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Impact of one or two visits strategy on hypertension burden estimation in HYDY, a population-based cross-sectional study: implications for healthcare resource allocation decision making

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ABSTRACT

Context: The prevalence of hypertension in developing countries is coming closer to values found in developed countries. However, surveys usually rely on readings taken at a single visit, the option to implement the diagnosis on readings taken at multiple visits, being limited by costs.

Objective: To estimate more accurately the magnitude and extent of the resource that should be allocated to the prevention of hypertension.

Design: Population-based cross-sectional survey with triplicate blood pressure (BP) readings taken on two separate home-visits.

Setting: Rural and urban locations in three areas of Yemen (capital, inland and coast).

Participants: A nationally representative sample of the Yemen population aged 15–69 years (5063 men and 5179 women), with an overall response rate of 92% in urban and 94% in rural locations.

Main outcome measure: Hypertension diagnosed as systolic BP ≥140 mm Hg and/or diastolic BP ≥90 mm Hg and/or self-reported use of antihypertensive drugs.

Results: Hypertension prevalence (age-standardised to the WHO world population 2001) based on fulfilling the same criteria on both visits (11.3%; 95% CI 10.7% to 11.9%), was 35% lower than estimation based on the first visit (17.3%; 16.5% to 18.0%). Advanced age, blood glucose ≥7 mmol/l or proteinuria ≥1+ at dipstick test at visit one were significant predictors of confirmation at visit 2. The 959 participants found to be hypertensive at visit 1 or at visit 2 only and thus excluded from the final diagnosis had a rate of proteinuria (5.0%; 3.8% to 6.5%) comparable to rates of the general population (6.1%; 5.6% to 6.6%), and of subjects normotensive at both visits (5.6%; 5.1% to 6.2%). Only 1.9% of Yemen population classified at high or very high cardiovascular (CV) risk at visit 1 moved to average, low or moderate CV risk categories after two visits.

Conclusions: Hypertension prevalence based on readings obtained after two visits is 35% lower than estimation based on the first visit, subjects were excluded from final diagnosis belonging to low CV risk classes.

ARTICLE SUMMARY

Article focus

- To investigate the effects on healthcare resource allocation decision making of taking blood pressure at one or two visits with cardiovascular risk stratification.
- To identify the characteristics of subjects who are excluded from the final diagnosis when restricting the diagnostic criteria.

Key messages

- The present study clarify that although there is a large discrepancy (35%) in the estimation of hypertension prevalence on the basis of one visit or two visits, only 1.9% of subjects classified at high or very high cardiovascular (CV) risk at visit 1 moved to average, low or moderate CV risk categories after two visits.
- Subjects excluded from the final diagnosis of hypertension, had rates of proteinuria and self-reported CV disease comparable with normotensive subjects and the general population.
- According to present data the choice of one or two visits is not relevant when a strategy that allows for a more comprehensive framework of CV risk is implemented.

Strenght and limitations of this study

- This study utilised data from nationally representative survey conducted with a door-to-door approach and a high response level in a developing country.
- Laboratory investigations were performed with the use of dry chemistry. However, the long distance to get to a service laboratory requires shipments under special conditions, often resulting in deterioration and spoilage of the specimen.

INTRODUCTION

The WHO has been indicating since 2001 that cardiovascular (CV) disease is the first cause of death worldwide.[1] More precisely,

80% of CV death are now occurring in low-income and middle-income countries.[2 3] Surveys performed in developing countries are revealing that changing lifestyle and urbanisation are associated with growing prevalence of hypertension[4] which is coming closer to values found in developed countries.[5] All these surveys rely on readings taken at a single visit, the option to implement the diagnosis on readings taken at multiple visits, as recommended by guidelines for clinical practice,[6 7] being limited due to costs. Diagnostic criteria based on readings collected at a single visit, might, however, lead to include subjects with high blood pressure (BP) variability and episodic hypertension, with a final overestimation of hypertension prevalence.[8 9] Although high BP variability potentially increases the risk of future CV events,[10] treatment decision is uncertain. Conversely, resource allocation in developing countries requires sound data. Finally, although the association between hypertension and target organ damage was recently reported to be independent by the diagnostic criteria,[9] the CV risk characteristics of subjects which are impacted more from the two survey strategies, being either included among hypertensives after a single visit survey or excluded when restricting the diagnostic criteria, is currently unknown.

In the Hypertension and Diabetes in Yemen (HYDY) survey, subjects received urine dipstick test for proteinuria combined with triplicate BP readings performed during two separate home-visits as recommended by guidelines for the clinical diagnosis of hypertension.[6 7] To estimate more accurately the magnitude and extent of the resource that should be allocated to the prevention of hypertension we (1) compared prevalence, awareness, treatment and control rates, and CV risk stratification when the definition of hypertension rely on data collected either at a single or at two visits carried out in different dates and (2) identified the characteristics of subjects who are excluded from the final diagnosis when restricting the diagnostic criteria.

