Effectiveness of an Integrated Approach to HIV and Hypertension Care in Rural South Africa: Controlled Interrupted Time-Series Analysis

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Background: South Africa faces a dual burden of HIV/AIDS and noncommunicable diseases. In 2011, a pilot integrated chronic disease management (ICDM) model was introduced by the National Health Department into selected primary health care (PHC) facilities. The objective of this study was to assess the effectiveness of the ICDM model in controlling patients' CD4 counts ($>$350 cells/mm^3) and blood pressure [BP ($<$140/90 mm Hg)] in PHC facilities in the Bushbuckridge municipality, South Africa.

Methods: A controlled interrupted time-series study was conducted using the data from patients' clinical records collected multiple times before and after the ICDM model was initiated in PHC facilities in Bushbuckridge. Patients ≥18 years were recruited by proportionate sampling from the pilot (n = 435) and comparing (n = 443) PHC facilities from 2011 to 2013. Health outcomes for patients were retrieved from facility records for 30 months. We performed controlled segmented regression to model the monthly averages of individuals' propensity scores using autoregressive moving average model at 5% significance level.

Results: The pilot facilities had 6% greater likelihood of controlling patients' CD4 counts than the comparison facilities (coefficient = 0.057; 95% confidence interval: 0.056 to 0.058; $P < 0.001$). Compared with the comparison facilities, the pilot facilities had 1.0% greater likelihood of controlling patients' BP (coefficient = 0.010; 95% confidence interval: 0.003 to 0.016; $P = 0.002$).

Conclusions: Application of the model had a small effect in controlling patients' CD4 counts and BP, but showed no overall clinical benefit for the patients; hence, the need to more extensively leverage the HIV program for hypertension treatment.

Key Words: Agincourt, HIV, integrated, primary health care, noncommunicable diseases, South Africa

(J Acquir Immune Defic Syndr 2017;75:472–479)

INTRODUCTION

The World Health Organization (WHO) defines chronic conditions as those requiring "ongoing management over a period of years or decades" covering a wide range of health problems expanding beyond the traditional noncommunicable diseases (NCDs) to include some communicable diseases such as HIV/AIDS.[1] This is because of the increasing recognition of the transformation of HIV to a chronic condition as a result of rapidly expanding antiretroviral treatment (ART) which fuels the emergence of age-related chronic diseases.[2,3]

NCDs are the leading cause of death globally.[4] In 2012, NCDs accounted for 38 million (68%) of the world's 56 million deaths, and nearly 3-quarter of these deaths occurred in low- and middle-income countries.[4] Mortality due to NCDs is estimated to increase to 55 million by 2030[5]; the greatest increase (27%) between 2010 and 2020 is projected for Africa.[6]

South Africa is undergoing an epidemiological transition with a dual burden of HIV and NCDs. In 2014, NCDs were responsible for 43% of all deaths[7] and an estimated 10.2% of the total population was HIV positive,[8] one of the highest in Africa.

The combined epidemics of HIV and NCDs have implications for South Africa's health care system which is yet to adapt to the long-term continuity of care for patients with chronic disease. Chronic disease care is fragmented within the public health care system in South Africa.[9,10] The relatively well-managed HIV program is vertically controlled,[10] whereas services for NCDs, which account for the highest morbidity and mortality, are poor.[11,12]

The concept of integration as a strategic approach to tackle NCDs is due to shared risk factors. Joint action on these risk factors is an efficient and effective way of reducing the burden of NCDs[13] within the primary health care (PHC) framework.[14] The argument for an integrated approach for NCD management becomes more compelling in the light of multiple morbidities and the consequent rising prevalence of polypharmacy because of drug interactions and side effects.[15]

A study in Cambodia demonstrated the feasibility of integrating HIV/AIDS services with those for NCDs.[16] Median CD4 count increased from 53 cells/mm^3 at baseline to 218 cells/mm^3 at month 12 and 316 cells/mm^3 at month 24 of treatment. Of all hypertension patients on regular treatment for more than 6 months, 68% had blood pressure (BP) values equal to or below the target of 160/90 mm Hg and 57% of diabetes patients had glycosylated hemoglobin values below or equal to 9%.[16] Following this evidence, the Joint United Nations Program on HIV/AIDS (UNAIDS) recommends an integrated approach in which the successful program, tools and approaches of the vertical HIV treatment program are leveraged to support or scale up services for NCDs.[2]

