Cardiovascular risk in Mozambique: who should be treated for hypertension?

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Aim: To estimate the proportion of Mozambicans eligible for pharmacological treatment for hypertension, according to single risk factor and total cardiovascular risk approaches.

Methods: A representative sample of Mozambicans aged 40–64 years (n = 1116) was evaluated according to the WHO STEPwise Approach to Chronic Disease Risk Factor Surveillance (STEPS). We measured blood pressure (BP) and 12-h fasting blood glucose levels and collected data on sociodemographic characteristics, smoking, and use of antidiabetic and antihypertensive drugs. We estimated the 10-year risk of a fatal or nonfatal major cardiovascular event (WHO/International Society of Hypertension risk prediction charts), and computed the proportion of untreated participants eligible for pharmacological treatment for hypertension, according to BP values alone and accounting also for the total cardiovascular risk (WHO guidelines for assessment and management of cardiovascular diseases).

Results: Among the Mozambicans aged 40–64 years and not taking antihypertensive drugs, less than 4% were classified as having cardiovascular risk at least 20% whereas the prevalence of SBP/DBP at least 140/90 mmHg was nearly 40%. A total of 19.8% of 40–64-year-olds would be eligible for pharmacological treatment of hypertension according to the WHO guidelines, all of whom had SBP/DBP at least 160/100 mmHg.

Conclusion: Among the Mozambicans aged 40–64 years and not taking antihypertensive drugs and having SBP/DBP at least 140/90 mmHg, only half were eligible for pharmacological treatment according to the WHO guidelines. Taking the latter into account, when defining strategies to control hypertension at a population level, may allow a more efficient use of the scarce resources available in developing settings.

Keywords: diabetes mellitus, hypertension, Mozambique, risk assessment, smoking

Abbreviations: BP, blood pressure; FBG, fasting blood glucose; ISH, International Society of Hypertension; STEPS, STEPwise Approach to Chronic Disease Risk Factor Surveillance; USD, United States Dollar

INTRODUCTION

Cardiovascular diseases are the leading cause of death worldwide [1], estimated to become responsible for almost 25 million deaths by 2030, mostly from heart disease and stroke [2]. Although the mortality rates have been declining in industrialized countries since the late twentieth century [3], they are rapidly increasing in most developing nations [4].

In Mozambique, hypertension affects one-third of the adult population [5] and cardiovascular diseases already have an important public health impact [6–8], especially stroke, and mainly among older dwellers from urban areas [9]. In 1994, cerebrovascular diseases were the leading cause of death among Maputo inhabitants aged over 60 [6]. Between 2005 and 2006, the incidence of stroke hospitalization in Maputo was estimated to be 148.7 per 100,000, one of the highest in developing settings [7], and the early case-fatality rates were also high [8].

The Framingham Heart Study led the way to the development of cardiovascular risk prediction equations for assessment of absolute risk that have resulted in a paradigm shift in prevention strategies, from addressing a single risk factor (e.g. hypertension) to a more cost-effective total cardiovascular risk approach [10]. More recently, the WHO and the International Society of Hypertension (ISH) developed a tool that enables cardiovascular risk assessment in low-income countries [11].

Thus, we aimed to estimate the proportion of the Mozambican population in different cardiovascular risk categories, according to the WHO/ISH risk prediction charts, as well as the prevalence of eligibility for treatment

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with antihypertensive drugs, following different criteria, both according to the single risk factor and the total risk approaches.

METHODS

The present study was based on a survey that evaluated a representative sample of the Mozambican adults aged 25–64 years, between September and November 2005, as previously described in detail [5]. Briefly, using a sampling frame derived from the 1997 Mozambican census, 95 geographical clusters were selected across 11 strata (provinces). In each cluster, all the households were listed and 25 randomly selected and visited. In each household selected, all the individuals in the eligible age range were invited to participate (n = 3378); 55 refused and the remaining (98.4% of the invited) were evaluated at their homes by trained interviewers, following the WHO STEPwise Approach to Chronic Disease Risk Factor Surveillance (STEPS) [12]. This consisted of a face-to-face interview using a structured questionnaire to collect information on sociodemographic characteristics, lifestyles (including tobacco smoking), and medical history (including the use of antihypertensive and antidiabetic drugs), as well as physical measurements (including blood pressure (BP)), and the assessment of 12-h fasting glucose levels.