METHODS

Study sites and study population

The Yemen population was estimated to be more than 21 million in 2007.[11] A multistage stratified sampling method was used. In the first stage, Yemen was stratified into three regions, the capital area, the inland and the coastal area. In addition to the governorate of Sana'a, the governorate of Taizz in the inland, and the governorates of Al Hudaydah and Hadramaut on the coast were selected to be representative of the geographic, economic and climatic characteristics of the country. In the second stage, rural and city regions were identified from each study area. In the third stage, districts were arbitrarily identified within each urban and rural region, boundaries being defined using local maps or in consultation with the local health workers. The total number of districts within each study area (20 in the capital area, 12 in the inland and 8 in the coastal area) was proportional to the estimated population size of the area. In the final stage, due to the lack of a national population register, a cluster of 300 participants was made for each district, participants being equally allocated by gender and age-group (6–14, 15–24, 25–34, 35–44, 45–54 and 55–69 years) to a total of 12 strata. All male and female subjects aged 6–69 years who lived permanently in the study areas were eligible. Pregnant women were excluded. A common set of rules for making a cluster was followed. Briefly, a sampling frame was established following enumeration of houses counting from the centre to the suburbs of the district and the first house to be surveyed was chosen at random by choosing a number on the list and selecting the corresponding house. Investigators then continued to call at every second address, always turning left. A household was defined as a group of people who usually live under the same roof and share meals. If more than one household was present in the same dwelling one was randomly selected. All of the eligible subjects in the same household were invited to take part in the study. About 182 subjects refused to participate, and 12 257 were evaluated between February 2008 and March 2009. Results obtained in subjects aged ≥15 years (5063 men and 5179 women) are reported in the present study.

The study was approved by the Ethical Committee of the University of Science and Technology, Sana'a, Yemen (Ref. 1–2007). Districts Leaders and local Chiefs also consented to the survey. Informed consent was obtained from every participant before data collection. No incentives were offered to study participants. Participants with untreated conditions identified during the examination were referred to a primary healthcare provider.

Data collection

The survey was performed following the three different levels of the WHO Stepwise Approach to Chronic Disease Risk Factor Surveillance (STEPS),[12] which included questionnaire, physical measurements and biochemical measurements, using standardised methods. The burden of hypertension in the population was assessed by taking triplicate BP measurements on two visits, separated by few days. Data collection was conducted at home by centrally trained survey teams composed by two investigators of the opposite gender.

Community sensitisation activities preceded each survey round, including local council briefings with the chiefs and elders of the villages. During the first visit (visit 1) the head of the household or spouse and the participant were informed about the objectives, and procedural details of the survey. Privacy of information was assured. After obtaining consent, a study questionnaire was administered. The study questionnaire included questions about demographics, lifestyle and medical history (WHO STEPS-Instrument V.2.0).[12] Participants were asked if they had been advised to change their diet

('special prescribed diet'), or to lose weight ('advice or treatment to lose weight'), or quit smoking ('advice or treatment to stop smoking') or do exercise ('advice to start or do more exercise') attributed to hypertension, by indication of a health professional. Close-ended questions were asked to find out if they had been seen by a traditional healer over the last year or if they had been using herbal or traditional remedies attributed to high BP. 'Known ischaemic heart disease' (IHD) was defined as a person with a history of heart attack requiring hospitalisation, or a person with physician-diagnosed IHD who was taking medication as confirmed by the survey team. 'Known stroke' was defined as a person with a history of abrupt-onset weakness or paralysis on one side of the body, with or without a history of hospitalisation, or a person with physician-diagnosed stroke and currently experiencing weakness or paralysis on one side of the body.

The mid-arm circumference was measured to use the appropriate cuff size (small, medium and large for mid-arm circumferences of 17–22, 22–32 and 32–42 cm, respectively). Three measurements of BP and pulse rate were taken at 2 min intervals on the dominant arm after a rest of at least 15 min, in the seated position.[7] Readings were obtained using a clinically validated semiautomatic sphygmomanometer (HEM 705 IT; Omron Matsusaka Co Ltd, Japan). The average of the last two readings for systolic and diastolic BP was defined as SBP1 and DBP1, respectively. Anthropometric measurements were taken on standing participants wearing light clothes and without shoes using standard techniques.[13] Body weight was measured to the nearest 0.1 kg using a spring balance and height to the nearest 0.5 cm using a stadiometer. Waist and hip circumference was measured to the nearest 0.1 cm. Finger-prick blood samples were then obtained from fasting (>8 h) subjects (aged ≥15 years) to measure glucose (Accutrend system, Roche Diagnostics, Mannheim, Germany), cholesterol and triglycerides blood values (MultiCare-in, HPS, Italy) using dry chemistry. The subject was then asked to void. A midstream specimen of urine was collected and dipstick test (Auction sticks, A.Menarini Diagnostics, Italy) was immediately performed and read manually to semiquantitate the occult blood (trace, 1+ to 4+) and protein (trace, 1+ to 4+). A new appointment was taken for non-fasting participants and for subjects who were menstruating. All subjects were then visited again within the next 10 days by the same survey team using the same measurement devices and procedures for the second session of BP (SBP2 and DBP2) and fasting glucose (FG2) measurements.

