Cardiovascular risk management and its impact on hypertension control in primary care in low-resource settings: a cluster-randomized trial

Shanthi Mendis,[a] S Claiborne Johnston,[b] Wu Fan,[c] Olulola Oladapo,[d] Ali Cameron[a] & Mohammed F Faramawi[a]

Objective To evaluate a simple cardiovascular risk management package for assessing and managing cardiovascular risk using hypertension as an entry point in primary care facilities in low-resource settings.

Methods Two geographically distant regions in two countries (China and Nigeria) were selected and 10 pairs of primary care facilities in each region were randomly selected and matched. Regions were then randomly assigned to a control group, which received usual care, or to an intervention group, which applied the cardiovascular risk management package. Each facility enrolled 60 consecutive patients with hypertension. Intervention sites educated patients about risk factors at baseline and initiated treatment with hydrochlorothiazide at 4 months in patients at medium risk of a cardiovascular event, according to a standardized treatment algorithm. Systolic blood pressure change from baseline to 12 months was the primary outcome measure.

Findings The study included 2397 patients with baseline hypertension: 1191 in 20 intervention facilities and 1206 in 20 control facilities. Systolic and diastolic blood pressure decreased more in intervention patients than in controls. However, at 12 months more than half of patients still had uncontrolled hypertension (systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg). Behavioural risk factors had improved among intervention patients in Nigeria but not in China. Only about 2% of hypertensive patients required referral to the next level of care.

Conclusion Even in low-resource settings, hypertensive patients can be effectively assessed and managed in primary care facilities.

Une traduction en français de ce résumé figure à la fin de l'article. *Al final del artículo se facilita una traducción al español.* الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

The burden of cardiovascular disease (CVD) is substantially greater in low- and middle-income countries than in high-income countries.[1,2] CVD is associated with several modifiable risk factors, and effective primary prevention requires total cardiovascular risk assessment and management.[3] Risk assessment approaches used in high-income countries may not be feasible in low-resource settings, where primary health care workers often find it difficult to assimilate multiple risk factors for accurate assessment of cardiovascular risk without clinical decision support tools that estimate risk. In 2000, the World Health Organization (WHO) developed and subsequently validated a CVD risk management package to facilitate multiple risk factor assessment and treatment in low-resource settings.[4] However, its effect on patient management outcomes has not been evaluated.

The WHO package is a simple tool that provides clinical decision support for the assessment and management of cardiovascular risk; it is designed to address three scenarios commonly encountered in low- and medium- resource settings.[4] Scenario 1 is built upon an algorithm that stratifies CVD risk status (high, medium or low) based on age, clinical history of CVD, diabetes, tobacco use and systolic blood pressure (Fig. 1). High-risk patients are referred to the next level of care, which allows access to specialist care if necessary. Those categorized as medium- and low-risk can be managed by primary care physicians or non-physician health workers who have been instructed to initiate a variety of medical and behavioural interventions to reduce cardiovascular risk, supported by standardized protocols.

The main objective of this study was to assess the effectiveness of the WHO CVD risk management package in reducing blood pressure in primary care settings and improving adherence to lifestyle-change interventions at both individual and cluster levels. A cluster randomized trial (CRT) design was used because it has several advantages: it is a strong study design for evaluating educational and intervention programmes in health-care units and it avoids potential contamination between compared groups because patients are managed in a similar manner within the same unit, with savings in cost and time.