The classification of the place of residence as urban (in any of the 23 cities and 68 towns) or rural (outside cities or towns) and the definition of categories for the highest level of education attained (<1; 1–5; ≥6 years) were done in accordance with the 1997 census [13].

To assess the smoking status, the participants were asked whether they currently smoked any tobacco product, including manufactured cigarettes, hand-rolled cigarettes, cigars, and pipe. Participants were also asked whether they smoked in the past on a daily basis and ex-smokers were asked for how long they quit smoking. Participants who were smokers at the time of the interview and ex-smokers who stopped smoking for less than 1 year were classified as smokers, according to the WHO guidelines for assessment and management of cardiovascular risk [14].

BP was measured in the sitting position on a single occasion by nonphysician trained interviewers using a semiautomatic sphygmomanometer (Omron 3) with an appropriate cuff size. After a 5-min rest, BP was measured twice, 1 min apart, and a third measurement was performed if the difference between the first two was more than 10 mmHg for SBP or DBP. For analysis, we used the mean of the two measurements or the mean of the last two when three measurements were taken.

Participants reporting the use of antihypertensive drugs in the previous 2 weeks were considered to be treated pharmacologically for hypertension and were not further considered for data analysis. The untreated participants (93%) were grouped according to the SBP/DBP cut-offs that underlie the WHO eligibility criteria for treatment with antihypertensive drugs, namely less than 130/80, at least 130/80 and less than 140/90, at least 140/90 and less than 160/100, and at least 160/100 mmHg [15].

Twelve-hour fasting blood glucose (FBG) levels were obtained in accordance with WHO standardized fingertip prick tests, using calibrated blood glucose meters and reagent strips (Accu-Chek Advantage meter; Roche Diagnostics Corporation, Indianapolis, Indiana, USA). Participants who reported to have diabetes diagnosed by a health professional within the previous 12 months were asked whether they currently use insulin or oral blood glucose-lowering drugs. Participants were classified as having diabetes when their FBG concentration was above 7.0 mmol/l, or when reporting to take insulin or oral antidiabetic drugs [14].

The WHO/ISH prediction charts for Africa E (WHO African subregion with high child and very high adult mortality) were used to classify each participant regarding the individual absolute cardiovascular risk, based on sex (male/female), age (40–49, 50–59, and ≥59 years), current smoking status (nonsmoker/smoker), SBP (<140, 140–159, 160–179, and ≥180 mmHg), and diabetes (presence/absence).

The WHO/ISH prediction charts estimate the 10-year risk of a fatal or nonfatal major cardiovascular event (myocardial infarction or stroke) expressed in four categories – less than 10% (low), 10–19% (moderate), 20–29% (high), and at least 30% (very high) – in people who do not have established cardiovascular diseases [14].

The eligibility for treatment with antihypertensive drugs was defined according to the single risk factor approach (SBP/DBP ≥140/90 mmHg or SBP/DBP ≥160/100 mmHg), and according to the WHO guidelines for assessment and management of cardiovascular risk [15]. The WHO guidelines recommend that all individuals with persistent BP at least 160/100 mmHg, and those with total risk at least 30% with persistent BP at least 130/80 mmHg, should be submitted to drug treatment, in addition to receiving specific lifestyle advice to lower their BP and risk of cardiovascular diseases. Antihypertensive drugs are also recommended for individuals with risk at least 20% with persistent BP at least 140/90 mmHg who are unable to lower BP through lifestyle strategies with professional assistance within 4–6 months [14] (Fig. 1).

Statistical analysis

For the present analyses, only the participants aged 40 or more years were considered, as those are the target population of the WHO/ISH prediction charts. From a total of 1519 participants aged 40–64 years, 315 were excluded because of missing information on BP and/or blood glucose; the latter were not significantly different from the 1204 participants considered for analysis regarding place of residence, sex, age, or education. Participants who did not follow the 12 h of fasting or with no information regarding the fulfilment of this prerequisite (n = 100) were not excluded; these were less educated (≥6 years: 10.6 vs. 20.9%, P = 0.012), but not significantly different from the remaining regarding place of residence, sex, or age. We further excluded 88 participants who were being treated with antihypertensive drugs, and 1116 participants were considered for data analysis (Fig. 2).