Diagnostic criteria

Arterial hypertension was defined as (1) systolic BP≥140 mm Hg and/or diastolic BP≥90 mm Hg and/or (2) self-reported use of antihypertensive drugs at the time of the interview.[7] More precisely, the prevalence of hypertension was based on values measured at the first visit (SBP1 and DBP1), at the second visit (SBP2 and DBP2) and on fulfilling the same criteria for hypertension on both visits. Awareness of hypertension was defined as self-report of any prior diagnosis of hypertension by a health-care professional among the population defined as having hypertension. Hypertension treatment was defined as a self-reported use of antihypertensive drugs within the 2 weeks preceding the interview. Hypertension control was defined as systolic BP<140 mm Hg and diastolic BP<90 mm Hg. The proportion of hypertension control was relative to hypertensive treated with drugs.

Diabetes mellitus (DM) was defined as (1) FG ≥7.0 mmol/l at the two visits or (2) self-reported use of hypoglycaemic medications at the time of the interview; impaired FG (IFG) as FG≥5.6 mmol/l and <7.0 mmol/l in the absence of hypoglycaemic medications; normal FG as FG<5.6 mmol/l at the two visits.[14] Overweight and obesity were defined as a body mass index (BMI) 25.0–29.9 and ≥30 kg/m^2, respectively. Abdominal obesity was defined as waist circumference >102 cm in men or >88 cm in women. Gender-specific tertiles for BMI and waist-to-hip (W/H) ratio were calculated using data of adult subjects without hypertension, normal FG, cholesterol <5.0 mmol/l, triglycerides <1.7 mmol/l and no protein at urine dipstick test. Resulting cut-offs were 20 and 23.2 kg/m^2 for men and 20.5 and 24.3 kg/m^2 for women for BMI and 0.849 and 0.907 in men and 0.815 and 0.887 in women for W/H ratio. On the basis of cholesterol and triglycerides assessments, subjects were classified as high cholesterol (>5.0 mmol/l) or high triglycerides (>1.7 mmol/l).[7 15] Results of dipstick urinalysis were classified as no protein (0), protein trace (±) or proteinuria (≥+1). A smoker was defined as one who smoked any form of tobacco on a daily (daily smoker) or a non-daily (occasional smoker) basis. Those who had smoked but had quit were designated as former smokers, and those who had never smoked at all were designated as never smokers. On the basis of education level, subjects were classified into six levels: (1) illiterate, (2) can read and write, (3) primary school, (4) preparatory school, (5) secondary and (6) university or post. Fruit and vegetable consumption were classified as (1) ≤1 day/week, (2) 2–4 day/week and (3) ≥5 days/week.

Participants were categorised as: sedentary if they walked or cycled for less than 10 min daily, if their work did not involve intense physical activity, and they did not usually practice any sport or recreational physical activities; engaging in light-to-moderate physical activity if they performed work or recreational physical activities 1 or 2 days/week; engaging in vigorous physical activity if they performed work or recreational vigorous physical activities 3 days or more/week.

According to the European Society of Hypertension/European Society of Cardiology (ESH/ESC) chart[7] risk stratification (average, low, moderate, high and very high added risk categories) was based on the presence of risk factors (average of SBP1/SBP2 and DBP1/DBP2 graded in five categories; age >55 years for men or >65 years for women; daily smoking; waist circumference >102 cm in

men or >88 cm in women; IFG; triglycerides >1.7 mmol/l; total cholesterol >5.0 mmol/l), DM, subclinical organ damage (protein trace at dipstick test) and established renal (proteinuria ≥1+ at dipstick test) or CV disease (self-reported stroke, myocardial infarction or peripheral artery disease). The cluster of three of four risk factors among abdominal obesity, altered fasting plasma glucose, BP>130/85 mm Hg and high triglycerides (as defined above) was considered as the presence of metabolic syndrome.

