Cardiovascular disease prevention in a health insurance program in rural Nigeria
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Chapter 5

Feasibility and quality of cardiovascular disease prevention within a community-based health insurance program in rural Nigeria: an operational cohort study


J Hypertens, accepted pending minor revisions
ABSTRACT

Objective
To assess the feasibility of providing guideline-based cardiovascular disease (CVD) prevention care within the context of a community-based health insurance program (CBHI) in rural Nigeria.

Methods
A prospective operational cohort study was conducted in a primary healthcare clinic in rural Nigeria, participating in a CBHI program. The insurance program provided access to care and improved the quality of the clinics participating in the program, including CVD prevention guideline implementation. Insured adults at risk of CVD were consecutively included upon clinic attendance. The primary outcome was quality of care determined by scoring of quality indicators on patient files of the cohort, 1.5 year after guideline implementation.

Results
Of 368 screened patients, 349 were included, 323 (93%) completed one year of follow up. The majority of patients (331, 95%) had hypertension. Process indicators showed that 114/115 (99%) new hypertension cases had a record of CVD risk assessment and 249/333 (75%) eligible cases a record of lifestyle advice. Outcome indicators showed that in 292/328 (64%) hypertension cases blood pressure was on target. Barriers to care included limited human resources, limited affordability of diagnostic tests and multidrug regimes for the healthcare provider, frequent doctor’s appointments, and inefficient drug supplies.

Conclusion
Implementation of CVD prevention care within the context of a CBHI program resulted in high quality care in rural SSA, comparable to high income countries. However, guideline implementation was resource intense and specific recommendations were not feasible. Simple models of care delivery are needed for rapid scale-up of CVD prevention services in SSA.

Trial registration
ISRCTN, ID number: ISRCTN47894401

Keywords
Cardiovascular diseases; primary prevention; hypertension; program evaluation; operational research; quality of health care; Africa South of the Sahara; Insurance, Health; Nigeria; developing countries.
INTRODUCTION

Cardiovascular disease (CVD) has become a leading contributor to the burden of disease in low- and middle-income countries (LMICs), including sub-Saharan Africa (SSA). The World Health Organization (WHO) has developed guidelines for CVD prevention in LMICs. However, it is unclear whether it is feasible to implement these guidelines in settings with dysfunctional health systems. CVD prevention care is unaffordable for many patients in SSA. Quality of care is often insufficient with a lack of facilities, qualified staff, essential equipment and supplies, and limited organizational capacity to provide chronic care. Operational research of CVD prevention care programs in SSA is urgently needed to evaluate how guidelines can be successfully translated into practice.

The operational research project QUality Improvement Cardiovascular care Kwara (QUICK) aimed to assess the feasibility of CVD prevention care according to WHO and other international guidelines, in the context of a community-based health insurance (CBHI) program in rural Nigeria. This insurance program ensured access to care for patients by covering the costs of care, and at the same time provided financial and technical support to improve the quality of care in the participating healthcare clinics. Here we report on the feasibility of CVD prevention care in this context, with quality of care as the main outcome. The financial feasibility of providing CVD prevention care is described elsewhere (chapter seven).

METHODS

The study protocol is described in detail elsewhere. A summary is described below.

Context

The Health Insurance Fund

The Health Insurance Fund (HIF) subsidizes CBHI programs for low- and middle-income groups in several African countries. The health maintenance organization Hygeia has contracted both private and public clinics to provide the care for the enrollees in HIF’s program in Nigeria, called the Hygeia Community Health Care (HCHC) program (see Text, Supplemental Digital Content 1, which describes the HCHC program in more detail).

Study site and context

Ogo Oluwa Hospital (OOH) in Kwara State is a private primary healthcare clinic participating in the HCHC program. It provides care for the population of Bacita, a rural, low-income community. Guidelines for CVD prevention were unavailable in OOH before the start of the HCHC program. Facilities to screen for target organ damage (TOD) were absent and registration of patient treatments and outcomes was poor. As part of the quality improvement component of the HCHC program, CVD prevention guidelines were introduced in OOH in June 2010 and included provision of equipment for diagnostic testing, introduction of treatment protocols (see Supplemental Digital Content 2, which shows the treatment algorithms for hypertension and diabetes treatment), quarterly staff training with feedback on guideline adherence,
and organizational support, including introduction of standardized patient files and laboratory forms. CVD prevention care, upgrading, and support were financed through the insurance program. However, as TOD screening was considered unaffordable within the insurer’s reimbursement fees by the medical director of OOH, consumables required for TOD were provided in the context of the QUICK study.

**Study design and study participants**

The QUICK study was an observational prospective hospital-based cohort study of 349 adults (see Text, Supplemental Digital Content 1, which provides more details on the sample size), recruited between June 2010, directly after guideline implementation, and January 2011. Patients at increased risk of CVD (i.e. diagnosed with hypertension, diabetes, renal disease or established CVD), who were enrolled in the HCHC program and attending the clinic, were consecutively included if none of the following exclusion criteria were present: pregnancy/lactating, suspected secondary hypertension, not residing in Kwara State. All patients were followed for one year and visited a study nurse every three months, in addition to the regular monthly doctors’ appointments (see Text, Supplemental Digital Content 1, which provides more details on data collection).

**Outcome measures and data collection**

The primary outcome was quality of care measured using the adjusted cardiovascular care quality indicators of the United Kingdom National Health Services Quality and Outcome Framework (QOF),\[^{12,13}\] 1.5 year after the implementation of CVD prevention guidelines. The indicators included process and patient outcome indicators. Scoring of quality of care was done by three independent medical doctors (i.e. not part of OOH staff, not involved in data analysis) in a cross-sectional audit of the medical records of all patients included in the QUICK cohort.

Secondary outcomes included 1) the proportion of patients who obtained risk factor control at 12 months of follow up, 2) operational and behavioural determinants of treatment success in hypertensive patients and 3) health system-related barriers to CVD prevention guideline implementation.

Blood pressure was measured at each study visit. Three measurements were performed with the patient in sitting position, after five minutes of rest, using a validated automatic blood pressure device with a cuff suitable for different arm circumferences (ranging from 22 cm to 42 cm) (OMRON M6 Comfort, OMRON Cooperation). The mean of the 2nd and 3rd measurement was used for analysis. Health system-related barriers to guideline implementation were identified during training sessions with the hospital staff using interviews. Perceived barriers were systematically recorded using standardized record forms. In addition, hospital records were collected to monitor stocks and staff-turnover.