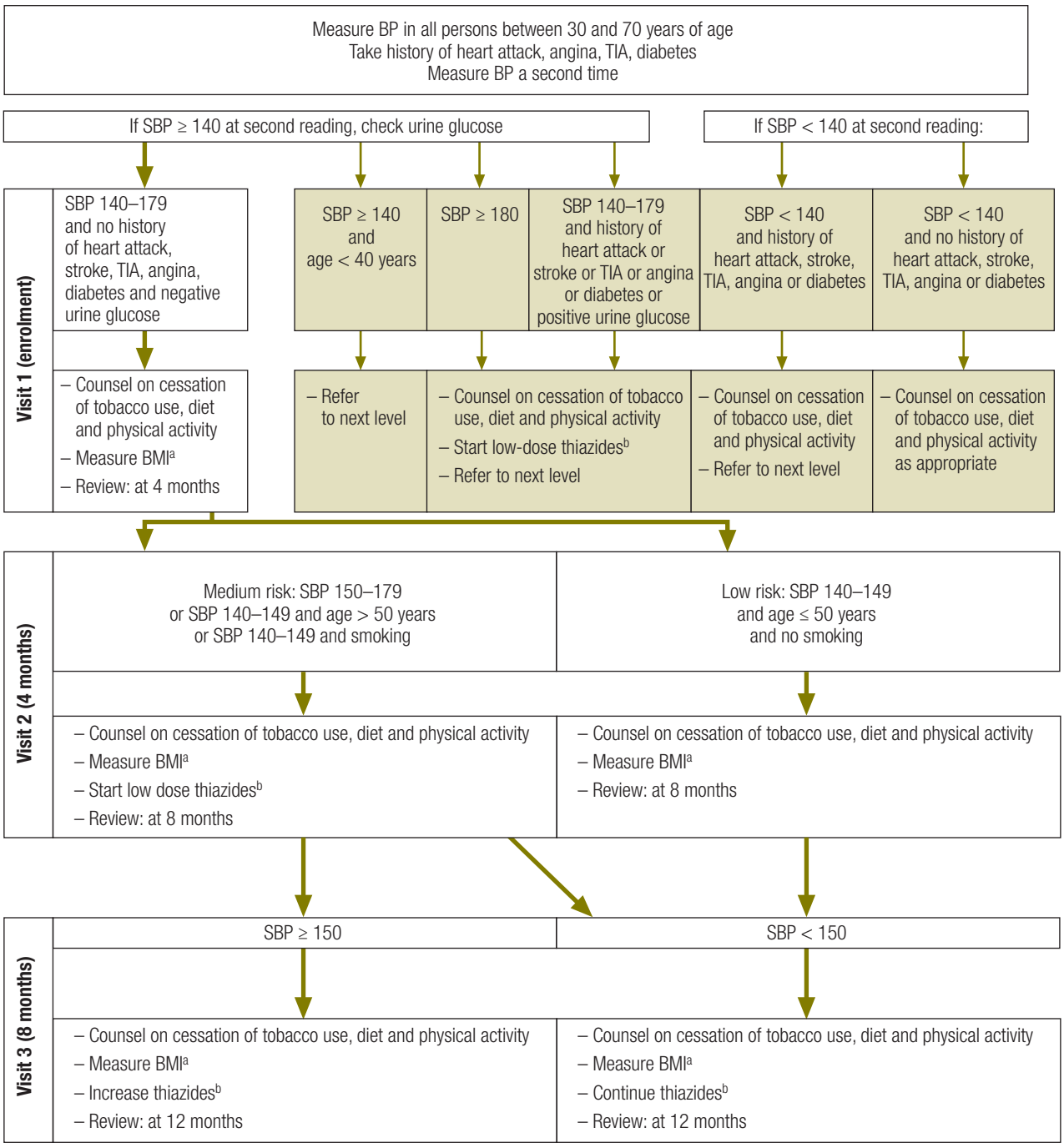
Methods

Design

Ten pairs of matched primary health care facilities in two regions in China and two regions in Nigeria (i.e. 10 facilities in each region) participated in the study. The flow of clusters and participants through the study is shown in Fig. 2. To be eligible, facilities had to be defined as primary care facilities in the specific country and had to have the minimum necessary capacity to implement the study algorithm. In consultation with local health officials, we selected two areas geographically distant from one another but similar socioeconomically and in terms of urban/rural mix. We identified all primary care centres

[a] Department of Chronic Disease and Health Promotion, World Health Organization, 20 avenue Appia, CH-1211, Geneva 27, Switzerland.
[b] Department of Neurology, University of California, San Francisco, United States of America.
[c] National Center for Chronic and Noncommunicable Disease Control and Prevention, Beijing, China.
[d] College of Medicine, University of Ibadan, Ibadan, Nigeria.
Correspondence to Shanthi Mendis (e-mail: mendiss@who.int).
(*Submitted: 15 December 2008 – Revised version received: 30 September 2009 – Accepted: 2 October 2009 – Published online: 8 December 2009*)

Fig. 1. **Protocol for cardiovascular risk assessment and management at the primary care level: scenario 1 of the World Health Organization risk management package for cardiovascular disease**



BP, blood pressure; BMI, body mass index; SBP, systolic blood pressure (mmHg); TIA, transient ischaemic attack.

[a] Alternatively, measure waist circumference or body weight.

[b] Thiazide diuretic: Hydrochlorothiazide starting dose 12.5 mg (low-dose), to be increased up to 25 mg (maximum dose).

in the two areas and matched them to form pairs based on their infrastructure, resources and function. We then randomly selected 10 pairs of matched primary care facilities to participate in the study. To reduce cross contamination, we randomly assigned one region and all its selected facilities to the intervention group, which used the WHO CVD risk management package, and the other region to the control group, which continued conventional treatment. Blinding was not feasible given the nature of the intervention.

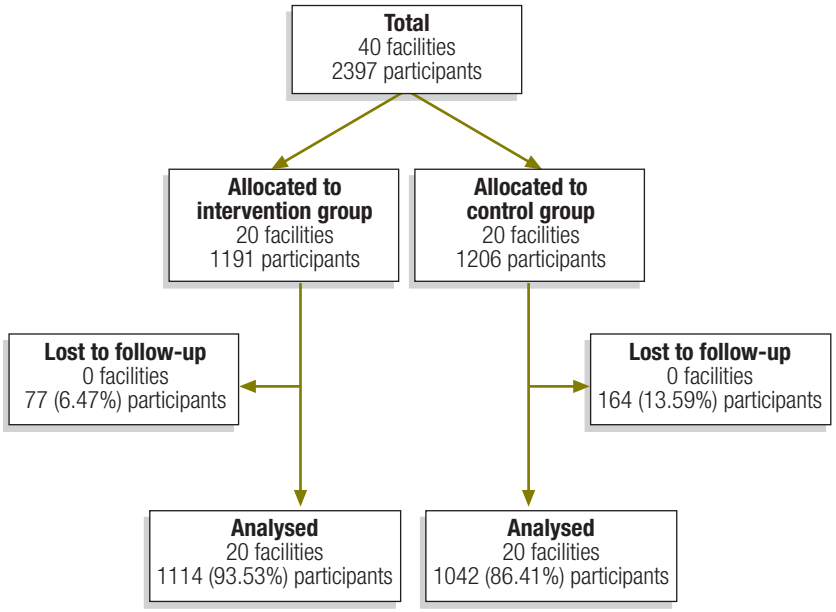
Recruitment and inclusion criteria

Patient recruitment started in 2005 and ended in 2006. Providers in the participating facilities assessed the eligibility of patients using information from the patient's health records, when available, and information provided by

the patient through direct interview and examination. Each facility recruited approximately 60 consecutive patients who met the eligibility criteria.

