia, Zimbabwe, Uganda, and Haiti [49-52]. Integrated depression care may reduce overall health expenditure in the long-term as patient treatment adherence and retention improves, though in the short-term it could lead to increased cost as previously undetected cases are identified and managed. In particular, medication expenditure will increase as patients are prescribed anti-depressants. However, integrated care may lead to immediate cost savings in other areas. While previous studies have estimated that only about 3-13% of all South African households face catastrophic out-of-pocket health expenditures [121,122], we estimated a much higher proportion of catastrophic expense in this sample. Untreated depression may place households at greater risk of catastrophic expenditure; integrated care may reduce that risk.

4.6 CONCLUSION

We assessed health service use, medication use, and health service expenditure among patients with depressive symptoms on ART in North West Province, South Africa, and estimated the effects of depression severity on use and expenditure. Depression severity was associated with aspects of use and expenditure in this population. Low rates of identification and referral into treatment of patients with depression may explain why depression severity was not a stronger driver of cost. Patients with co-morbid HIV and depression may be particularly vulnerable to catastrophic out-of-pocket expenditure.

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VITA

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