Data monitoring procedures were implemented to assure the quality of study data (see Text, Supplemental Digital Content 1, which provides more details on data monitoring).
Data analysis

Quality indicator scoring
For each indicator, the denominator to calculate percentage passed was the total number of patients for which a quality indicator was applicable. The nominator was the number of patients for whom the indicator was achieved. Each indicator allowed for exception reporting as recommended by the QOF Framework, for example if there was a contraindication for a specific test or treatment, in which case the record did not count in the denominator. Therefore, the denominator for a specific indicator, for example for hypertension control, and the number of patients with hypertension included in the cohort varied.

Secondary outcomes
The proportion of patients who achieved risk factor control after one year of follow up was determined using descriptive statistics. Determinants of treatment success in hypertension patients, defined as blood pressure below 140 mmHg systolic and 90 mmHg diastolic, were evaluated using multivariable logistic regression. All follow up visits (at 3, 6, 9 and 12 months) were included. Mixed models, corrected for clustering at patient level, accounted for repeated observations on the same patient. The following operational and behavioural predictors for treatment success were explored: missing doctor’s appointments, travel time to and waiting time in the clinic, travel mode, travel costs, income or productivity losses due to clinic visits, out-of-pocket expenditures for healthcare, drug stock-outs, adherence to drugs and lifestyle advices, drug side effects, use of traditional medicine, consultation of other healthcare providers, and doctor’s prescription of maximum indicated drug doses. Plausible confounders explored in all analyses were biological (age, gender, baseline blood pressure, co-morbidities, BMI) and socio-economic patient characteristics (ethnicity, marital status, education, wealth, job type) that may have altered the probability of successful treatment. To account for initial drug titration in patients not on treatment upon inclusion, other confounders tested were being on treatment upon inclusion, duration of study follow-up and drug intensity (number and dose of anti-hypertensive agents). Plausible interactions were explored. The decision to include a variable in the final model was based on a significant change (greater or equal to 5%) in the overall fit of the model. Predictors for the main determinants of treatment success were also explored using the same methodology. Data were analyzed using STATA, version 12.1 (StataCorp LP, Texas, USA).

Health system barriers to guideline implementation were reported according to the framework for chronic disease care as reported by Maimaris et al.

Definitions
The QOF quality indicators used blood pressure targets that differed from international guidelines of CVD prevention care because the audit standard is less stringent than targets recommended in treatment guidelines. We used the QOF definition of blood pressure control for the primary outcome for comparability with other studies that reported quality of care according to QOF indicators. This is defined as a blood pressure of ≤ 150 mmHg systolic and ≤ 90 mmHg diastolic for hypertensive patients without diabetes and ≤ 145 mmHg systolic and ≤ 85 mmHg diastolic for hypertensive patients with diabetes. For all secondary outcomes,
blood pressure control was defined as < 140 mmHg systolic and < 90 mmHg diastolic, irrespective of co-morbidities, similar to other studies from SSA.\textsuperscript{14-17} The remaining definitions can be found in the Supplemental Digital Content (see Text, Supplemental Digital Content 1, which describes all outcome definitions).

**Ethical Review**

Ethical clearance was obtained from the Ethical Review Committee of the University of Ilorin Teaching Hospital in Nigeria. Informed consent was obtained from all study participants by written signature or fingerprint.

**RESULTS**

**Patient characteristics**

The QUICK cohort consisted of 349 patients. Participants flow is shown in Figure 1. Ninety-five percent (n = 331) of the patients were included based on a diagnosis of hypertension. Other reasons for inclusion are shown in Table 1. Of the 118 hypertensive patients who were not receiving treatment at baseline, 45.8% had grade 2 hypertension and 31.4% grade 3 hypertension. The prevalence of TOD at baseline was 58.5% (Table 1).

\footnotesize*229 patients were in active follow-up and receiving CVD preventive drug treatment upon inclusion, 120 patients had not been on CVD preventive treatment for at least 1 year upon inclusion.
Table 1 Baseline characteristics QUICK cohort