Males and females 30–70 years of age with systolic blood pressure between 140 and 179 mmHg were selected for the study if they were not on treatment for hypertension and did not have any exclusion factor. Exclusion criteria included previously diagnosed conditions resulting in secondary hypertension, other types of circulatory disorders (e.g. heart attack, stroke, transient ischaemic attacks, angina), pregnancy, trauma or other acute condition as presenting complaint, history of diabetes or positive urine glucose test, inability to comply with the follow-up requirements or inability to provide informed consent. Patients whose systolic blood pressure was over 179 mmHg or who had a positive history of heart attack, stroke, transient ischaemic attacks, angina, diabetes or a positive urine glucose test were referred to the next level of care.

Fig. 2. **Flowchart showing how clusters and participants proceeded through clinical trial of the World Health Organization risk management package for cardiovascular disease, China and Nigeria, 2005–2006**



Intervention sites

Training workshops on the study protocol, data collection forms and exit interviews were used to ensure standardization and data quality. These workshops were organized by the participating intervention centres before commencing enrolment. A follow-up training session was conducted 2 to 4 months later to reinforce knowledge about the intervention. The training included instruction in obtaining written informed consent; filling out the data collection forms; tasks and responsibilities of the staff involved; blood pressure measurement; the CVD risk management protocol for the primary care level (scenario 1 of the WHO CVD risk management package), including procedures and patient flow; and assessment and management of cardiovascular risk factors according to the package algorithm.

Blood pressure was measured using a validated automatic device. Two readings were taken with at least a 5-minute interval, with the subject at rest and the arm supported at heart level. The second reading was used for the analysis. Assessment and management of cardiovascular risk factors were standardized as much as possible by ensuring close adherence to the WHO package. The following protocols were provided for maximum standardization: cardiovascular risk assessment and management, counselling on cessation of tobacco use, evidence-based recommendations on treatment of blood pressure and recommendations on the use of blood pressure measurement devices.

The study included four visits: baseline, 4 months, 8 months and 12 months. The cost of visits was not covered. At the baseline visit all subjects at intervention sites were counselled on risk factor control (tobacco cessation, diet, physical activity), but no drug treatment was given. Patient information materials, translated to the local language, were given to each subject, along with follow-up cards to encourage adherence. The cards documented blood pressure measurements and indicated future visit dates. The back of the cards contained a summary of the counselling on diet, tobacco cessation and physical activity.

At the second visit (at 4 months), subjects were classified into low and medium CVD risk categories based on the WHO package as shown in Fig. 1, and medium-risk patients were started on low-dose hydrochlorothiazide. Those with systolic blood pressure > 179 mmHg were referred to a higher level of care. At the third visit (at 8 months), the hydrochlorothiazide dose was increased for patients with systolic blood pressure of ≥ 150 mmHg. Body mass index was measured and counselling on tobacco cessation, diet and physical activity was provided at all visits.

Control sites

Control facilities screened and followed subjects, but did not apply the WHO CVD package protocol or provide other instruction about risk factor assessment and management. Health-care workers from these facilities received initial training in filling out data collection forms and using blood pressure measurement devices. They were asked to continue to provide care following their usual practice patterns, which were not guided by evidence-based protocols. This often results in patients not receiving appropriate medications in a timely fashion.[5] Hydrochlorothiazide is an effective and inexpensive antihypertensive medication that is well suited for use as a first-line therapy in low-resource settings; however, it is underutilized and often replaced with more expensive medications such as methyldopa.[6]

Measurements

Data collection was done using the following forms: registry, inclusion visit, follow-up visits and exit interview. To assess possible bias in inclusion, sites kept a registry of all patients whose blood pressure was measured during the enrolment period. After inclusion, the following data were collected at each study visit: demographic and personal data; level of education; CVD risk factors; concomitant diseases; concomitant medications;

systolic and diastolic blood pressure; onset of angina, acute myocardial infarction, transient ischaemic attack or stroke since previous visit; and anti-hypertensive treatment.

The data collection forms were transferred from each site to a central coordinating centre. Photocopies of all forms were kept at the participating primary care facilities. A first visual check of data quality was done immediately upon receipt of the forms at the coordinating centre. Data were then entered into a database at the coordinating centre using Epi Info software version 6 (Centers for Disease Control and Prevention, Atlanta, GA, United States of America). Entries were validated to prevent invalid entries such as out-of-range values, illogical entries and other errors. The data were then transferred electronically every month to the project office in Geneva, Switzerland, where a third quality control check was performed. The original data collection forms were also sent to the project office every month.

Outcomes

The primary outcome measure was absolute reduction of systolic blood pressure at 12-month follow-up with respect to the baseline measurement. We also evaluated several secondary outcome measures at 12-month follow-up, including: rates of smoking cessation, change in body mass index compared to baseline, change in fruit and vegetable consumption and prescription of cost-effective antihypertensive drugs.