We estimated the proportion of participants classified in different categories of total cardiovascular risk, as well as the proportion of subjects eligible for treatment with antihypertensive drugs (according to different criteria), by sociodemographic characteristics. Adjusted prevalences
and respective 95% confidence intervals (95% CIs) were computed through unconditional logistic regression.

Data analysis was conducted using STATA, version 11.2 (Stata Corporation, College Station, Texas, USA). As stratified sampling resulted in a similar number of participants across strata with unequal population size, sampling weights were computed taking into account the number of participants evaluated in each stratum in relation to the number of participants expected per stratum, according to the population projections for the same period [16]. All analyses were conducted considering the sampling weights, to ensure that the computed estimates reflect the prevalence in Mozambique. The standard errors were estimated taking into account the effect of stratification, and clustering at the primary sampling unit level. All statistical tests were two-sided.

Ethics
The study protocol was approved by the National Mozambican Ethics Committee and written informed consent was obtained from all participants.

RESULTS
Characteristics of the study sample
Approximately two-thirds of the population under study lived in rural areas, nearly 15% were older than 59 years, and almost half of the participants had no formal education. Nearly 40% of the participants showed a SBP above 139 mmHg, and approximately 2% were classified as having diabetes. Smoking was reported by approximately one-third of the population (Table 1).

Total cardiovascular risk
Most of the participants were classified as having low (<10%) 10-year cardiovascular risk (90.2%; 95% CI 87.0–93.3). The prevalences were 6.7% (95% CI 4.0–9.4), 1.7% (95% CI 0.8–2.5), and 1.4% (95% CI 0.5–2.3), for the cardiovascular risk categories 10–19, 20–29, and at least 30%, respectively. The prevalence of total cardiovascular risk at least 20% increased with age and was higher among the urban participants (Fig. 3).

Eligibility for treatment with antihypertensive drugs
All the participants eligible for treatment with antihypertensive drugs according to the WHO guidelines for assessment and management of cardiovascular risk (19.8%) also had SBP/DBP at least 160/100 mmHg, and most of these were classified as having low (<10%) cardiovascular risk. Approximately, one-fifth of the overall sample was estimated to have a cardiovascular risk under 10%, but SBP/DBP at least 140/90 mmHg, meeting therefore the criteria for continuing lifestyle strategies to lower BP and to have their BP and total cardiovascular risk reassessed every 2–5 years depending on clinical circumstances and resource availability (Fig. 4). Among the diabetic patients, 58.6% were eligible for treatment with antihypertensive drugs and 14.7% had SBP/DBP at least 140/90, but total cardiovascular risk less than 10%.

FIGURE 1 Criteria used to define eligibility for pharmacological treatment for hypertension, according to WHO guidelines [15]. BP, blood pressure; CV, cardiovascular.
The prevalence of eligibility for pharmacological treatment of hypertension was 41.0%, if all participants with SBP/DBP at least 140/90 mmHg were to be considered and 19.8% according to the WHO guidelines. The prevalences were higher in urban areas and among women, and increased with age regardless of the criteria used. There were also higher proportions of more educated participants eligible for treatment, although the differences were not statistically significant (Table 2).

## DISCUSSION

Among the Mozambicans aged 40–64 years, less than 4% were classified as having cardiovascular risk at least 20%, whereas the prevalence of SBP/DBP at least 140/90 mmHg was nearly 40%. According to the WHO guidelines for assessment and management of cardiovascular diseases, almost one-fifth of the participants would be eligible for treatment with antihypertensive drugs.