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>On treatment at inclusion</th>
<th>Not on treatment at inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>N=349</td>
<td>N=229</td>
<td>N=120</td>
</tr>
<tr>
<td></td>
<td>154 (44.1)</td>
<td>90 (39.3)</td>
<td>64 (53.3)</td>
</tr>
<tr>
<td><strong>Age, median (IQR)</strong></td>
<td>57.0 (50.0-65.0)</td>
<td>56.3 (50.0-65.0)</td>
<td>57.7 (49.0-65.2)</td>
</tr>
<tr>
<td><strong>Reason inclusion, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HT</td>
<td>294 (84.2)</td>
<td>184 (80.3)</td>
<td>110 (91.7)</td>
</tr>
<tr>
<td>DM</td>
<td>18 (5.2)</td>
<td>16 (7.0)</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>HT/DM</td>
<td>28 (8.0)</td>
<td>22 (9.6)</td>
<td>6 (5.0)</td>
</tr>
<tr>
<td>HT/DM/renal disease</td>
<td>1 (0.3)</td>
<td>1 (0.4)</td>
<td>-</td>
</tr>
<tr>
<td>HT/renal disease</td>
<td>1 (0.3)</td>
<td>-</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>HT/Stroke</td>
<td>2 (0.6)</td>
<td>2 (0.9)</td>
<td>-</td>
</tr>
<tr>
<td>HT/Angina Pectoris</td>
<td>3 (0.9)</td>
<td>3 (1.3)</td>
<td>-</td>
</tr>
<tr>
<td>HT/DM/Stroke</td>
<td>2 (0.6)</td>
<td>1 (0.4)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td><strong>Systolic BP, median (IQR) (if HT)</strong></td>
<td>135 (120.0-162.5)</td>
<td>125 (114.5-134.5)</td>
<td>168.3 (158.5-181.5)</td>
</tr>
<tr>
<td><strong>Diastolic BP, median (IQR) (if HT)</strong></td>
<td>84 (75.0-96.5)</td>
<td>87 (71.0-84.5)</td>
<td>98.3 (91.5-107.5)</td>
</tr>
<tr>
<td><strong>BP classification, n (%) (if HT)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>162 (48.9)</td>
<td>160 (75.1)</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>HT grade 1</td>
<td>67 (20.2)</td>
<td>42 (19.7)</td>
<td>25 (21.2)</td>
</tr>
<tr>
<td>HT grade 2</td>
<td>63 (19.0)</td>
<td>9 (4.2)</td>
<td>54 (45.8)</td>
</tr>
<tr>
<td>HT grade 3</td>
<td>39 (11.8)</td>
<td>2 (0.9)</td>
<td>37 (31.4)</td>
</tr>
<tr>
<td><strong>BMI, median (IQR)</strong></td>
<td>24.6 (21.5-28.7)</td>
<td>25.3 (21.8-30.1)</td>
<td>23.4 (20.9-26.8)</td>
</tr>
<tr>
<td><strong>Abdominal Obesity (waist circumference), n (%)</strong></td>
<td>138 (39.7)</td>
<td>110 (48.3)</td>
<td>28 (23.3)</td>
</tr>
<tr>
<td><strong>High total cholesterol, n (%)</strong></td>
<td>35 (10.0)</td>
<td>29 (12.7)</td>
<td>6 (5.0)</td>
</tr>
<tr>
<td><strong>High LDL cholesterol, n (%)</strong></td>
<td>44 (12.6)</td>
<td>34 (14.9)</td>
<td>10 (8.3)</td>
</tr>
<tr>
<td><strong>Low HDL cholesterol, n (%)</strong></td>
<td>144 (41.3)</td>
<td>87 (38.0)</td>
<td>57 (47.5)</td>
</tr>
<tr>
<td><strong>High total triglycerids, n (%)</strong></td>
<td>15 (4.3)</td>
<td>7 (3.1)</td>
<td>8 (6.7)</td>
</tr>
<tr>
<td><strong>Smoking, n (%)</strong></td>
<td>13 (3.7)</td>
<td>5 (2.2)</td>
<td>8 (6.7)</td>
</tr>
<tr>
<td><strong>Any alcohol use, n (%)</strong></td>
<td>19 (5.4)</td>
<td>9 (3.9)</td>
<td>10 (8.3)</td>
</tr>
<tr>
<td><strong>Heart Failure, n (%)</strong></td>
<td>8 (2.3)</td>
<td>4 (1.8)</td>
<td>4 (3.3)</td>
</tr>
<tr>
<td><strong>Presence of microalbuminuria, n (%)</strong></td>
<td>41 (11.7)</td>
<td>26 (11.4)</td>
<td>15 (12.5)</td>
</tr>
<tr>
<td><strong>Any target organ damage</strong>, n (%)</td>
<td>204 (58.5)</td>
<td>130 (56.8)</td>
<td>74 (61.7)</td>
</tr>
<tr>
<td><strong>Presence of LVH</strong>, n (%)</td>
<td>108 (30.9)</td>
<td>61 (26.6)</td>
<td>47 (39.2)</td>
</tr>
<tr>
<td><strong>Presence of renal impairment</strong>, n (%)</td>
<td>42 (12.0)</td>
<td>36 (15.7)</td>
<td>6 (5.0)</td>
</tr>
<tr>
<td><strong>Presence of pathological Q waves on ECG</strong>, n (%)</td>
<td>36 (10.3)</td>
<td>19 (8.3)</td>
<td>17 (14.2)</td>
</tr>
<tr>
<td><strong>Stroke</strong>, n (%)</td>
<td>4 (1.1)</td>
<td>3 (1.3)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td><strong>Angina Pectoris (doctors diagnosis, exl screening Rose at baseline)</strong></td>
<td>3 (0.9)</td>
<td>3 (1.3)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Angina Pectoris (Rose questionnaire)</strong></td>
<td>61 (17.5)</td>
<td>38 (16.6)</td>
<td>23 (19.2)</td>
</tr>
<tr>
<td><strong>Job, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farmer</td>
<td>91 (26.1)</td>
<td>57 (24.9)</td>
<td>34 (28.3)</td>
</tr>
<tr>
<td>Trader</td>
<td>117 (33.5)</td>
<td>82 (35.8)</td>
<td>35 (29.2)</td>
</tr>
<tr>
<td>No paid job</td>
<td>61 (17.5)</td>
<td>41 (17.9)</td>
<td>20 (16.7)</td>
</tr>
<tr>
<td>Other</td>
<td>80 (22.9)</td>
<td>49 (21.4)</td>
<td>31 (25.8)</td>
</tr>
<tr>
<td><strong>Highest degree in school completed, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No school at all</td>
<td>198 (56.7)</td>
<td>126 (55.0)</td>
<td>72 (60.0)</td>
</tr>
</tbody>
</table>

Feasibility and quality of cardiovascular disease prevention
Retention in care, mortality and CVD events

One year follow up was completed for 323 patients (92.5%). Eleven patients died during the study period (3.2%). Causes of death and reasons for study drop out are shown in Figure 1. Out of the 349 patients included in the QUICK cohort, four patients were diagnosed with stroke, one with angina pectoris, and three patients had newly developed pathological Q waves on ECG, during the follow up period.

Quality of care

Quality of care scoring was performed for the following QOF disease categories: primary prevention, hypertension, diabetes, smoking and obesity. Heart failure, stroke, and chronic kidney disease were excluded as the limited number of patients in the cohort with these conditions did not allow reliable scoring of the indicators. Amongst 349 patients, three medical files could not be retrieved. All three patients had died during the follow up. The results of the scoring on all indicators are described in Table 2.

Process indicators

A record of CVD risk factor and TOD screening during the follow-up period was found in 114 of 115 (99.1%) files of eligible patients with newly diagnosed hypertension. A record of lifestyle advice was found in 249 of 333 (74.8%) files of patients eligible for lifestyle advice. A recent record of blood pressure measurement was found in 292 of 328 (89%) files of eligible patients with hypertension (Table 2).