Statistical analysis

To detect an effect for the intervention at the individual level, the sample size calculation was based on published evidence that the type of intervention proposed is associated with a 2–6 mmHg reduction in systolic blood pressure in the intervention group.[7] A sample size of 293 patients per treatment arm was calculated using the uncorrected χ^2 test and the following parameters: α, 0.05; power, 0.8; P_0 (proportion of those who achieve control with usual care), 0.2; P_1 (proportion of those who achieve control in the intervention arm), 0.3; m (ratio between the two treatment arms), 1.1. To detect an effect at the facility level, the sample size was calculated by a method that takes into account the intraclass correlation coefficient. An intraclass correlation of $\rho = 0.15$ was assumed. A sample size of 2 clusters per group with 10 individuals per cluster achieves 80% power to detect a difference of 2.0 mmHg in systolic or diastolic blood pressure between the group means when the standard deviation is 0.600 and the intraclass correlation is 0.15 with a significance level of 0.05. Intention-to-treat analysis was performed in all cases.

Generalized estimation equation models were used to examine the clustering effect of the facility. No pooled analysis was carried out, and sample size was based on the number of subjects required in each participating country. Unvaried comparisons were performed with *t*-tests for continuous variables and Fisher's exact test was performed for dichotomous variables. The observed intraclass correlation of the outcomes (systolic and diastolic blood pressure) was calculated according to the formula derived by Donner & Klar.[8] An estimate for ρ was obtained by performing one-way analysis of variance, a valid method for both binary and continuous outcomes.[9]

Ethical issues

WHO Research Ethics Review Committee clearance was obtained for this study (SCRIHS project No. RPCO50). Informed consent was obtained from each subject before participation. For subjects incapable of reading and signing, the consent form was read aloud and additional explanations were given if needed; after the patient's questions were answered satisfactorily, a thumb print was used to represent the patient signature. Study forms and documents collected for the purpose of this project did not reveal the names of participants. Confidentiality was ensured by identifying subjects on all study forms by a unique patient number. All data at the project office were kept secure. No subject identifiers were included in any files transmitted to any committee or institution. The study was sponsored by WHO.

Table 1. **Baseline characteristics of cohorts in a clinical trial of the World Health Organization risk management package for cardiovascular disease, China and Nigeria, 2005–2006**

Characteristic	Site A[a]		Site B[b]	
	Intervention (*n* = 603)	Control (*n* = 606)	Intervention (*n* = 588)	Control (*n* = 600)
No. of males (%)	292 (48.4)	281 (46.4)	253 (43.0)	245 (40.9)
Mean age (SD)	53.2 (8.7)	54.8 (8.2)*	54.6 (10.1)	55.5 (10.8)
Mean years of education (SD)	4.6 (3.7)	5.3 (3.3)*	4.9 (4.4)	4.5 (4.5)
Mean BMI in kg/m^2 (SD)	24.7 (3.2)	24.8 (3.2)	27.4 (4.3)	27.4 (4.9)
Mean SBP in mmHg (SD)	150.5 (9.6)	149 (9.2)*	151.6 (11.2)	154.8 (13.5)*
Mean DBP in mmHg (SD)	91.6 (6.5)	91.1 (7.8)	94 (9.6)	94.1 (9.8)
No. of smokers (%)	194 (32.2)	199 (32.8)	22 (3.7)	43 (7.2)*

* $P < 0.05$.

BMI, body mass index; DBP, diastolic blood pressure; mmHg, millimetres of mercury; SD, standard deviation; SBP, systolic blood pressure.

[a] China.

[b] Nigeria.

Results

Baseline characteristics of the intervention and control groups were generally similar in both site A and site B (Table 1), although systolic blood pressure was greater in intervention subjects in site A and in controls in site B. There were also small differences between control and intervention subjects in age and years of education in site A and in smoking rates in site B.

Follow-up was nearly 100% at the 4-, 8-, and 12-month visits, except among controls in site B, 99% of whom attended follow-up at 8 months, but only 75% at 12 months (Table 2). At 4 months, the majority of patients in both groups were defined as medium-risk based on the WHO CVD risk management package (Table 2). In site A, all medium-risk patients in the intervention group were treated with hydrochlorothiazide, in accordance with the protocol, with 483 receiving the recommended 12.5 mg and 1 receiving 25 mg; in the control group, 200 medium-risk patients (38.8%) received a generic antihypertensive medication ($P < 0.0001$). In site B, 392 of 444 intervention patients (88.3%) were prescribed 12.5 mg of hydrochlorothiazide at the 4-month visit, while 321 of 483

Table 2. **Risk distribution of sample at follow-up visits among participants in a clinical trial of the World Health Organization risk management package for cardiovascular disease, China and Nigeria, 2005–2006**

Characteristic	Site A[a]				Site B[b]			
	Intervention (*n* = 603)		Control (*n* = 606)		Intervention (*n* = 588)		Control (*n* = 600)	
	No.	%	No.	%	No.	%	No.	%
4 month follow-up								
Attended visit	601	99.7	605	99.8	588	100.0	598	99.7
Low risk[c]	104	17.3	80	13.2	136	23.1	96	16.1
Medium risk[d]	484	80.5	516	85.3	444	75.5	483	80.8
SBP > 179 mmHg[e]	13	2.2	7	1.2	8	1.4	15	2.5
Missing data	0	0.0	2	0.3	0	0.0	4	0.7
8 month follow-up								
Attended visit	597	99.0	605	99.8	588	100.0	596	99.3
Low risk[f]	459	76.9	505	83.5	382	65.0	280	47.0
Medium risk[g]	138	23.1	99	16.4	206	35.0	315	52.9
Missing data	0	0.0	1	0.2	0	0.0	1	0.2
12 month follow-up								
Attended visit	584	96.8	605	99.8	530	90.1	447	74.5

mmHg, millimetres of mercury; SBP, systolic blood pressure.
[a] China.
[b] Nigeria.
[c] SBP < 150 mmHg, and age ≤ 50, and non-smoker.
[d] SBP 150–179 mmHg; or SBP < 150 mmHg and age > 50; or SBP < 150 mmHg and smoker; or SBP < 150 mmHg and age > 50 and smoker.
[e] Referred to higher level of care.
[f] SBP < 150 mmHg.
[g] SBP ≥ 150 mmHg.