Integrated chronic care for HIV and NCDs is underway in some African Countries. In 2013, a multidisciplinary initiative for integrated management of NCDs was formed in Uganda.[17] In Swaziland and Ethiopia, pilot studies have been conducted in health facilities to further understand the status of NCD services, and the feasibility and effectiveness of adapting HIV program-related tools and systems for patients with diabetes mellitus.[18] In Ethiopia, the quality of care provided to diabetes patients improved significantly after 6 months.[2] A study in Kenya showed the feasibility of integrating NCD care for HIV patients along with HIV-negative patients in primary care.[19]

In South Africa, the National Department of Health (NDoH) in 2011 initiated a national integrated chronic disease management (ICDM) model pilot program in selected PHC facilities in 3 districts selected from 3 of South Africa's 9 provinces (Gauteng, North West, and Mpumalanga).[20–22] The ICDM model aims to improve health outcomes for patients being managed for HIV/AIDS, tuberculosis, hypertension, diabetes, chronic obstructive pulmonary disease, asthma, epilepsy, and mental health illnesses in PHC facilities.[20]

At the core of ICDM model implementation are facility reorganization and clinical management support at the facility level; "assisted" self-management to promote individual responsibility at the community level; and health promotion and population screening to increase awareness of chronic diseases at the population level.[20]

The focus of the facility component is on designation of chronic care area; use of guidelines for management of chronic diseases; human resource audit; capacity building; supply of critical medicines; prepacking of medication; and appropriate referral. To prepare the community for chronic disease care, each clinic has ward-based outreach teams operating within the community that the clinic serves, and consists of one professional nurse, 3 staff nurses, and 6 community health workers. It is anticipated that at least 80% of defined health problems of the catchment population are managed with the outreach team being responsible for 6000 individuals in 1500 households (250 households per 1 community health worker).[20]

There is a dearth of information on the effectiveness of the ICDM model in improving health outcomes of patients since initiation of the ICDM model. The objective of this study was to assess the effectiveness of the ICDM model in improving key indicators of health outcomes, eg, patients' CD4 count and BP, using the data from patients' clinical records in PHC facilities in a rural municipality of South Africa.

METHODS

Study Setting

This study was conducted in 12 PHC facilities in the Bushbuckridge municipality situated in Ehlanzeni health district, Mpumalanga Province, northeast South Africa. In this district the Medical Research Council/Wits Agincourt Research Unit has surveyed the population since 1992 using a Health and Demographic Surveillance System (HDSS). As of first July 2011, the population under surveillance in the Agincourt HDSS was 90,000 people in 16,000 households living in 27 villages.[23] At the time data collection for this study was commenced in June 2013, the ICDM model was being implemented in 17 of the 38 PHC facilities in the

Bushbuckridge municipality. Seven of these 17 health facilities were purposively selected in this study, as they serve the population in the Agincourt subdistrict, and we referred to them as the ICDM pilot facilities. Five of the remaining 21 PHC facilities, where the ICDM model was not piloted, were randomly selected into the comparison arm of this study; henceforth referred to as the comparison facilities.

Study Design and Population

This was a controlled interrupted time-series (ITS) study of patients with chronic disease 18 years and older receiving treatment in the PHC facilities in the study settings. The defining feature of ITS design is that each participant in the sample is observed multiple times before and after an intervention.[24] The ITS study design is the strongest quasi-experimental design to evaluate longitudinal effects of a non-experimental intervention.[24] This quantitative research is part of a larger mixed method study that aimed to contribute to understanding the effectiveness of the ICDM model in improving patients' health outcomes and the quality of integrated chronic disease care.