Table 2 Quality scoring 1.5 year after the implementation of CVD prevention guidelines in the study clinic

<table>
<thead>
<tr>
<th>Description</th>
<th>N*</th>
<th>Passed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRIMARY PREVENTION</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of patients with a new diagnosis of hypertension (including those with pre-existing coronary heart disease, diabetes, stroke and/or transient ischemic attack) who have a record of a face to face cardiovascular risk assessment using an agreed risk assessment tool including blood tests.</td>
<td>115</td>
<td>114 (99.1)</td>
</tr>
<tr>
<td>Percentage of patients diagnosed with hypertension who have a record of given lifestyle advice for: increasing physical activity, smoking cessation, safe alcohol consumption and healthy diet.</td>
<td>333</td>
<td>249 (74.8)</td>
</tr>
<tr>
<td><strong>HYPERTENSION</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Process indicators</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The practice can produce a register of patients with established hypertension.</td>
<td></td>
<td>Yes</td>
</tr>
</tbody>
</table>
A recent record of blood glucose measurement was found in 51 of 53 (96.2%) files of patients with diabetes, 52 (98.1%) files had a record of blood pressure measurement. Screening for microalbuminuria, impaired estimated Glomerular Filtration Rate and high cholesterol was recorded in 98.1% of diabetes cases. Physical examination to screen for retinal damage, peripheral artery disease and neuropathy was recorded in 43.4%, 18.9% and 17% of the files respectively (Table 2).

Outcome indicators
Of the 328 hypertensive patients who were eligible for the blood pressure outcome indicator, 211 (64.3%) cases had a blood pressure that was measured in the last nine months and that
was on target (≤ 150 mmHg systolic and ≤ 90 mmHg diastolic) (Table 2). In 22 of 53 (41.5%) patients with diabetes, blood glucose was controlled. Blood pressure and cholesterol control in diabetes patients was observed in 29 out of 53 (54.7%) and 37 out of 53 (69.8%) patients respectively (blood pressure target ≤ 145 mmHg systolic and ≤ 85 mmHg diastolic) (Table 2).

Secondary Outcomes

Risk factor control

Blood pressure was controlled in 207 out of 308 (67.2%) patients with hypertension at 12 months of follow up compared to 162 out of 331 (48.9%) patients at baseline (p< 0.001) (blood pressure target < 140 mmHg systolic and < 90 mmHg diastolic). Glucose was controlled in 19 out of 43 (44.2%) diabetic patients at 12 months compared to 17 out of 49 (34.7%) patients at baseline (p=0.35) (see Table 1, Supplemental Digital Content 3, which describes risk factor control at baseline and 12 months for each risk factor).

Predictors for hypertension treatment success

Predictors for hypertension treatment success were evaluated using multivariable regression analyses. Patients who had missed an appointment with their doctor in the last three months were less likely to have controlled blood pressure (< 140 mmHg systolic and < 90 mmHg diastolic) compared to patients who did not miss appointments (OR 0.58, 95%CI 0.36-0.95 for 1 missed appointment ranging to OR 0.35, 0.17-0.70 for >2 missed appointments; Table 3). Patients with a medium or high adherence to drug treatment according to the Morisky adherence scale\(^{18}\) were more likely to have controlled blood pressure (medium adherence OR 1.91, 95%CI 1.09-3.36; high adherence OR 2.68, 1.59-4.53, Table 3) compared to patients with low adherence. Other variables that were significantly associated with successful treatment were shorter waiting time in the clinic during doctor’s appointments, and a healthy lifestyle (Table 3). Only 6 of the 331 (1.8%) hypertension patients were prescribed the maximum recommended dose of three anti-hypertensive drugs and none of them continued the maximum dose during follow up.

Factors significantly associated with missing appointments included low adherence to drugs, long waiting time in the clinic, high travel costs, loss of income due to doctor’s appointments and travelling to the clinic with private travel means. Patients who reported missing appointments with the doctor, or who reported drug stock-outs or drug side effects, were less likely to be highly adherent to drugs (see Table 2, Supplemental Digital Content 3, which provides predictors for missing appointments and for high adherence using multivariable regression analyses).

Health system barriers to guideline implementation

Table 4 lists the main barriers to effective guideline implementation encountered during QUICK follow up. Challenges were observed in the following health system domains: human, physical and intellectual resources, health system financing, and health system governance and delivery.

Chapter 5
Table 3 Operational and behavioral predictors of a blood pressure on target in hypertension patients during follow up visits at 3,6,9 and 12 months.

<table>
<thead>
<tr>
<th>Blood pressure on target, n=1236*</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed appointments in past 3 months: 1^</td>
<td>0.58</td>
<td>(0.36 - 0.95)</td>
<td>0.030</td>
</tr>
<tr>
<td>Missed appointments in past 3 months: 2</td>
<td>0.36</td>
<td>(0.19 - 0.68)</td>
<td>0.002</td>
</tr>
<tr>
<td>Missed appointments in past 3 months: &gt;2</td>
<td>0.35</td>
<td>(0.17 - 0.70)</td>
<td>0.003</td>
</tr>
<tr>
<td>Medium drug adherence Score#</td>
<td>1.91</td>
<td>(1.09 - 3.36)</td>
<td>0.024</td>
</tr>
<tr>
<td>High drug adherence Score</td>
<td>2.68</td>
<td>(1.59 - 4.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinic time 4-5 hours$</td>
<td>0.62</td>
<td>(0.36 - 1.07)</td>
<td>0.085</td>
</tr>
<tr>
<td>Clinic time 5-6 hours</td>
<td>0.51</td>
<td>(0.30 - 0.88)</td>
<td>0.016</td>
</tr>
<tr>
<td>Clinic time 6-7 hours</td>
<td>0.57</td>
<td>(0.33 - 1.00)</td>
<td>0.048</td>
</tr>
<tr>
<td>Clinic time 7+ hours</td>
<td>0.63</td>
<td>(0.36 - 1.11)</td>
<td>0.107</td>
</tr>
<tr>
<td>Smoking at baseline</td>
<td>0.27</td>
<td>(0.10 - 0.77)</td>
<td>0.015</td>
</tr>
<tr>
<td>Performing (moderate) exercise</td>
<td>1.89</td>
<td>(1.08 - 3.30)</td>
<td>0.025</td>
</tr>
<tr>
<td>Adding extra salt to meals</td>
<td>0.57</td>
<td>(0.34 - 0.98)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Note: Logistic regression adjusted for repeated measurements per patient using mixed models, 95%CI = 95% Confidence Interval. ^Reference: no missed appointments, #Reference: low adherence score, $Reference Clinic time 0-4 hours. Operational and behavioral variables significantly associated with treatment success are shown in the table. Confounding variables that were significantly associated with treatment success are listed in the legend below.