control subjects (66.0%) were started on a generic antihypertensive medication ($P < 0.0001$). In both countries, no intervention patient received any antihypertensive other than hydrochlorothiazide, while control subjects received a variety of antihypertensive medications but never hydrochlorothiazide. In Nigeria (site B), about one-fourth of the control subjects were lost to follow-up and were not included in the final analysis. Those subjects had a higher mean systolic blood pressure, higher mean diastolic blood pressure and consumed fewer fruits and vegetables. If we had been able to include them in the final analysis, the effect of the intervention would have been greater because those who dropped out were less healthy than those who remained in the study until the end.

Systolic blood pressure at 12-month follow-up – the primary outcome measure – was lower compared to baseline in all groups, but reductions were greater in intervention patients than in controls (Table 3) in both site A ($P < 0.0001$) and site B ($P = 0.0002$). Results were similar for diastolic blood pressure. Elevated blood pressure was also lowered more frequently in intervention patients in both countries ($P < 0.0001$), but remained uncontrolled (systolic blood pressure ≥ 140 and/or diastolic blood pressure ≥ 90 mmHg) in the majority of these patients. Among intervention patients with uncontrolled hypertension at 12 months, 264 of 320 (82.5%) in site A and 270 of 364 (74.2%) in site B were prescribed, and reported taking, hydrochlorothiazide.

When generalized estimation equation models were applied after adjustment for the potential effect of the visits and the country on blood pressure, the mean systolic blood pressure of subjects in the facilities that implemented the intervention was 2 mmHg lower ($P < 0.05$), and the mean diastolic blood pressure was 1 mmHg lower ($P = 0.07$) than among subjects in the facilities that did not implement the intervention.

Modification of risk factors other than hypertension was more variable (Table 3). In site B, intervention subjects showed greater reductions in body mass index, higher rates of smoking cessation and greater increases in fruit and vegetable consumption compared to control subjects. In site A, no significant change was observed in these parameters in the intervention group compared to the control group.

Discussion

The WHO CVD risk management package provides a simple protocol for assessment and management of CVD risk, including treatment of hypertension and educational materials for counselling. These materials are based on guideline recommendations and are optimized for primary prevention in low-resource settings.[4] In this trial of 2397 patients from 40 centres in two countries, we showed that the protocol can be implemented consistently, with recommended antihypertensive medications being initiated in a large proportion of appropriate candidates at intervention sites. Blood pressure was lower and rates of hypertension control higher in intervention subjects at 12-month follow-up. Behavioural interventions (smoking cessation, increase in fruit and vegetable consumption) appeared less effective: we observed an effect among study subjects in site B (Nigeria) but not in site A (China). Only about 2% of the subjects had to be referred to the next level of care; the majority could be managed at the primary care level. This highlights the importance of the primary care approach for prevention and control of non-communicable diseases.

Table 3. **Differences in risk factors at 12-month follow-up among participants in a clinical trial of the World Health Organization risk management package for cardiovascular disease, China and Nigeria, 2005–2006**

Characteristic	Site A[a]			Site B[b]		
	Intervention (*n*=584)	Control (*n*=605)	*P*-value	Intervention (*n*=530)	Control (*n*=447)	*P*-value
Mean change in SBP in mmHg (SD)	–13.28 (12.25)	–9.42 (11.77)	<0.0001	–11.01 (15.37)	–6.61 (20.57)	0.0002
Mean change in DBP in mmHg (SD)	–6.07 (7.54)	–4.54 (7.57)	0.0005	–5.36 (9.99)	–2.03 (13.20)	<0.0001
Mean change in BMI in kg/m^2 (SD)	0.06 (1.71)	0.07 (2.03)	0.66	–0.22 (1.56)	0.92 (1.28)	<0.0001
No. who quit smoking (%)[c]	7.00 (3.6)	4.00 (2.00)	0.38	22.00 (100.0)	32.00 (74.4)	0.023
No. with increased fruit consumption (%)[b]	219 (37.7)	218 (36.1)	0.30	495.00 (93.4)	84.00 (18.8)	<0.0001
No. with increased vegetable consumption (%)[d]	91.00 (15.6)	108 (17.9)	0.17	75.00 (14.2)	31.00 (7.00)	0.0002

BMI, body mass index; DBP, diastolic blood pressure; mmHg, millimetres of mercury; SBP, systolic blood pressure; SD, standard deviation.
[a] China.
[b] Nigeria.
[c] Subjects who quit smoking during the study as a result of the counselling provided.
[d] From "seldom" to "several times per week", or from "several times per week" to "daily".