At the time of the study, eligibility criteria for ART initiation were CD4 count ≤350 cells/mm³; WHO clinical stage 3 or 4; and pregnancy or breastfeeding status.[25] For those on ART, viral load was repeated 12 monthly and CD4 count repeated 6 monthly for ART monitoring purposes with the expectation that CD4 count would be >350 cells/mm³. Supplemental Digital Content 1, http://links.lww.com/QAI/B22 showed the treatment regimens recommended for HIV/AIDS patients in South Africa during the duration of the study.[25] At every visit, adherence to treatment was assessed by pill count and record of clinic attendance. A pill count of more than 95% of ART doses was considered good adherence.[25] Adherence to hypertension treatment was subjectively assessed by nurses based on the number of antihypertension medicines remaining from the last visit and brought forward to the index visit; and documented as good or poor in patients' clinic records. Unstable (uncontrolled) HIV and hypertension patients were reviewed monthly until stability was achieved, whereas stable patients were reviewed every 2–3 months. All patients were routinely referred to the doctor for review every 6 months.

Hypertension is defined as currently taking antihypertensive drugs; or systolic BP ≥140 mm Hg or diastolic BP ≥90 on 3 separate measurements 2–3 days apart.[25] Antihypertensive drugs used in the study setting are shown in SDC 1.

Inclusion and Exclusion Criteria for the Patients

Study participants comprised patients 18 years and older receiving treatment for the markers of chronic diseases in the study area (HIV, hypertension or diabetes)[26–28] from January 2011 to June 2013. Patients transferred between ICDM pilot and comparison facilities after the study was commenced were excluded.

Sample Size Calculation and Sampling Technique

We calculated a minimum sample size of 435 patients in each study arm after adjusting for a 10% nonresponse using Diggle's sample size formula for repeated measures in which changes in BP (hypertension being the most prevalent marker of chronic diseases in the study area) are consistently compared between 2 groups across 30 time points of observation in a longitudinal study,[29] assuming an effect size of 0.22; 0.90 correlations of repeated outcomes; 90% power ($Z_\beta = 1.28$); and 5% significance level for a 2-sided hypothesis test ($Z_{\alpha/2} = 1.96$).

A 3-step process was used to recruit the study participants (Supplemental Digital Content 2a and 2b, http://links.lww.com/QAI/B22). First, the number of patients to be recruited in each of the 12 health facilities was determined by proportionate sampling. Second, the patients in each health facility were stratified by HIV, hypertension and diabetes using the health facility-specific sampling frame. Third, systematic sampling (sampling interval determined by disease-specific sampling fraction) was used to recruit patients in the disease-specific clinical appointment roster daily until the desired sample size in each clinic was achieved. A total sample of 435 patients from the ICDM pilot facilities and 443 patients from the comparison facilities were included in this study.

Data Collection and Variables

Clinical records of patients were reviewed to collect the data for this study. After patient recruitment in June 2013, data were collected retrospectively from January 2011 to June 2013. The HIV treatment form was designed for monthly recording of CD4 count and viral load results, BP values, and other variables. Depending on the level of control, the BP records of HIV-negative hypertension patients were documented during each clinic visit which varied between 1 to 3 months. We retrieved key outcome variables such as viral load, CD4 count and BP values during the 30-month period of data collection. BP and CD4 count control were defined as BP <140/90 mm Hg and CD4 count >350 cells/mm³, respectively.

Data Management and Statistical Analyses

We hypothesized that the ICDM model leads to changes in the CD4 counts and BP of patients receiving care in the PHC facilities implementing the ICDM model with an allowance of 8 time points before and after initiation of the model.[30]

Data were entered into Access 2010 and imported into Stata 14.0 (College Station, TX, USA) for statistical analyses. Two periods were specified[1]: preintervention (January–June 2011)—6 months before initiation of the ICDM model, including the month of June 2011 when the model was initiated; and[2] postintervention (July 2011–June 2013)—24 months of implementation of the model.