* Estimates corrected for gender, age, baseline blood pressure, having had a cardiovascular disease in the past, BMI, ethnicity, on treatment at inclusion, number and dose of drugs, number of follow-up visit, having smoked in the past, missing values in missed visit categories (n=12), interaction between number/dose of drugs and treatment status at inclusion, interaction between number of follow-up visit and treatment status at inclusion.

Table 4 Health system related barriers to effective guideline implementation as identified in QUICK, presented per health system framework domain.

<table>
<thead>
<tr>
<th>Barriers to care per health systems framework domain</th>
<th>Example from this study</th>
<th>Implication for care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human resources</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High turn-over of doctors</td>
<td>Besides the medical director, 10 doctors worked to fill 2 doctor vacancies in OOH between June 2010-Dec 2011, employment duration ranged from 1 month to 10 months.</td>
<td>Loss of knowledge and skills acquired during guideline training.</td>
</tr>
<tr>
<td>High workload doctors</td>
<td>No time for internal training or case review meetings.</td>
<td>Limited knowledge translation between doctors on guideline-based care.</td>
</tr>
<tr>
<td>Physical resources</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination drug formulas or higher dose formulations CVD prevention drugs not available</td>
<td>Over 90% of hypertension patients in QUICK cohort received multidrug therapy leading to large numbers of pills prescribed per day.</td>
<td>Risk of poor adherence to drugs.</td>
</tr>
<tr>
<td>Facilities for diabetes care insufficient</td>
<td>HbA1c tests not available, home-based insulin treatment not available (no facilities for home monitoring of glucose, insulin not affordable)</td>
<td>Only oral anti-diabetic treatment available.</td>
</tr>
<tr>
<td>Drug stock-outs</td>
<td>Several drug stock-outs. Patients needed to buy drugs outside clinic and pay out-of-pocket.</td>
<td>Risk of poor adherence to drugs.</td>
</tr>
<tr>
<td>Intellectual resources</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited knowledge and skills doctors</td>
<td>CVD risk stratification including TOD screening perceived as too complicated (e.g. ECG interpretation)</td>
<td>TOD screening not feasible in primary care settings.</td>
</tr>
</tbody>
</table>
DISCUSSION

Our study demonstrated that high quality CVD prevention care according to international guidelines\textsuperscript{2,8-10} can be provided within the context of a CBHI program, in a rural primary care setting in SSA. We observed a very high patient retention in care of over 90% and high scores on process and outcome quality indicators. Several factors are likely to have contributed to these results. First, the availability of insurance has most likely contributed to the high patient retention by removing the barrier of costs of care for patients. A pilot study in a health facility nearby the study clinic with a similar patient population but without access to insurance showed that many patients did not return after initial diagnosis. Most other prospective studies from SSA describing CVD prevention care programs, also report high loss to follow up rates, the majority over 50% at one year of follow up.\textsuperscript{19-24} Studies reporting higher patient retention provided free care.\textsuperscript{14,25} Second, the insurance program provided resources for quality improvement. Other elements that have likely contributed to the high quality of care include implementation of treatment algorithms based international guidelines, training and feedback sessions, and standardization of patient files and laboratory forms.
Our study also identified several health system barriers to CVD prevention care despite the availability of health insurance. The high workload and high turnover of doctors constrained knowledge translation between healthcare professionals. TOD screening as recommended by WHO guidelines was considered too complicated, too time consuming, and too expensive for use in routine clinic settings within the reimbursement system of the insurer. Similar financial constraints were reported for high dose multidrug regimes and insulin and HbA1c tests. The unaffordability of multidrug regimes may explain why almost none of the patients with uncontrolled blood pressure were prescribed the recommended maximum dose drug regime, although patient-related factors, such as poor drug adherence, may also have discouraged doctors from prescribing more drugs. The unavailability of insulin may have resulted in the relatively low blood glucose control in diabetes patients. Long waiting times in the clinic, travel costs to the clinic and income loss due to frequent clinic visits were shown to compromise patient adherence to monthly doctor’s appointments, thereby increasing the risk of treatment failure. However, monthly doctor’s appointments were considered necessary for patient retention in care and because alternative drug supply systems were not available. Similar barriers have also been reported by other studies from SSA.

We included patients attending a single private primary healthcare clinic in our study. Inclusion of patients attending public facilities and secondary and tertiary care facilities would have allowed us to measure setting-specific variations. However, 69% of total health expenditure in Nigeria are private expenditures and private facilities account for a high percentage of health expenditures. In addition, CVD prevention care should preferably be provided at a primary care level. Therefore, our study clinic represents a typical primary healthcare setting in SSA and many of our health system related findings can be generalized to other settings in SSA.

The facilitation of TOD screening may have led to a bias towards better blood pressure control rates, since guidelines recommend a multidrug regime for patients with grade 1 hypertension and TOD. However, only 15 patients with grade 1 hypertension combined with TOD were receiving monotherapy at baseline, other patients were already on multidrug regimes. In only 10 of these patients treatment was intensified. Therefore, we believe the TOD screening facilitation did not affect the blood pressure control rates observed in our study.

Studies from high income countries describing quality of CVD prevention care in primary care practices using the QOF indicators, reported similar scores on the outcome indicators as observed in our study. Achievement of process indicators ranged between 70% to over 90% Achievement of outcome indicators ranged from 33% to 81% for blood pressure control in hypertensive and diabetes patients, 40% to 71% for diabetes control (based on HbA1c values) and 34% to 83% for cholesterol control in diabetes. Studies from high income countries examining blood pressure control in black populations, in whom blood pressure control is more difficult to achieve than in Caucasian populations, reported lower control rates than observed in our study, ranging from 14% to 59% in treated hypertension patients. In addition, several prospective studies from SSA evaluated CVD prevention
Most studies focused on treatment outcomes only, without reporting process outcomes or systematically collected data on health system related barriers to guideline implementation. The inclusion of quality indicators and health system barriers to care as outcome measures in our study allowed analysis of the problems that limit effective CVD prevention care implementation. Other strengths of our study include the prospectively collected data, the intensive monitoring of data quality and the low loss to study follow up. Therefore, our study provides high quality data from an understudied region in the world that can be used for the design of urgently needed CVD prevention programs in SSA.