This study had many advantages. First, it is one of only a few studies to report intraclass correlation coefficients for important CVD risk measures such as systolic and diastolic blood pressure at the primary care level in developing countries. These observed intraclass correlation coefficients could be used to calculate sample size for future cluster-based intervention studies in primary care settings.[10] The larger the class correlation value, the larger the sample size needed to detect a difference. The sample size calculation was based on an interclass correlation coefficient of 0.15. The observed intraclass correlations for systolic and diastolic blood pressure were 0.04 and 0.06, respectively. Therefore, we believe that we had an adequate sample size and sufficient power to detect a difference between the intervention and control groups.

Second, there are no previous published studies of assessment and management of CVD risk in resource-constrained primary care settings. Several randomized trials of guideline implementation strategies have been conducted in developed countries and have generally demonstrated only modest effects.[11] Walsh et al. reviewed randomized and non-randomized trials of interventions aimed at improving the achievement of treatment goals for patients on antihypertensive therapy.[12] They reported a median increase in the proportion of patients achieving recommended targets of systolic and diastolic blood pressure of 16.2% (interquartile range, IQR: 10.3–32.2) and 6.0% (IQR: 1.5–17.5), respectively, similar to those seen in our trial. The greatest effect sizes were achieved with interventions involving organizational change and patient education. Our intervention had no organizational change but did have components that focused on education of health-care providers and patients. The intervention was multifaceted, and it is therefore not possible to say which of the various components were most important for overall effectiveness.

Third, the use of the package also resulted in a significant increase in the prescribing of antihypertensive medicines, particularly of an inexpensive diuretic (hydrochlorothiazide). Control subjects were prescribed antihypertensive medicines less frequently and a variety of medications were used, including expensive non-generic preparations and medicines with more unfavourable side effect profiles, such as methyldopa and reserpine. These findings are in line with those of other randomized trials that have found tailored interventions to be effective at changing prescribing practices.[13]

Despite the success of the intervention, hypertension control was achieved in fewer than 50% of subjects in both intervention countries. Most of those with uncontrolled hypertension were prescribed recommended doses of hydrochlorothiazide and reported taking their medications. The recommended doses were small, however, and may have been inadequate to control hypertension fully in many subjects. Even at maximum dose, many patients require the addition of other agents.[14] Furthermore, patient adherence was not monitored, and lack of adherence may therefore have reduced the effectiveness of the intervention. Additional studies are required to assess a multi-step protocol for further escalating treatment in appropriate subjects; patient adherence should be monitored in such studies.

The effect of the intervention on blood pressure was consistent in both countries when the analysis was conducted at the individual subject level and at the facility level. An effect on behavioural risk factors, such as diet and smoking, was less consistent, particularly in site A. Non-adherence to behavioural interventions often limits their impact.[15] Although the intervention did include patient counselling and education, it is unclear how aggressively this component was implemented and how well the messages were understood and taken to heart. Future studies in limited-resource settings should gather more information for understanding the effect of patient education and counselling.

Our study had several important limitations. First, although it was a randomized trial, randomization was at the regional level. We devoted much effort to matching sites to ensure balance, but there were differences in the baseline characteristics of subjects in the intervention and control groups in both countries. Our focus on change may have reduced any bias introduced, but residual confounding due to imbalanced randomization cannot be entirely ruled out. The health-care workers in control facilities were trained in filling out data collection forms and using the blood pressure measurement devices, and this may have biased the practice in control centres and reduced the apparent effect size of the intervention. Second, information on smoking cessation and fruit and vegetable consumption was based on self-reporting to physicians. It is possible that patients in the intervention group tended to report higher rates of smoking cessation and fruit and vegetable consumption because they

had been encouraged to make these behavioural changes. We did not attempt to validate self-reports of behavioural change, which have been reported to be inaccurate in some settings.[16] Third, the quality of data sources varied; routine medical records were used to derive some variables, and the completeness and accuracy of recording may have affected the results. However, these errors were probably evenly distributed between the intervention and control groups, and thus should not bias conclusions about whether the intervention was effective.

The generalizability of our study is also somewhat limited. In addition to China and Nigeria, one other country was invited to participate but was dropped from the study when the participating facilities failed to initiate and maintain adequate data collection, which suggests that implementation may be more difficult in some resource-constrained settings. Furthermore, in the two countries that did participate, facilities in only limited geographical areas were invited to take part in the trial, and those facilities may not have been representative of all primary care facilities in those countries. Nonetheless, the selection of sites was random within each region, so self-selection of sites most interested in improvement was not a problem. The increase in vegetable and fruit consumption and tobacco cessation seen in the intervention arm in site B at 12-month follow-up may have been due to more effective counselling methods or better understanding of the health messages by patients. Future studies should gather more information and use objective evidence of tobacco cessation to ensure data quality.

Conclusion

A simple intervention using standardized treatment based on cardiovascular risk improved blood pressure control and the prescribing of antihypertensive drugs in randomly selected sites in primary care facilities in two resource-limited countries. Although blood pressure remained uncontrolled in the majority of intervention patients, the doses of hydrochlorothiazide prescribed in the study were low and therefore may not have been sufficient to achieve complete control in many subjects. Our results suggest that the majority of patients with hypertension can be effectively managed in primary care facilities, even in low-resource settings. ■

Acknowledgements

We are grateful to Eugene Zheleznyakov for his input and for revising the paper.

Competing interests: None declared.