Measures have been taken to attain complete reliability and to reduce variation to reasonable limits. All study personnel successfully completed the specific 1-week training programme organised in Sana'a (December 2007) on the aims of the study and the specific methods used to standardise the procedure for sampling and contacting individuals, questionnaire administration and form filling, BP measurements using electronic devices, performing blood biochemical assay, performing urine assay and data entry into computerised data base. The training programme included a pilot testing performed on a population sample of 400 individuals in urban and rural areas of Sana'a.

Statistical methods

A sample size of at least 1117 subjects was required to achieve a 1% precision around an estimated prevalence of diabetes of 3% with 95% confidence level (Cl). Estimated required sample size for two-sample comparison of diabetes prevalence of 2.25% versus 3.75% with the assumption of 0.05 α (two-sided), 80% power, was 2161 subjects for each group. Cleaning the data, handling missing data and outliers were done according to the guidelines of WHO for STEPS data management.[12] Prevalence estimates were calculated for the five age groups in the overall population and by gender. Data are expressed as mean ±SD with 95% Cl for continuous variables, and as rates with 95% CI for categorical variables. Prevalence was also weighted to represent the total Yemen population aged 15–69 years (2008 estimated Yemen population),[11 16] and age standardised for age ranges 15–69 years using WHO World Standard Population.[17] For hypertension awareness and treatment the analysis was done on the subpopulation of hypertensive patients; for hypertension control, analysis was done on the subpopulation of treated people. As there were no national data available for these two subpopulations for the purpose of weighting, at this stage of analysis, we did not weigh the data. Prevalence rates were compared using χ^2 analysis and risk ratio (RR).[16] When appropriate, test of hypothesis was done at significance level 0.05 two-sided. Associations between socio-demographic, anthropometric and clinical factors and the prevalence of hypertension were explored with logistic regression analysis, the diagnosis of hypertension being entered as a dependent dichotomic variable. Results of regression analysis are expressed as RR with 95% Cl for each independent variable.[18] All analyses were performed with SPSS software, V.17.0 (SPSS).

RESULTS

Characteristics of study population

Characteristics of HYDY participants are reported in table 1. Distribution among age decades and living location (urban and rural) were identical among men and women. Overall, the prevalence of illiterate subjects was higher in women (51%) than in men (19%). The prevalence of obesity and abdominal obesity were also higher in women (13.4%; 95% Cl 12.5% to 14.4%; and 26.5%; 95% Cl 25.3% to 27.7%) than in men (6.9%; 95% Cl 6.2% to 7.6%; and 3.4%; 95% Cl 2.9% to 3.9%).

All subjects received two visits at home separated by a median interval of 5.36 days (95% Cl 5.30% to 5.42%; range 1–13 days), with no differences between gender. The average of the last two of the three BP and heart rate readings taken at each visit is reported in table 1. Values measured at visit 2 were lower than values obtained at visit 1 both in men and in women.

Hypertension rate and diagnostic criteria

Overall, the rate of hypertension at visit 1 was 19.1% (95% Cl 18.3% to 19.8%), being 15.9% (95% Cl 15.2% to 16.6%) at visit 2. In particular 1307 and 7930 participants were found to be hypertensive and normotensive at both visits, respectively; 642 subjects had an hypertension diagnosis at visit 1 only, whereas 317 were hypertensive at visit 2 only (χ^2 test p<0.001). Therefore, when the diagnosis was based on fulfilling the same criteria on both visits the estimated hypertension rate was lowered by 33% (12.8%; 12.1% to 13.4%). When data were standardised to the Yemen population (15–69 years) prevalence was 7.7% (95% CI 7.2% to 8.1%). This value, considering both the visits, is lower than estimations obtained when visit 1 (12.8%; 95% CI 12.2% to 13.4%) or visit 2 (10.5%; 95% CI 9.9% to 11%) are considered independently (figure 1). Hypertension prevalence age-standardised to the WHO world population 2001 aged 15–69 years was 11.3% (10.7% to 11.9%) when based on both visits and 17.3% (16.5% to 10%) when based on the first visit (gender-specific values are reported in table 2).

Overall 528 subjects were on antihypertensive treatment. Rates of awareness and treatment importantly varied according to the criteria adopted for hypertension diagnosis being higher when based on the results of both visits. The estimation of control rates was more restrictive when based on the result of both visits than of single visits (table 2). In both genders the proportion of hypertensive subjects aware of their hypertension, the proportion of subjects under current treatment increased with age. Conversely, as expected, the proportion of treated subjects whose hypertension was controlled decreased with age (table 2). When excluding individuals already on antihypertensive drug treatment and estimating hypertension prevalence on BP measurements, the rate of hypertension among participants was 17.2% (16.4% to 18%) at visit 1 (n=1425), 12.8% (12.1% to 13.5%) at visit 2 (n=1098), 8.7% (8.1% to 9.3%) of subjects (n=779) fulfilling the criteria at both visits.