Two dependent stages of analysis were conducted in our study. The first stage was the individual patient level

analysis with binary outcomes (CD4 counts >350 vs. ≤350 cells/mm^3 or BP <140/90 vs. BP ≥140/90 mm Hg) using mixed effects logistic regression models adjusting for the study arms (clusters) in which patients received health care. This yielded the postlogistic regression probabilities (propensity scores) of controlling CD4 counts or BP for each person on each visit. We did a propensity score matching to balance the effects of age, sex, looking for a paid job, and reception of grant.[31]

The second stage of the analysis was based on the monthly averages of all the individuals' propensity scores seen in that month (continuous outcomes) from stage one. We performed a segmented analysis using the autoregressive moving average (ARMA) models on the monthly average data over time. The segmented analytical approach is a statistical method for estimating the effects of longitudinal intervention in ITS data.[24,30] Autocorrelation inherent in the time-series data were accounted for via the ARMA models.

The ARMA models considered the main effects (ie, controlled CD4 counts and BP) as well as the interactions of the time periods and intervention/control arms across the whole time span to assess the effect of the intervention. The inverse of the SDs was used in the ARMA models as the analytic (importance) weights.

The *P*-values and the 95% confidence interval of the parameters were reported to ascertain statistical significance (*P* <0.05). The goodness of fit of the models was assessed by testing the residuals for normality in addition to the visual assessment of the fitted vs. observed time-series plots.

Analysis of diabetes patients could not be undertaken because of the small number in each of the study groups (n = 2).

Ethical Considerations

Ethical clearance for this research was granted by the Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand, Johannesburg, South Africa (Ref No. M120943), and the Mpumalanga Provincial Research and Ethics Committee. Written informed consent was obtained from the study participants and confidentiality was assured.

RESULTS

A significantly (*P* < 0.001) higher percentage of patients in the ICDM pilot (67%) than the comparison (43%) facilities were ≥ 50 years (Table 1). The percentage of hypertension patients was significantly higher in the ICDM pilot facilities (48% vs. 21%; *P* < 0.001), whereas the comparison facilities had more HIV patients (64% vs. 32%; *P* < 0.001).

Figure 1 showed that the slopes of the probability of controlling patients' CD4 counts in the pilot and comparison facilities decreased in both pre- and post-ICDM model periods. The pilot facilities had a consistently higher probability of controlling patients' CD4 counts than the comparison facilities at the time of initiation of the ICDM model (97.5% vs. 95.0%) and 2 years after the model was implemented (96.5% vs. 94.0%).

TABLE 1. Sociodemographic Characteristics of the Patients in the ICDM Pilot and Comparison Facilities, Bushbuckridge Municipality, 2011–2013

Characteristic	Total (n = 878)		ICDM Fac. (n = 435)		Comparison Fac. (n = 443)		Two-Sided *P* Value of Difference
	No.	%	No.	%	No.	%	
Age group, yrs							
18–29	58	6.6	19	4.4	39	8.8	<0.001
30–39	179	20.4	60	13.8	119	26.9	
40–49	151	17.2	59	13.6	92	20.8	
50–59	169	19.2	84	19.2	85	19.2	
≥60	302	34.4	197	45.3	105	23.7	
Missing	19	2.2	16	3.7	3	0.6	
Sex							
Female	731	83.3	363	83.4	368	83.1	0.881
Male	147	16.7	72	16.6	75	16.9	
Education (completed years)							
No formal education	339	38.6	172	39.6	167	37.7	0.170
1–6	343	39.1	174	40.0	169	38.1	
>6	144	16.4	71	16.3	73	16.5	
Missing	52	5.9	18	4.1	34	7.7	
Looking for a paid job							
Yes	246	28.0	126	29.0	120	27.0	0.725
No	592	67.4	291	66.9	301	68.0	
Missing	40	4.6	18	4.1	22	5.0	
Reception of grant							
None	412	46.9	202	46.4	210	47.4	0.927
HIV	13	1.5	5	1.2	8	1.8	
Disability	28	3.1	15	3.5	13	2.9	
Old age	385	43.9	195	44.8	190	42.9	
Missing	40	4.6	18	4.1	22	5.0	
Chronic disease status							
Hypertension	301	34.3	210	48.3	91	20.5	<0.001
HIV	423	48.2	141	32.4	282	63.7	
Diabetes	4	0.5	2	0.4	2	0.5	
Comorbidities	150	17.0	82	18.8	68	15.3	

Five patients in the ICDM model facilities were transferred to other facilities also implementing the ICDM model. This was also the case for 3 patients in the comparison facilities.