In 2009, we reported on the prevalence, awareness, treatment, and control of hypertension in adult Mozambicans [5]; one of the most important findings was that less than 10% of the participants classified as hypertensive were under pharmacological treatment. The present study adds to our previous research on this topic the assessment of the 10-year risk of a fatal or nonfatal major cardiovascular event in the population aged at least 40 years who was not receiving pharmacological treatment for hypertension. This provided the basis to estimate the proportion of individuals eligible for treatment with antihypertensive drugs according to different criteria, including those defined in the WHO guidelines for assessment and management of cardiovascular diseases, which account simultaneously for the levels of BP and the total cardiovascular risk. However, some potential limitations need to be discussed.

We used the WHO/ISH prediction charts for settings in which blood cholesterol cannot be measured, as no such data were available in our study [11]. In the clinical context, lipid assays may also be used only in patients with high cardiovascular risk defined by other criteria, and therefore not considering cholesterol in a risk-prediction model does not necessarily limit the ability to assess cardiovascular risk at a population level [17].

We opted to include in the analyses the participants who did not follow the 12-h fasting or those with no information regarding the fulfilment of this prerequisite. This may have contributed to an overestimation of the cardiovascular risk, but is expected to have a minor impact on our results and conclusions, given the very low prevalence of diabetes in this population.

BP was measured on a single occasion instead of two occasions as recommended by the WHO/ISH [15], which may have contributed to an overestimation of BP [18] and consequently cardiovascular risk and prevalence of eligibility for treatment with antihypertensive drugs. Nevertheless, among participants classified as having SBP/DBP at least 160/100 mmHg, the mean SBP and DBP was 176 and 97 mmHg, respectively. Furthermore, this is not expected to compromise the comparison of estimates of eligibility according to different criteria.

People with established cardiovascular diseases, namely angina or intermittent claudication, or who have had a myocardial infarction, transient ischemic attack, or stroke, should be considered to be at very high cardiovascular risk of coronary, cerebral and peripheral vascular events and death, regardless of their risk factor levels. Although we do not have such information in this study, the prevalence of these conditions is expectedly low, due to the high case fatality associated with major cardiovascular events [7,8].

According to the WHO guidelines, the individuals with cardiovascular risk between 20 and 29% and SBP/DBP at least 140/90 mmHg and less than 160/100 mmHg are eligible for drug treatment, if they are unable to lower BP through lifestyle strategies with professional assistance within 4–6 months. Although the latter information was not available in our STEPS survey, there were no participants in this category.

Our estimates of the cardiovascular risk distribution in Mozambique are in line with those described in Seychelles [19] and in Nigeria [20], where the prevalence of total cardiovascular risk at least 20% was 5%, and similar figures were reported in other non-African low-income and middle-income countries [20,21]. In a survey aiming at estimating the total cardiovascular risk in eight countries from different regions, the proportion of the population with cardiovascular risk at least 20% ranged from 1.1% in
China to 10.0% in Pakistan [20]. More recently, in a study based on data from STEPS surveys conducted in Asian countries [21], the prevalence of WHO/ISH cardiovascular risk at least 20% was 1.3% in Cambodia, 2.3% in Malaysia, and 6% in Mongolia. In these multicountry surveys, the prevalence of BP at least 140/90 mmHg was three-fold to 20-fold higher than the prevalence of high and very high cardiovascular risk (≥20%), in accordance with our observations in Mozambique.

The total cardiovascular risk approach seems to be more cost-effective to prevent cardiovascular events than the single risk factor approach. Gaziano et al. [22] compared six strategies for initiation of drug treatment – two based on BP levels alone (SBP/DBP: >160/95 and >140/90 mmHg) and four based on the total cardiovascular risk approach (10-year risk of a fatal or nonfatal major cardiovascular event: 40, 30, 20, and 15%) in South Africa. The authors concluded that hypertension treatment based on the total cardiovascular risk is more effective at saving lives and less costly than those based only on the BP level. Also, a study conducted in Seychelles [19] compared distinct risk management strategies for the prevention of cardiovascular events – single risk factor management (high BP and/or high serum cholesterol), total cardiovascular risk