Factors affecting misclassification of hypertension at visit one

When considering untreated subjects, 53% of the 1094 participants who had hypertension grade 1 at the first visit, and 24% of the 239 subjects with hypertension grade 2, did not fulfil the criteria for hypertension at visit 2 reassessment. Conversely, only 8% of the 92 untreated participants with grade 3 hypertension had normal BP values at visit 2 reassessment. Misclassification also varied by subject age. The younger the subjects were, the wider

Table 1 Characteristics of Hypertension and Diabetes in Yemen study participants

	Men	Women
Participants, n	5063	5179
Living in urban location, n (%)	2519 (49.8)	2590 (50.0)
Age (years), mean (95% CI)	39.4 (39.0 to 39.9)	39.2 (38.7 to 39.6)
15–24 years, n (%)	1016 (20.1)	1058 (20.4)
25–34 years, n (%)	1020 (20.1)	1047 (20.2)
35–44 years, n (%)	1008 (19.9)	1021 (19.7)
45–54 years, n (%)	990 (19.6)	1057 (20.4)
55–69 years, n (%)	1029 (20.3)	996 (19.2)
Smokers (daily), n (%)	1428 (28.2)	458 (8.8)
Education (years), mean (95% CI)	7.7 (7.5 to 7.9)	4.4 (4.2 to 4.5)
Illiterate, n (%)	986 (19.5)	2666 (51.5)
Can read and write, n (%)	830 (16.4)	375 (7.2)
Primary school, n (%)	685 (13.5)	661 (12.8)
Secondary school, n (%)	832 (16.4)	542 (10.5)
High school, n (%)	774 (15.3)	504 (9.7)
College or post, n (%)	950 (18.8)	428 (8.3)
Self-reported physical activity, n (%)		
Sedentary	914 (21.1)	1465 (32.8)
Light to moderate	2606 (60.1)	2586 (57.9)
Vigorous	814 (18.8)	418 (9.4)
Self-reported fruit consumption, n (%)		
≤1 day/week	2357 (46.7)	2470 (47.8)
2–4 day/week	1947 (38.6)	1962 (37.9)
≥5 days/week	744 (14.7)	740 (14.3)
Self-reported vegetable consumption, n (%)		
≤1 day/week	1101 (21.8)	1040 (20.1)
2–4 day/week	1362 (26.9)	1437 (27.8)
≥5 days/week	2597 (51.3)	2692 (52.1)
Treated with antihypertensive drugs, n	215	313
Height (cm), mean (95% CI)	161.6 (161.4 to 161.8)	153.1 to (152.9 to 153.3)
Weight (kg), mean (95% CI)	60.5 (60.1 to 60.9)	56.9 (56.5 to 57.3)
Waist circumference (cm), mean (95% CI)	78.5 (78.1 to 78.9)	80.0 (79.6 to 80.4)
Abdominal obesity, n (%)	171 (3.4)	1372 (26.5)
Body mass index (kg/m^2), mean (95% CI)	23.1 (22.9 to 23.3)	24.3 (24.1 to 24.5)
Overweight (25.0–29.9 kg/m^2), n (%)	1174 (23.2)	1321 (25.5)
Obesity (≥30.0 kg/m^2), n (%)	349 (6.9)	695 (13.4)
High cholesterol (≥5 mmol/l), n (%)	593 (11.7)	803 (15.5)
High triglycerides (≥1.7 mmol/l), n (%)	2007 (39.6)	1887 (36.4)
Diabetes	257 (5.1)	281 (5.4)
Interval between visits (days), mean (95% CI)	5.2 (5.2 to 5.3)	5.5 (5.4 to 5.6)
First visit (mean, 95% CI)		
Systolic blood pressure (BP) (mm Hg)	123.0 (122.6 to 123.4)	122.7 (122.1 to 123.3)
Diastolic BP (mm Hg)	76.9 (76.5 to 77.3)	76.9 (76.7 to 77.1)
Heart rate (mm Hg)	79.3 (79.1 to 79.5)	2.2 (82.0 to 82.4)
Air temperature (°C)	24.4 (24.2 to 24.6)	24.3 (24.1 to 24.5)
Second visit (mean, 95% CI)		
Systolic BP (mm Hg)	121.5 (121.1 to 121.9)	120.6 (120.2 to 121.0)
Diastolic BP (mm Hg)	76.2 (76.0 to 76.4)	76.0 (75.8 to 76.2)
Heart rate (mm Hg)	78.5 (78.3 to 78.7)	81.1 (80.9 to 81.3)
Air temperature (°C)	24.4 (24.2 to 24.6)	24.2 (24.0 to 24.4)
Dipstik test ≥1+, n (%)	339 (6.7)	270 (5.2)
Self report of MI, stroke, POAD, n (%)	47 (0.9)	38 (0.7)