Two patients in the ICDM model facilities and one in the comparison facilities were transferred to health facilities in other provinces.

One HIV patient died in the ICDM model facilities while 3 deaths (one hypertension and 2 HIV/AIDS patients) were recorded in the comparison facilities.

Fac, facilities.

Figure 2 showed decreasing slopes of the probability of patients having a controlled BP in the pilot and comparison facilities before the ICDM model was initiated. After initiation of the ICDM model, comparison of the 2 study arms showed a consistently higher probability of controlling patients' BP in the pilot facilities than in the comparison facilities at the time the ICDM model was initiated (50% vs. 47%) and 2 years after the model was implemented (47% vs. 40%).
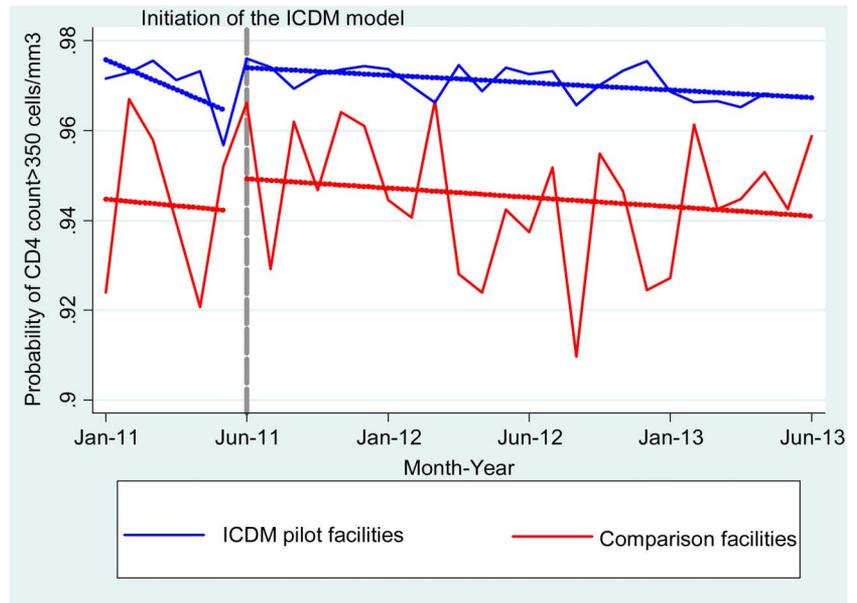
FIGURE 1. Monthly probabilities of having a CD4 count >350 cells/mm³ after propensity score matching in the ICDM pilot and comparison facilities in the Bushbuckridge municipality, 2011–2013.

The ARMA[1] model was fit with the covariates shown in Table 2. The pilot facilities had about 6% greater likelihood of controlling patients' CD4 counts than the comparison facilities [coefficient = 0.057; 95% confidence interval (CI): 0.056 to 0.058; $P < 0.001$]. There was a 0.3% drop in the probability of controlling patients' CD4 counts in the postintervention period (coefficient = −0.003; 95% CI: −0.004 to −0.002; $P < 0.001$). The interaction of study groups with the periods showed that CD4 count control was greater by 0.2% in the pilot facilities during the 24 months of implementation of the ICDM model compared with the comparison facilities during the 6 months preceding the initiation of the ICDM model (coefficient = 0.002; 95% CI: 0.001 to 0.003; $P < 0.001$).