### TABLE 1. Characteristics of the participants

<table>
<thead>
<tr>
<th></th>
<th>Participants (n = 1116)</th>
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<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>Unweighted (%)</td>
<td>Weighted (%)</td>
</tr>
<tr>
<td>Place of residence</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Urban</td>
<td>549 (49.2)</td>
<td>49.2</td>
<td>31.8</td>
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<tr>
<td>Rural</td>
<td>567 (50.8)</td>
<td>50.8</td>
<td>68.2</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Women</td>
<td>629 (56.4)</td>
<td>56.4</td>
<td>51.7</td>
</tr>
<tr>
<td>Men</td>
<td>487 (43.6)</td>
<td>43.6</td>
<td>48.3</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>257 (23.0)</td>
<td>23.0</td>
<td>21.7</td>
</tr>
<tr>
<td>50–59</td>
<td>138 (12.4)</td>
<td>12.4</td>
<td>10.3</td>
</tr>
<tr>
<td>60–64</td>
<td>94 (8.4)</td>
<td>8.4</td>
<td>6.7</td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>26 (2.3)</td>
<td>2.3</td>
<td>1.8</td>
</tr>
<tr>
<td>≥1 and &lt;6</td>
<td>514 (46.1)</td>
<td>46.1</td>
<td>42.7</td>
</tr>
<tr>
<td>≥6</td>
<td>174 (15.6)</td>
<td>15.6</td>
<td>11.4</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;140</td>
<td>627 (56.2)</td>
<td>56.2</td>
<td>61.3</td>
</tr>
<tr>
<td>≥140 and &lt;160</td>
<td>257 (23.0)</td>
<td>23.0</td>
<td>21.7</td>
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<tr>
<td>≥160 and &lt;180</td>
<td>138 (12.4)</td>
<td>12.4</td>
<td>10.3</td>
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<tr>
<td>≥180</td>
<td>94 (8.4)</td>
<td>8.4</td>
<td>6.7</td>
</tr>
<tr>
<td>Diabetes*</td>
<td>26 (2.3)</td>
<td>2.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Smoking</td>
<td>320 (28.7)</td>
<td>28.7</td>
<td>33.9</td>
</tr>
</tbody>
</table>

*Fasting blood glucose more than 7.0 mmol/l or treatment with insulin or oral hypoglycemic drugs.

FIGURE 3 Prevalence of total cardiovascular risk groups among Mozambicans aged 40–64 years, according to place of residence, sex, and age.
management, and WHO guidelines. The number of individuals eligible for treatment is much lower when considering the total risk approach (total cardiovascular risk $\geq 10\%$) while averting a higher number of cardiovascular events than when treating patients with BP at least 140/90 mmHg. Considering the WHO guidelines, the number of individuals eligible for treatment (both with antihypertensive and/or lipid-lowering drugs) would be approximately twice higher than if treating those with total cardiovascular risk at least 10%, and the number of events prevented would be also higher (147 per 100,000 vs. 137 per 100,000 individuals aged 40–64 years) [19].

According to the WHO guidelines, about 20% of the Mozambican adults aged 40–64 years were eligible for pharmacological treatment of hypertension, corresponding to approximately half million people. Treating all these individuals with hydrochlorothiazide (25 mg) and amiloride (2.5 mg), the first line of pharmacological treatment recommended by the Mozambican guidelines for the diagnosis, treatment, and control of hypertension [23] would correspond to an overall estimated annual cost of 0.8 million US dollars (USD), based on the costs of these medicines to the Mozambican Ministry of Health (personal communication). Although the accuracy of these values is limited by the fact that we have no empirical data to estimate the proportion of hypertensive patients requiring second and third line therapies, these results show that the pharmacological treatment of hypertension according to the WHO guidelines would be difficult to afford in this setting. Furthermore, these figures underestimate the burden associated with hypertension because patients aged below 40 and above 64 years were not considered in our analyses. Although the latter correspond to less than 5% of the population, there are 3.9 million Mozambicans aged 25–39 years, among whom the prevalence of SBP/DBP at least 160/100 mmHg is 10.7% (prevalence observed in this STEPS survey among patients who were not treated with antihypertensive drugs).

In addition to the financial resources necessary to cover the unmet needs regarding the pharmacological treatment of hypertension in Mozambique, it should be noted that a large proportion of the Mozambicans never had their BP measured (64% in our sample). Therefore, improving awareness is also a major challenge in this setting.