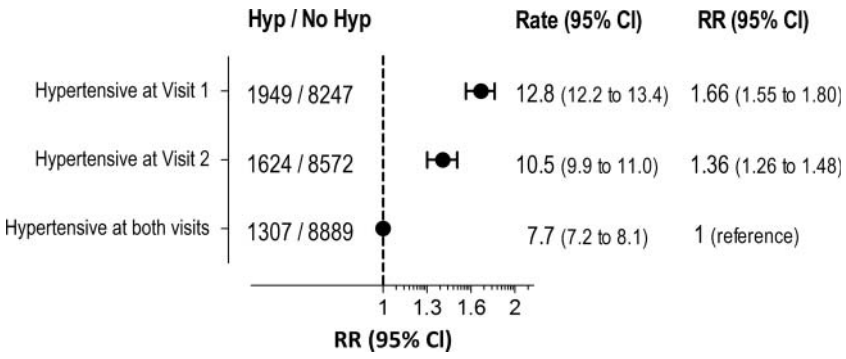

Figure 1 Diagnosis of hypertension (systolic blood pressure (BP) ≥140 mm Hg and/or diastolic BP ≥90 mm Hg and/or self-reported use of antihypertensive drugs at the time of the interview) performed on the basis of measurements taken at the first visit (visit 1), at the second visit (visit 2) or both. The number of subjects with and without the condition and age-weighted rates (to the 15–69 years Yemen population) are reported.

the difference was between estimates based on one or two visits (table 2). As a result, only 43% of men and 44% of women <35 years of age found to be hypertensive at visit one were hypertensive at both visits. These percentages were 72% and 76% for men and women, respectively, aged >45 years of age (table 3).

When characteristics of misclassified participants were compared to untreated subjects with hypertension diagnosis confirmed at both visits (logistic regression analysis including 1396 subjects), misclassification was found to be independent by gender, education level, BMI and W/H ratio tertiles. The probability to have the diagnosis confirmed was directly associated with age decades, grade of hypertension, provisional diagnosis of diabetes at visit 1 (FG≥7.0 mmol/l or self-reported use of hypoglycaemic medications), and proteinuria ≥1+ at dipstick test.

Rates of proteinuria (≥1+ at dipstick test), or the self-report of CV disease (MI, stroke and POAD) at questionnaire, were comparable among subjects classified as hypertensive at the first, the second or at both visits (table 3). However, the 959 participants found to be hypertensive at visit 1 or at visit 2 only, and thus excluded from the final diagnosis of hypertension (not confirmed), had rates of proteinuria and self-reported CV disease comparable with normotensive subjects (at both visits) and the general population (table 4).

Cardiovascular risk stratification after one or two visits

BP readings taken at the first visit (SBP1/DBP1) or average of BP readings taken at the first and the second visits (SBP1–SBP2/DBP1–DBP2) were used to stratify HYDY participants in the five BP categories according to ESH/ESC guidelines.[7] As indicated by figure 2 the different prevalence of hypertension when the diagnosis rely on measurements taken at the first visit or at two visits is mainly due to misclassification of subjects with grade 1 hypertension.

CV risk stratification according to the ESH/ESC chart[7] using average BP values at visit1 and at both visits is reported in table 5. Most people had average or low 10-year CV risk, and a large fraction (84.3% after visit 1 and 86.2% after two visits) had CV risk <20% (average, low or moderate). The age-weighted percentage of the population with a CV risk ≥20% (high or very high CV risk) was 13.8% after visit 1 and 12% after two visits (table 5). Overall, only 1.9% of Yemen population classified at high or very high CV risk at visit 1 moved to average, low or moderate CV risk categories after two visits (figure 3).

DISCUSSION

This study provides helpful results to clarify the impact of survey strategy on the final estimation of hypertension burden in developing countries. One of the major contributions is the information that a strategy based on two visits allows one to exclude from final diagnosis subjects at low CV risk with a resultant 35% reduction of the estimated prevalence of hypertension. This information is essential for estimating drug costs and budget allocation in national prevention programmes.