The covariates in the ARMA[1,2] model for BP control are shown in Table 3. The pilot facilities had a 1.0% greater likelihood of controlling patients' BP than the comparison facilities (coefficient = 0.010; 95% CI: 0.003 to 0.016; $P = 0.002$). The postintervention period had a 3% decrease in the probability of controlling patients' BP (coefficient = −0.030; 95% CI: −0.036 to −0.024; $P < 0.001$). The interaction of study groups with period showed that BP control was greater by 4% in the pilot facilities during the 24 months of implementation of the ICDM model compared with the comparison facilities during the 6 months preceding initiation of the ICDM model (coefficient = 0.036; 95% CI: 0.029 to 0.043; $P < 0.001$).
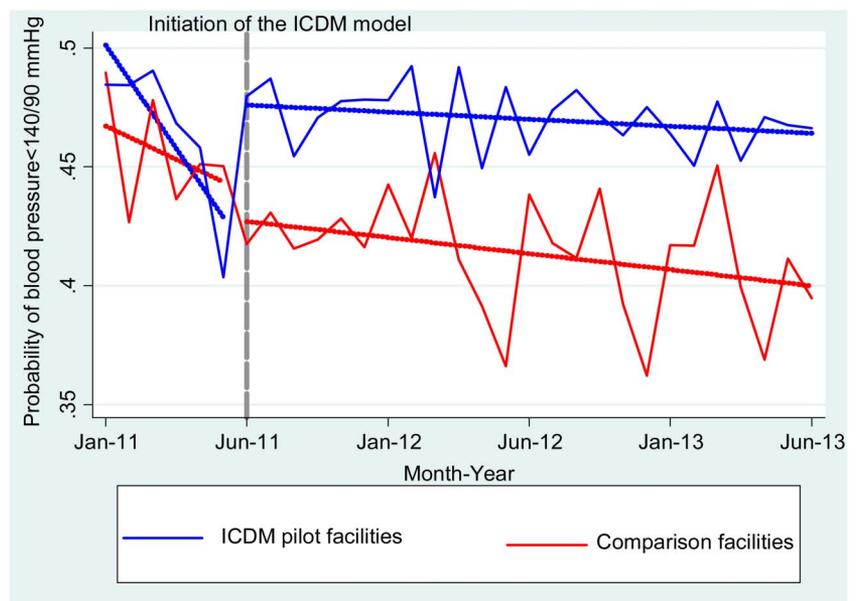
FIGURE 2. Monthly probabilities of having a BP <140/90 mm Hg after propensity score matching in the ICDM pilot and comparison facilities in the Bushbuckridge municipality, 2011–2013.

TABLE 2. The Autoregressive Moving Average Model for CD4 Count Control in PHC Facilities in the Bushbuckridge Municipality, 2011–2013

Characteristic	Coefficient	Standard Error	95% Confidence Interval	P
Facility				
Comparison	1			
ICDM model pilot	0.057	0.0002	0.056 to 0.058	<0.001
Period				
Preintervention	1			
Postintervention	−0.003	0.0001	−0.004 to −0.002	<0.001
Interaction of facility and period				
Comparison and preintervention	1			
ICDM pilot and postintervention	0.002	0.0003	0.001 to 0.003	<0.001

The number of monthly visits of sampled patients who used PHC facilities from January 2011 to June 2013 in the 2 study arms are shown in Supplemental Digital Content 3, http://links.lww.com/QAI/B22.

DISCUSSION

To the best of our knowledge, this is the first study in sub-Saharan Africa to assess the effectiveness of an integrated chronic disease model in improving health outcomes of hypertension and patients with HIV receiving treatment in PHC facilities. The main findings showed that the ICDM model had a small but significant effect in controlling patients' CD4 counts and BP compared with the preintervention period. However, there was no overall clinical benefit for the patients due to nonreversal of the downward trends observed before the implementation of the model.

The higher percentage in the control of CD4 counts in the pilot than in the comparison facilities may have been because of reduced HIV stigma in settings of integrated care,

TABLE 3. The Autoregressive Moving Average Model for BP Control in PHC Facilities in the Bushbuckridge Municipality, 2011–2013

Characteristic	Coefficient	Standard Error	95% Confidence Interval	P
Facility				
Comparison	1			
ICDM model pilot	0.010	0.0031	0.003 to 0.016	0.002
Period				
Preintervention	1			
Postintervention	−0.030	0.0030	−0.036 to −0.024	<0.001
Interaction of facility and period				
Comparison and preintervention	1			
ICDM pilot and postintervention	0.036	0.0029	0.029 to 0.043	<0.001

which was reported by operational managers in the qualitative sub-study of our broader research.[32] Reduced HIV/AIDS-related stigma may have led to increased uptake of HIV services because HIV and NCD patients received care in the same consultation rooms as was reported in a Cambodia pilot study.[2,16] Although the WHO recommends virological monitoring as the preferred approach to treatment monitoring for those on ART,[33] we used CD4 counts for treatment monitoring because CD4 counts are still important indicators for initiating and monitoring ART[34] and HIV disease progression[35] in resource-limited settings such as rural South Africa.