Our study demonstrated that implementation of CVD prevention care was feasible within a CBHI program. However, provision of high quality care was resource intense and involved considerable costs (chapter seven). Rapid scale-up of CVD prevention care in SSA according to current WHO CVD prevention guidelines may be too demanding, especially in settings where CBHI programs are not available. Therefore, more efficient models of care delivery should be explored. Simplified treatment protocols could facilitate task-shifting to nurses and community-health workers and facilitate alternative drug supply systems such as mobile pharmacies. A fixed-dose combination pill (the so-called “polypill”) containing cheap generic anti-hypertensive drugs and a statin for all patients at risk of CVD may be a promising opportunity for primary care settings in SSA due to its simplicity, promise of better patient adherence and potential for cost reduction. Expensive TOD screening and complicated drug regimes with step-wise drug titration would no longer be needed for the majority of patients as all patients at risk of CVD would receive multi-drug therapy irrespective of individual risk profiles. Simple treatment protocols with combination pills and partial task-shifting to medical assistants were also key elements of a recent, very successful, quality improvement program for hypertension within an insurance program from the United States that resulted in blood pressure control rates of over 80%. However, more research is needed to establish effectiveness and safety of these new interventions.

CONCLUSION

Our study demonstrated that high quality CVD prevention care can be successfully implemented in a primary care setting in rural SSA within the context of a CBHI program. However, provision of guideline-based care was resource intense and the identified health system related barriers to care may threaten the rapid scale-up of services. Therefore, more simple models of CVD prevention care delivery are needed to expand coverage of CVD prevention services in SSA.

ACKNOWLEDGEMENTS

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REFERENCES


SUPPLEMENTAL DIGITAL CONTENT 1

Study setting
The Health Insurance Fund
The insurance program was funded by the Health Insurance Fund (HIF). The HIF is a program which originated from the international development organization PharmAccess. The PharmAccess Group is committed to providing access to quality healthcare for low- and middle-income groups in several African countries through innovative financing mechanisms and improvement of the quality of healthcare. The HIF is developing and supporting the implementation of community-based health insurance (CBHI) programs, which focus on the informal sector. Although a clear definition of CBHI (also called health insurance for the informal sector or micro-health insurance) is lacking, the term usually refers to not-for-profit, voluntary health insurance with a focus on individuals who work in the informal sector or who are unemployed, and community empowerment. The aim of the HIF program is twofold: improving the demand for and access to healthcare, by introducing CBHI for individuals with low and middle incomes as well as improving the quality of care provided in these communities. The key elements on the demand side of the HIF program are the focus on organized groups in the informal sector and their dependents, for example communities of farmers; the provision of subsidized insurance premiums; co-payment of the premium by enrollees to encourage the groups to demand quality care; and voluntary enrolment. On the supply side, the key elements include capacity building, quality assurance, involvement of the private and public sector, focus on performance-based financing, and management support.

The HIF program uses a public-private partnership model and is implemented by PharmAccess and private African Health Maintenance Organizations (HMOs) or health insurance companies. The HMOs are responsible for execution of the program and for contracting a network of healthcare providers to provide the care for the enrollees. Donor money - from both international and local sources - is used to develop and set up the insurance program and to upgrade the medical and administrative capacity of the insurers and healthcare providers contracted under the program. The payment of healthcare providers is related to their performance. The program started in Lagos and Kwara State in Nigeria in 2007 in collaboration with the HMO Hygeia Limited under the name of Hygeia Community Health Care (HCHC).

Quality assurance within HCHC program
Quality and efficiency of care in health facilities participating in the HCHC program are monitored through independent audits of an international quality improvement and assessment body called SafeCare, a partnership of PharmAccess, the American Joint Commission International and the South-African Council for Health Services Accreditation of Southern Africa. When a healthcare provider is contracted by an HMO, a baseline assessment in the health facility is conducted by SafeCare and a quality improvement plan is formulated. The improvement plans are implemented by the healthcare providers with technical and financial support from the HMO while SafeCare monitors the progress on quality improvement through annual follow-up assessments with the SafeCare Quality Standards. Examples of quality improvement
interventions include implementation of treatment guidelines (for example for hypertension), training of staff in guideline-based care, upgrading of laboratory equipment and training of laboratory staff to enable basic laboratory testing, assurance of continuous essential drug supplies, adequate medical file keeping, waste management protocols and hospital infection control protocols.

The HCHC program in Kwara
Since 2007, the HCHC program has been rolled out in three regions in Kwara State. Over 64,000 people were enrolled in the HCHC program in April 2014 in all three regions. The details and advantages of the health insurance program were communicated to the public by the HMO through several channels. Activities included face to face information sharing (e.g. through house visits by enrolment officers, health education and advocacy visits to community opinion leaders) and large-scale communication and marketing activities in the target communities (through billboards, comics, brochures, flyers and announcements on the radio). All households living in the districts in which the program is operational are eligible for enrolment. Individuals can register in the communities during community outreach activities of the insurer or in the health facilities participating in the program. There is no pre-enrolment screening for chronic diseases. After enrolment, new members can access care from the first day of the next month. Beneficiaries are enrolled individually (as opposed to household enrolment) on an annual basis and pay a share of the premium, the so called co-premium. The co-premium ranges from 0.15% of the average annual per capita consumption (a socioeconomic measure of wealth based on household expenditures on food and non food items) for the lowest wealth quintile to 0.04% for the highest wealth quintile (consumption data 2009, corrected for inflation). The program does not include deductibles. The total cost of the yearly insurance premium was 28 USD in May 2014. The Kwara State Government pays 60% of the premium, the participants 12% and the HIF 28%. The Kwara State Government started contributing to the premium subsidies in 2009. Its contribution has increased from 20% to 60% and it plans to eventually take over all costs of the premium subsidy. Prior to 2009, the HIF paid the greater part of the premium subsidy through a grant from the Dutch Ministry of Foreign Affairs. The transfer of premium payment from the HIF to the Kwara State Government is evidence of local political commitment and ownership which is needed to ensure the financial sustainability of the program.