الملخص

التدبير العلاجي لعوامل خطر الإصابة بالأمراض القلبية الوعائية وتأثيره على مكافحة فرط ضغط الدم في الرعاية الأولية بالمواقع المنخفضة الموارد: تجربة عنقودية معَشّاة

الغرض تقييم حزمة بسيطة من التدابير العلاجية لعوامل خطر الإصابة بالأمراض القلبية الوعائية من أجل التقييم والتدبير العلاجي لعوامل خطر الإصابة بهذه الأمراض وذلك باستخدام فرط ضغط الدم بوصفه نقطة لدخول مرافق الرعاية الصحية في المواقع المنخفضة الموارد.

الطريقة اختير إقليمان نائيان جغرافياً في بلدين (هما الصين ونيجريا) واختير عشوائياً عشرة أزواج من مرافق الرعاية الصحية في كل إقليم وأجري توافق بينها. ثم صنفت الأقاليم عشوائياً إلى مجموعة الشواهد، وهي التي تلقت الرعاية المعتادة، وإلى مجموعة المداخلات، وهي التي طبقت الحزمة الخاصة بالتدبير العلاجي لعوامل خطر الإصابة بالأمراض القلبية الوعائية. وضم كل مرفق صحي 60 مريضاً متعاقباً مصاباً بفرط ضغط الدم. وفي مواقع المداخلات تم تثقيف المرضى بعوامل الخطر كأساس قاعدي وبدأ العلاج باستخدام الهيدروكلوروثيازيد في الشهر الرابع بالنسبة للمرضى المعرضين لخطورة متوسطة للإصابة بالأمراض القلبية الوعائية، وذلك وفقاً لخوارزمية المعالجة المعيارية. وكان تغير ضغط الدم الانقباضي من المستوى القاعدي وحتى 12 شهراً هو قياس النتيجة الأولي.

الموجودات شملت الدراسة 2397 مريضاً مصاباً بفرط ضغط الدم كمستوى قاعدي: 1191 مريضاً في 20 مرفقاً للمداخلات، و 1206 في 20 مرفقاً لمجموعة الشواهد. وقد انخفض ضغط الدم الانقباضي والانبساطي في مرضى مجموعة المداخلات أكثر منهم في مرضى مجموعة الشواهد. غير أنه بحلول الشهر 12 ظل أكثر من نصف المرضى يعانون من فرط ضغط الدم غير المتحكم فيه (كان ضغط الدم الانقباضي أعلى من 140 ملي متر زئبق وضغط الدم الانبساطي أكثر من 90 ملي متر زئبق). وتحسنت عوامل الخطر السلوكية بين مرضى المداخلات في نيجيريا ولم تتحسن في الصين، واحتاج 2% فقط من مرضى فرط ضغط الدم إلى الإحالة إلى المستوى التالي من الرعاية.

الاستنتاج حتى في المواقع المنخفضة الموارد يمكن تقييم ومعالجة مرضى فرط ضغط الدم بفعالية في مرافق الرعاية الأولية.

Résumé

Prise en charge du risque cardiovasculaire et impact sur le contrôle de l'hypertension par les soins de santé primaires dans les pays disposant de faibles ressources: essai en grappes randomisé

Objectif Évaluer un module simple de prise en charge du risque cardiovasculaire permettant d'estimer et de prendre en charge le risque cardiovasculaire en utilisant l'hypertension comme point d'entrée dans les établissements de soins de santé primaires des pays à faibles ressources.

Méthodes Deux régions géographiquement distantes ont été choisies dans deux pays (Chine et Nigéria) et 10 paires d'établissements de soins de santé primaires ont été sélectionnés au hasard dans chaque région et appariés. Les régions ont ensuite été réparties au hasard entre un groupe témoin qui recevait les soins habituels et un groupe d'intervention, auquel était appliqué le module de prise en charge du risque cardiovasculaire. Chaque établissement a recruté successivement 60 patients hypertendus. Sur les sites d'intervention, on a fourni au départ aux patients un enseignement sur les facteurs de risque et débuté au bout de 4 mois un traitement par l'hydrochlorothiazide chez ceux présentant un risque moyen d'accident cardiovasculaire, conformément à un algorithme de traitement standardisé. La variation de la pression artérielle systolique du stade de départ à 12 mois a constitué la principale mesure de résultat.

Résultats L'étude a porté sur 2397 patients présentant une hypertension au départ: 1191 dans 20 établissements mettant en oeuvre l'intervention et 1206 dans 20 établissements témoins. Les pressions systolique

et diastolique ont davantage diminué chez les patients bénéficiant de l'intervention que chez les patients témoins. Cependant, à 12 mois, plus de la moitié des patients présentaient encore une hypertension non contrôlée (pression systolique > 140 mm Hg et/ou pression diastolique > 90 mm Hg). Les facteurs de risque comportementaux s'étaient améliorés chez les patients bénéficiant de l'intervention au Nigéria, mais pas en Chine. Seuls 2 % environ des patients hypertendus ont dû être orientés vers le niveau de soins supérieur.

Conclusion Même dans les pays disposant de faibles ressources, il est possible d'évaluer et de prendre en charge efficacement les patients hypertendus dans les établissements de soins de santé primaires.

Resumen

La gestión del riesgo cardiovascular y su impacto en el control de la hipertensión arterial en la atención primaria en los entornos con recursos escasos: ensayo aleatorizado por conglomerados

Objetivo Evaluar un paquete sencillo de gestión del riesgo cardiovascular para evaluar y gestionar ese riesgo usando la hipertensión como punto de acceso en los centros de atención primaria en los entornos con pocos recursos.