Our study showed small but significant control of patients' CD4 count and BP. A similar study conducted in Cambodia using cohort analysis showed an increase in median CD4 count and the percentage of hypertension patients with controlled BP after 2 years of implementation of the pilot study.[16] From a health system perspective, our study does not entirely support the findings of the Cambodian study in terms of achieving optimal control of patients' BP.

Optimal BP control is difficult to achieve.[36–41] The suboptimal (<50%) control of BP observed in the pilot facilities implies that the purpose for which the ICDM model was initiated—to leverage HIV programs, tools, and systems to scale up services for NCDs—is yet to be fully achieved. The failure to achieve optimal BP control in the study setting may be attributed to health system and individual factors.

Three health system factors may have negatively impacted optimal BP control in the study setting. First, a study conducted at the time the ICDM model was initiated revealed that South Africa's public health sector vertical HIV program was not administratively integrated with the horizontal general health system.[10] Second, a quantitative component of our broader study showed that 5 of the 8 dimensions of care (referral system, defaulter tracing, prepacking of drugs, appointment system, and long patient waiting time) identified as the priority areas for leveraging the HIV program for NCDs in the ICDM model did not reflect their intended constructs for good quality of care.[42] Finally, the qualitative component of our broader study showed that facility managers and patients reported that nurses were overburdened by an increased workload resulting from integrated services. Furthermore, staff shortage, malfunctioning BP machines, and antihypertensive drug stock-out were reported by patients and facility managers in these facilities.[32]

Based on the literature evidence, individual-level factors that may have constituted a bottleneck in achieving optimal BP control in our study included ignorance of the complications of high BP[38]; obesity and physical inactivity[39]; poor adherence to pharmacological[40,41] and nonpharmacological treatment; and low socioeconomic status.[41]

Although the 7 pilot facilities implemented all components of the ICDM model through a "trial and learning" phased approach,[43] negative staff behavior (eg, resistance to improvement efforts in the implementation of the ICDM model), suboptimal involvement of doctors in the clinical management of patients, redeployment of professional nurses who received training in the implementation of the ICDM model, and poor infrastructure may have led to the decline in

CD4 count and BP control in the pilot facilities.[43] Some of these factors may have been responsible for these declines in the comparison facilities because these facilities were being managed by the same administrative and managerial structures in the municipality.

Achieving optimal health outcomes in the ICDM model used in South Africa will require strengthening of the health system in which the ICDM model is embedded. Health system interventions that focus on improving performance of the structural/hardware or social/software components of the health system's building blocks are needed.[44] Furthermore, a people-centered interventional model targeting hypertension patients could lead to increased awareness of the complications of poor compliance with treatment and better patient self-management.[44]

The steeper decline in the control of CD4 counts and BP in the pilot facilities than in the comparison facilities before implementation of the model may have been because of a "crowding-out" of the integrated services through routine training activities in preparation for the implementation of the ICDM model.[44]

Strengths and Limitations

The main strengths of this study were the ability to control for secular trends in the data; evaluate outcomes using the covariates adjusted propensity scores; and presentation of the results graphically. Our study findings must be interpreted in the light of the limitations imposed by the use of routine health care data. More specifically, some facility-level data were incomplete or unavailable because of one or more of the following reasons[1]: missing laboratory results of CD4 counts and viral load and[2] missing records of BP measurements because of BP machines being out of order. Other limitations included the paucity of information on facility-level factors such as unavailability of comparative data on staffing, patient load, medication supply chain, and inability to use viral load values for monitoring those on ART because of not having enough data time points obtained before and after implementation of the ICDM model.

Our study contributes to the national and global debates on an integrated health systems approach. The main findings of our research have implications for the nationwide implementation of the ICDM model that is underway in PHC facilities in South Africa and for the planning of an integrated chronic care in other low- and middle-income countries.

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