Coverage within the HCHC program in Kwara
The insurance package provides coverage for consultations, diagnostic tests and drugs for all disease categories, including hypertension and diabetes, that can be managed at a primary care level and limited coverage of secondary care services. Secondary care services provided include radiological and more complex laboratory diagnostic tests, hospital admissions for different disease categories, minor and intermediate surgery, antenatal care and delivery care, neonatal care, immunizations, annual check-ups and HIV/AIDS treatment. Excluded from the program are high technology investigations (CT, MRI), major surgeries and complex eye surgeries, family planning commodities, treatment for substance abuse/addiction, cancer care requiring chemotherapy and radiation therapy, provision of spectacles, contact lenses and hearing aids, dental care, intensive care treatment and dialyses. Management of acute cardiovascular events such as
thrombolysis for stroke or for myocardial infarction is excluded. In case of an acute cardiovascular event, admission to a hospital for supportive care is covered including for example treatment with intravenous fluids, and antibiotics for infectious complications. The HMO has contracted 18 public and private health facilities to provide the care for their enrollees. Most health facilities are primary and secondary care clinics that provide outpatient services and have admission capacity. Referral to two tertiary health facilities in Ilorin, the Kwara State capital, is possible if needed. There is no limit to the number of visits to the health facilities for patients but as a large share of the payment from the insurer to the healthcare provider is paid through capitation fees, healthcare providers are encouraged to prevent overutilization of services.

Methods

Sample size

The number of patients needed for reliable scoring of quality indicators differs per indicator and ranges from less than 50 patients to over 100 patients to achieve 90% confidence intervals of +/- 10 points on estimated pass rates. Therefore, the target sample size of 300 patients was based on the secondary outcome of number of patients in whom CVD risk factors were treated successfully. Assuming 30% of patients would be treated successfully, 300 patients would provide sufficiently narrow confidence limits around the estimate (95% CI: 24.9% - 35.5%). The aim was to include 150 patients who were attending the clinic for CVD preventive drug treatment prior to the start of the study, and 150 patients who had not received any CVD preventive drug treatment for at least one year upon inclusion. Evaluation of the feasibility to reach the distribution across the two subgroups took place three months after the start of inclusion, according to protocol. Because the majority of included patients were already receiving treatment upon inclusion, the sample size was increased to 350 and the last 50 patients included were limited to patients who were not yet receiving treatment.

Definitions

Glucose at target level was defined as fasting plasma glucose < 7.0 mmol/l or random plasma glucose of <12 mmol/l.

Lipid control was defined according to World Health Organization recommendations. Target levels for primary prevention were total cholesterol < 5.0 mmol/L and LDL cholesterol < 3.0 mmol/l. Targets for secondary prevention were total cholesterol < 4.0 mmol/L and LDL cholesterol < 2.5 mmol/l.

Presence of renal impairment was defined as an estimated Glomerular Filtration Rate < 60 mL/min/1.73m2.

Target organ damage was defined as ECG-based LVH according to Sokolov Lyon criteria, renal impairment, pathological Q waves on ECG, stroke or angina pectoris. Microalbuminuria was excluded from this definition as a community-based study in an area nearby demonstrated microalbuminuria was also prevalent in non-hypertensive subjects, indicating it was not a good marker for hypertensive target organ damage in this population. Proteinuria was excluded as it was not feasible to get accurate results based on a quantitative dipstick analysis.
Hypertension was classified according to JNC7 guidelines, adherence was scored using the Morisky scale.

Data collection
Patients were seen by a study nurse every three months, in addition to their regular doctor’s appointments. Patients were reminded of their study visits by telephone and text messages or during market days in the community. If patients could not be reached and did not show for study visits, a home visit by the study nurse was undertaken to assess the reason for no show. For regular doctor’s appointments, no reminders were sent and no home visits were undertaken.

Data monitoring
All Case Record Forms at the study site were checked weekly by a clinical research associate (CRA) for inconsistencies before double data entry. Entered data were also monitored for inconsistencies and data query reports were resolved at the study site on a three monthly basis using source documents. Three monthly monitoring visits to the study site and data entry unit were conducted by a CRA to monitor adherence to the study protocol and procedures by study staff.

REFERENCES
Chapter 5


SUPPLEMENTAL DIGITAL CONTENT 2

Figure 1 Flowchart for treatment of diabetes used in Ogo Oluwa hospital

DM  Diabetes mellitus
FBG  Fasting blood glucose
PE  Physical Examination
RBG  Random blood glucose
TOD  Target organ damage
**TOD/RF screening:** smoking, dyslipidemia, family history premature CVD (age < 55 M < 65 F), (abdominal) obesity
Blood tests: potassium, creatinine, lipid profile, glucose
Urine tests: microalbuminuria/proteinuria
ECG

---

**Screening**
Blood pressure (see CVD risk assessment chart) + PE
TOD/additional risk factors once p/year**
Neuropathy screening once per year
Retinal screening/check vision once p/y
Foot examination once per year (ulcers/puslions)

---

**Lifestyle advice**

FBG ≥ 7 mmol/L
Or RBG ≥ 12 mol/l

---

metformin 500mg o.d.*

---

FBG ≥ 7 mmol/L
Or RBG ≥ 12 mol/l

---

Increase metformin to 500mg b.d., then t.d.s, then 1000mg t.d.s.*

---

FBG ≥ 7 mmol/L
Or RBG ≥ 14 mol/l

---

Add glibenclamide 5 mg o.d., then 5 mg b.d., then 5 mg t.d.s.*

---

FBG ≥ 7 mmol/L
Or RBG ≥ 14 mol/l

---

Refer patient

---

Visit frequency every 2 weeks during treatment installation/increase of dosage. If stable once per 1-3 months
2 measurements needed before dosage increase

---

*Do not increase dose/add drugs in case of symptoms of hypoglycemia
Visit frequency every 2 weeks during treatment installation/increase of dosage. If stable once per 1-3 months
2 measurements needed before dosage increase

---

Feasibility and quality of cardiovascular disease prevention
COMPELLING INDICATIONS:
- Heart Failure
- Post myocardial infarction/Angina pectoris
- Diabetes
- Chronic Kidney Disease
- Recurrent stroke prevention
- High coronary disease risk: 3 out of 5 of the following risk factors: smoking, dyslipidemia, family history premature CVD (age < 55 M <65 F), microalbuminuria, left ventricular hypertrophy.