Métodos Se seleccionaron dos regiones geográficamente distantes de dos países (China y Nigeria), para proceder luego a elegir al azar y emparejar diez pares de centros de atención primaria de cada región. Las regiones fueron asignadas aleatoriamente a un grupo de control, que recibió la atención habitual, o a un grupo de intervención, al que se aplicó el paquete de gestión del riesgo cardiovascular. En cada establecimiento se estudió a 60 pacientes consecutivos con hipertensión arterial. En los centros de intervención se informó a los pacientes acerca de los factores de riesgo al comienzo del estudio y se instauró tratamiento con hidroclorotiazida a los 4 meses en los pacientes con riesgo medio de evento cardiovascular, de acuerdo con un algoritmo de tratamiento normalizado. El criterio de valoración principal fue la variación de la tensión arterial sistólica respecto al nivel basal al cabo de 12 meses.

Resultados El estudio abarcó a 2397 pacientes con hipertensión basal: 1191 en 20 centros de intervención y 1206 en 20 centros de control. La tensión arterial, sistólica y diastólica, disminuyó más en los pacientes del grupo de intervención que en los de control. Sin embargo, transcurridos 12 meses, más de la mitad de los pacientes seguían con la hipertensión no controlada (tensión arterial sistólica > 140 mmHg, o diastólica > 90 mmHg). Los factores de riesgo asociados al comportamiento habían mejorado entre los pacientes del grupo de intervención en Nigeria, pero no en China. Solo un 2% de los pacientes hipertensos tuvieron que ser derivados al siguiente nivel asistencial.

Conclusión Incluso en los entornos con recursos escasos, es posible evaluar y tratar eficazmente a los pacientes hipertensos en los centros de atención primaria.

References

1. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 2006;367:1747–57. doi:10.1016/S0140-6736(06)68770-9 PMID:16731270
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006;3:e442. doi:10.1371/journal.pmed.0030442 PMID:17132052
3. *Prevention of cardiovascular disease: guidelines for assessment and management of total cardiovascular risk*. Geneva: World Health Organization; 2007.
4. *WHO CVD-risk management package for low- and medium-resource settings*. Geneva: World Health Organization; 2002. Available from: http://www.who.int/cardiovascular_diseases/resources/pub0401/en/index.html [accessed 5 October 2009].
5. Moser M, Feig PU. Fifty years of thiazide diuretic therapy for hypertension. *Arch Intern Med* 2009;169:1851–6. doi:10.1001/archinternmed.2009.342 PMID:19901136
6. Wright JM, Musini VM. First-line drugs for hypertension. *Cochrane Database Syst Rev* 2009:CD001841.PMID: 19588327.
7. Ebrahim S, Beswick A, Burke M, Davey Smith G. Multiple risk factor interventions for primary prevention of coronary heart disease. *Cochrane Database Syst Rev* 2006:CD001561. PMID:17054138
8. Donner A, Klar N. *Design and analysis of cluster randomization trial in health research*. London: Arnold; 2000.
9. Smeeth L, Ng ES. Intraclass correlation coefficients for cluster randomized trials in primary care: data from MRC Trial of the Assessment and Management of Older People in the Community. *Control Clin Trials* 2002;23:409–21. doi:10.1016/S0197-2456(02)00208-8 PMID:12161083
10. Campbell MK, Grimshaw M, Elbourne D. Intraclass correlation coefficients for cluster randomized trials:empirical insights into how should they be reported. *BMC Med Res Methodol* 2004;4:9–13. doi:10.1186/1471-2288-4-9 PMID:15115554
11. Hakkennes S, Dodd K. Guideline implementation in allied health professions: a systematic review of the literature. *Qual Saf Health Care* 2008;17:296–300. doi:10.1136/qshc.2007.023804 PMID:18678729
12. Walsh JM, Sundaram V, McDonald K, Owens DK, Goldstein MK. Implementing effective hypertension quality improvement strategies: barriers and potential solutions. *J Clin Hypertens (Greenwich)* 2008;10:311–6. doi:10.1111/j.1751-7176.2008.07425.x PMID:18401229
13. Fretheim A, Oxman AD, Håvelsrud K, Treweek S, Kristoffersen DT, Bjørndal A. Rational prescribing in primary care (RaPP): a cluster randomized trial of a tailored intervention. *PLoS Med* 2006;3:e134. doi:10.1371/journal.pmed.0030134 PMID:16737346
14. Mendoza MD, Stevermer JJ. Hypertension with metabolic syndrome: think thiazides are old hat? ALLHAT says think again. *J Fam Pract* 2008;57:306–10. PMID:18460295.
15. Borgermans L, Goderis G, Broeke CV, Mathieu C, Aertgeerts B, Verbeke G. A cluster randomized trial to improve adherence to evidence-based guidelines on diabetes and reduce clinical inertia in primary care physicians in Belgium: study protocol [NTR 1369]. *Implement Sci* 2008;3:42. doi:10.1186/1748-5908-3-42 PMID:18837983
16. Fendrich M, Mackesy-Amiti ME, Johnson TP, Hubbell A, Wislar JS. Tobacco-reporting validity in an epidemiological drug-use survey. *Addict Behav* 2005;30:175–81. doi:10.1016/j.addbeh.2004.04.009 PMID:15561458