The fall in BP over repeated readings mainly rely to a transient elevation of BP in persons submitted to BP measurements, and was reported to be inversely related with age and directly related to BP values.[8] From a clinical prospective, the uncertainty about the patient's true BP at clinic measurement may cause uncertainty in treatment decisions.[19] Therefore, guidelines for clinical practice commonly recommend that the diagnosis of hypertension rely on multiple measurements obtained at different visits.[6 7] At the population level, the relevant logistic difficulties and personnel costs of a strategy based on two separate visits, and the negative prognostic role of high BP variability and episodic hypertension,[10] may sometimes lead to accept the adoption of a single visit strategy. Ignoring the difference in hypertension definition criteria may however lead to erroneous conclusions when comparing results of surveys assessing the prevalence of hypertension, awareness and control in different countries.[20] In two epidemiological studies where the estimation of hypertension prevalence based on two visits was compared with the estimation based on a single visit, the reduction was 12% in a cohort of

Table 2 Prevalence of hypertension, and awareness based on the first visit (visit 1), the second visit (visit 2) or both visits to the 10242 study participants

	Hypertension				Awareness among hypertensive subjects			
	Visit 1	Visit 2	Both	Δ	Visit 1	Visit 2	Both	Δ
Men (n=5063)								
Age decades, n (%)								
15–24 years	48 (4.7)	42 (4.2)	15 (1.5)	–68.1	4 (8.3)	4 (9.5)	4 (26.7)	220.0
25–34 years	82 (8.0)	68 (6.7)	41 (4.0)	–50.0	13 (15.9)	13 (19.1)	13 (31.7)	100.0
35–44 years	142 (14.1)	101 (10.0)	73 (7.2)	–48.6	20 (14.1)	20 (19.8)	20 (27.4)	94.5
45–54 years	263 (26.6)	234 (23.7)	188 (19.0)	–28.7	85 (32.3)	85 (36.3)	85 (45.2)	39.9
55–69 years	375 (36.5)	315 (30.6)	272 (26.4)	–27.5	118 (31.5)	118 (37.5)	118 (43.4)	37.9
Prevalence, % (95% CI)								
Crude	18.0 (16.9 to 19.1)	15.0 (14.0 to 16.0)	11.6 (10.8 to 12.5)	–35.3	26.4 (23.7 to 29.4)	31.3 (28.1 to 34.7)	39.9 (36.0 to 43.9)	54.5
Age standardised*	16.2 (15.1 to 17.3)	13.5 (12.5 to 14.4)	10.2 (9.4 to 11.0)	–37.0	–	–	–	–
Women (n=5179)								
Age decades, n (%)								
15–24 years	56 (5.3)	40 (3.8)	17 (1.6)	–69.7	1 (1.8)	1 (2.5)	1 (5.9)	229.4
25–34 years	97 (9.3)	68 (6.5)	46 (4.4)	–52.6	16 (16.5)	16 (23.5)	16 (34.8)	110.9
35–44 years	163 (16.0)	136 (13.4)	105 (10.3)	–35.6	54 (33.1)	54 (39.7)	54 (51.4)	55.2
45–54 years	371 (35.1)	325 (30.8)	285 (27.0)	–23.2	138 (37.2)	138 (42.5)	138 (48.4)	30.2
55–69 years	356 (35.7)	297 (29.8)	265 (26.6)	–25.6	133 (37.4)	133 (44.8)	133 (50.2)	34.3
Prevalence, % (95% CI)								
Crude	20.1 (19.1 to 21.2)	16.7 (15.7 to 17.8)	13.9 (12.9 to 14.8)	–31.2	33.8 (31.0 to 36.8)	39.8 (36.6 to 43.1)	46.9 (43.3 to 50.6)	45.3
Age standardised*	18.3 (17.2 to 19.4)	15.1 (14.1 to 16.1)	12.3 (11.4 to 13.2)	–32.8	–	–	–	–

Δ=(percentage based on visit 1−percentage based on both visits)/percentage based on visit 1.
To the WHO standard population 2001.

Table 3 Prevalence of treatment and control based on the first visit (visit 1), the second visit (visit 2), or both visits to the 10 242 study participants