High and very high cardiovascular risk ($\geq 20\%$) was more frequent in urban areas, in accordance with the higher mortality from cardiovascular diseases among urban dwellers [9], and reflects the urban/rural distribution of risk factors that underlie the construct of cardiovascular risk, as hypertension [5], diabetes [24], and manufactured cigarette smoking [25] are more common among urban Mozambicans.

* Only one participant was classified with total cardiovascular risk $\geq 40\%$

- Eligible for drug treatment and specific lifestyle advice to lower blood pressure and total cardiovascular risk (19.8%).
- Eligible for drug treatment if unable to lower blood pressure through lifestyle strategies with professional assistance within 4-6 months (0%).
- Eligible to continue lifestyle strategies to lower blood pressure and reassess blood pressure and total cardiovascular risk annually (0%).
- Eligible to continue lifestyle strategies to lower blood pressure and reassess blood pressure and total cardiovascular risk every 2-5 years (21.2%).

**FIGURE 4** Prevalence of Mozambicans aged 40–64 years eligible for pharmacological treatment for hypertension according to WHO guidelines [15].
The high proportion of population at low total cardiovascular risk (<10%) stresses the potential for reduction of cardiovascular risk through the implementation of public health policies to create supportive environments for quitting tobacco, eating healthy, and being physically active. Although these behaviors are influenced by economic growth and unplanned urbanization, it is feasible to implement multisectorial policies to counteract the adverse influences of the global environment. A set of measures, namely, for controlling tobacco use (e.g. raising taxes on tobacco products and taking into account the potential for transition from smokeless and traditional forms of tobacco consumption to manufactured cigarettes [26]), and improving diet (e.g. controlling salt intake, enforcing farming production, namely fruit and vegetables, and promoting moderate alcohol intake in habitual drinkers), may contribute in decreasing the exposure to the cardiovascular risk factors. Beyond those environmental supportive policies, monitoring their distribution and providing access to effective and comprehensive educational and public awareness programs on the healthy behaviors, are key aspects to minimize cardiovascular diseases, especially in a country with very low levels of awareness [5].

In conclusion, only half of the nearly 40% of Mozambicans aged 40–64 years with SBP/DBP at least 140/90 mmHg meet the eligibility criteria for pharmacological treatment according to the WHO guidelines. Taking into account the available evidence on the effectiveness of different approaches to manage hypertension at a population level, the substantial differences in the number of individuals eligible for treatment according to the distinct criteria suggest that considering the total cardiovascular risk may allow a more efficient use of the scarce resources available in developing settings.

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Conflicts of interest

There are no conflicts of interest.

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**Reviewers’ Summary Evaluations**

**Reviewer 1**

Limited healthcare resources should be used in the most efficient way to reduce cardiovascular morbidity and mortality in developing countries. The authors compare the single risk factor approach (conventional BP) with the total cardiovascular risk approach (based on dedicated WHO/ISH risk prediction charts). Compared to the 40% eligibility for antihypertensive treatment based on BP ≥140–90 mmHg (though measured at only one visit), just 20% were eligible according to the total risk approach, but outcome data from randomized comparative trials are not available to define the most effective strategy. The authors stress the importance of preventive measures, because even the 20% would be difficult to afford.

**Reviewer 2**

This progressive paper from Mozambique, a poor but dynamic southern African country, generated a remarkable 98% response by stratified random sampling, hence representative of the whole country. Two-thirds were rural and 15% >60 years old. Building on their 2009 paper, instead of arbitrary prevalence at say 140 or 90 mmHg, the authors show that using WHO’s total cardio-
vascular risk approach, some 20% of Mozambique’s 40–64 year olds would be eligible for antihypertensive treatment, half that from prevalence alone. Remarkably, all 20% had blood pressures (BP) >160 or 100mmHg, including those with known or tested type 2 diabetes. Even if based on a mean BP from 1 home visit, the paper offers the way forward for treatment strategies in ‘resource-
poor’ settings.

A final point: about half those surveyed had no formal education. How those found above this ‘WHO’ risk threshold would react to being ‘offered’ treatment, and then whether these new ‘patients’ would genuinely take treatment long-term is the challenge every such country and its health staff face.