Figure 2 CVD risk assessment and treatment. Choices of drugs are based on international guidelines+5 and local availability

ACEI Angiotensin Converting Enzyme Inhibitor
AP Angina pectoris
DBP Diastolic blood pressure
SBP Systolic blood pressure
MI Myocardial infarction
RF Risk factors
TC Total Cholesterol
TOD target organ damage

Visit frequency every 2 weeks during treatment
Installation/increase of dosage.
If stable once per month.

Women in fertile age
- NO ACEI (Captopril)
- Treat with Methyldopa (start 250 mg b.d.) and Nifedipine SR (start 20mg b.d.).
- Pregnant women (cut off 160/110 mmHg):
  - NO ACEI, quit smoking during pregnancy.
  - Treat with Methyldopa (start 250 mg b.d.).
  - If not on target: add Nifedipine SR (start 20mg b.d.), or Hydralazine 20 mg t.d.

Add simvastatin 20 mg o.d.

BP not on target: increase dose or add new drug
ADD Captopril 12.5 mg b.d

BP not on target: increase dose or add new drug
ADD Moduretic 5/50 mg o.d.

BP not on target: increase dose to Nifedipine SR 60 mg b.d
Captopril 50 mg b.d.
Moduretic 5/50 o.d.
Refer if this is insufficient
Table 1  Risk factor control at baseline compared to at 12 months follow up per risk factor

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Baseline</th>
<th>12 months</th>
<th>p-value</th>
<th>Baseline</th>
<th>12 months</th>
<th>p-value</th>
<th>Baseline</th>
<th>12 months</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure control in HT</td>
<td>331 (48.9)</td>
<td>162 (67.2)</td>
<td>&lt;0.001</td>
<td>213 (75.1)</td>
<td>160 (69.8)</td>
<td>(1.7)</td>
<td>118 (106)</td>
<td>106 (66)</td>
<td>(62.3)</td>
</tr>
<tr>
<td>Glucose control in DM</td>
<td>49 (34.7)</td>
<td>17 (44.2)</td>
<td>0.352</td>
<td>40 (37.5)</td>
<td>15 (45.7)</td>
<td></td>
<td>9 (22.2)</td>
<td>2 (8)</td>
<td>3</td>
</tr>
<tr>
<td>Lipid control</td>
<td>349 (54.2)</td>
<td>189 (57.6)</td>
<td>0.371</td>
<td>229 (50.7)</td>
<td>116 (35.6)</td>
<td>(60.8)</td>
<td>120 (107)</td>
<td>73 (66)</td>
<td>(61.7)</td>
</tr>
<tr>
<td>Presence of LVH</td>
<td>349 (10.9)</td>
<td>323 (29.7)</td>
<td>0.933</td>
<td>229 (26.6)</td>
<td>61 (26.4)</td>
<td>(19.2)</td>
<td>120 (39)</td>
<td>47 (39)</td>
<td>(36.4)</td>
</tr>
<tr>
<td>Presence of renal impairment</td>
<td>349 (12.0)</td>
<td>323 (7.1)</td>
<td>0.011</td>
<td>229 (15.7)</td>
<td>36 (8.8)</td>
<td></td>
<td>120 (6)</td>
<td>6 (4)</td>
<td>4</td>
</tr>
<tr>
<td>Smoking</td>
<td>349 (3.7)</td>
<td>13 (2.8)</td>
<td>0.504</td>
<td>229 (2.2)</td>
<td>5 (1.9)</td>
<td></td>
<td>120 (8)</td>
<td>4 (5)</td>
<td>5</td>
</tr>
</tbody>
</table>

HT= hypertension, DM= diabetes, LVH = left ventricular hypertrophy

Table 2  Operational and behavioral predictors of a missed doctor appointment, and high adherence to drugs in hypertension patients during follow up visits at 3, 6, 9 and 12 months

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odds ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed appointment, n=1236*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium drug adherence score</td>
<td>0.20 (0.12 - 0.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High drug adherence score</td>
<td>0.06 (0.03 - 0.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High travel costs</td>
<td>1.96 (1.01 - 3.84)</td>
<td>0.048</td>
</tr>
<tr>
<td>Clinic time 4-5 hours $</td>
<td>1.30 (0.70 - 2.40)</td>
<td>0.400</td>
</tr>
<tr>
<td>Clinic time 5-6 hours</td>
<td>2.18 (1.21 - 3.94)</td>
<td>0.010</td>
</tr>
<tr>
<td>Clinic time 6-7 hours</td>
<td>1.74 (0.96 - 3.16)</td>
<td>0.070</td>
</tr>
<tr>
<td>Clinic time 7+ hours</td>
<td>1.50 (0.82 - 2.75)</td>
<td>0.191</td>
</tr>
<tr>
<td>Income loss due to appointment</td>
<td>1.53 (1.03 - 2.27)</td>
<td>0.036</td>
</tr>
<tr>
<td>Private travel means</td>
<td>3.00 (1.04 - 8.68)</td>
<td>0.042</td>
</tr>
<tr>
<td>High adherence to drugs, n= 1210**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Having missed an appointment in the past 3 months</td>
<td>0.32 (0.20 - 0.52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High adherence to lifestyle advice</td>
<td>2.71 (1.53 - 4.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Experiencing side effects of drugs</td>
<td>0.13 (0.08 - 0.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patient ran out of drugs</td>
<td>0.07 (0.04 - 0.13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Expenditure on drug (when out of stock)</td>
<td>10.50 (5.47 - 20.17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Expenditure on drug (without out of stock)</td>
<td>1.20 (0.24 - 5.93)</td>
<td>0.825</td>
</tr>
</tbody>
</table>

Note: Logistic regression adjusted for repeated measurements per patient using mixed models. 95%CI = 95% Confident Interval. Reference: low adherence score, $Reference Clinic time 0-4 hours. Operational and behavioral variables significantly associated with missing appointments and high adherence are shown in the table. Confounding variables that were significantly associated with treatment success are listed for each model in the legend below. * Estimates corrected for gender, age, on treatment at inclusion, missing values in any income loss (n=12), adherence (n=26) and high travel costs (n=9). **Estimates corrected for gender, age, number of follow-up visit and missing values for high adherence to lifestyle.