	Current treatment among hypertensive subjects				Blood pressure control among treated subjects			
	Visit 1	Visit 2	Both	Δ	Visit 1	Visit 2	Both	Δ
Men (n=5063)								
Age decades, n (%)								
15–24 years	3 (6.3)	3 (7.1)	3 (20.0)	220.0	1 (33.3)	1 (33.3)	1 (33.3)	–
25–34 years	10 (12.2)	10 (14.7)	10 (24.4)	100.0	3 (30.0)	2 (20.0)	0 (0.0)	–
35–44 years	17 (12.0)	17 (16.8)	17 (23.3)	94.5	7 (41.2)	9 (52.9)	7 (41.2)	–
45–54 years	73 (27.8)	73 (31.2)	73 (38.8)	39.9	19 (26.0)	23 (31.5)	14 (19.2)	–26.3
55–69 years	112 (29.9)	112 (35.6)	112 (41.2)	37.9	19 (17.0)	33 (29.5)	15 (13.4)	–21.1
Prevalence, % (95% CI)								
Crude	23.6 (20.9 to 26.5)	28.3 (25.2 to 31.6)	36.5 (32.7 to 40.5)	54.5	22.8 (17.7 to 28.8)	31.6 (25.8 to 38.1)	17.2 (12.8 to 22.6)	–24.5
Women (n=5179)								
Age decades, n (%)								
15–24 years	1 (1.8)	1 (2.5)	1 (5.9)	229.4	0 (0.0)	0 (0.0)	0 (0.0)	–
25–34 years	13 (13.4)	13 (19.1)	13 (28.3)	110.9	8 (61.5)	9 (69.2)	6 (46.2)	–25.0
35–44 years	50 (30.7)	50 (36.8)	50 (47.6)	55.2	27 (54.0)	29 (58.0)	22 (44.0)	–18.5
45–54 years	124 (33.4)	124 (38.2)	124 (43.5)	30.2	36 (29.0)	47 (37.9)	31 (25.0)	–13.9
55–69 years	125 (35.1)	125 (42.1)	125 (47.2)	34.3	38 (30.4)	41 (32.8)	31 (24.8)	–18.4
Prevalence, % (95% CI)								
Crude	30.0 (27.3 to 32.9)	36.1 (33.0 to 39.4)	43.6 (40.0 to 47.2)	45.3	34.8 (29.7 to 40.2)	40.3 (35.0 to 45.7)	28.7 (24.0 to 34.0)	–17.4

Δ=(percentage based on visit 1—percentage based on both visits)/ percentage based on visit 1.

Table 4 Rates of proteinuria and self-reported cardiovascular (CV) disease in Hypertension and Diabetes in Yemen participants found to be hypertensive at visit 1, at visit 2 or at both visits, in subjects finally excluded from the final diagnosis of hypertension (not confirmed), in normotensive subjects and in all participants

	Subjects	DIPSTIK test ≥1+		Self-report of CV disease	
Diagnosis	n	n	% (95% CI)	n	% (95% CI)
Hypertension at visit 1	1938	153	7.9 (6.8 to 9.2)	58	3.0 (2.3 to 3.8)
Hypertension at visit 2	1614	141	8.7 (7.5 to 10.2)	55	3.4 (2.6 to 4.4)
Hypertension at both	1296	123	9.5 (8.0 to 11.2)	53	4.1 (3.1 to 5.3)
Not confirmed	959	48	5.0 (3.8 to 6.6)	7	0.7 (0.0 to 1.5)
Normotensives	7769	438	5.6 (5.1 to 6.2)	25	0.3 (0.2 to 0.5)
All participants	10 025	609	6.1 (5.6 to 6.6)	85	0.8 (0.7 to 1.0)

subjects aged 62±11 years,[9] being >35% in a cohort of subjects aged 39±9 years.[18] In particular, two-thirds of men <30 years of age had normal BP values at the second visit.[18] In both studies, the majority of subjects misclassified as hypertensive were in the less severe hypertensive grade.[9 18] In a recent small survey the estimation of hypertension prevalence had, as expected, a strong association with the presence of left ventricular hypertrophy independently from diagnostic criteria (one or two visits).[9] However, the most critical issue, the CV risk of subjects excluded from final diagnosis, is still poorly investigated. This information is especially crucial in low resource setting where budget allocation to CV prevention programmes might compete with other priorities. HYDY study participants were stratified by cardiovascular risk according to ESH/ESC criteria[7] thus allowing one to investigate characteristics of misclassified subjects. Subjects misclassified at first visit most frequently belonged to low or moderate CV risk categories, having a rate of proteinuria comparable to the general population and to subjects found to be normotensive at both visits. This does not necessarily imply that subjects with high BP at both visits are 'real' hypertensives but that they are higher-risk hypertensives. Therefore, when resources are limited the estimation of hypertension prevalence might be based on only one visit, while resources can be more efficiently used to target high-risk people who will benefit the most.

Heart attack and stroke are preventable either through conventional management of single risk factors (hypertension), or by applying a total CV risk approach which could permit providers to focalise drug treatment use only in high-risk subjects. CV risk has a continuous relationship with BP values. In particular, the present study clarifies that although there is a large discrepancy (35%) in the estimation of hypertension prevalence on the basis of one visit or two visits, only 1.9% of the Yemen population classified at high or very high CV risk at visit 1 moved to average, low or moderate CV risk categories after two visits. Current treatment strategies are indeed based on CV risk stratification. It is recommended that pharmacological treatment should be provided for all people when their calculated 10-year CV risk is at least 30% or more. The risk threshold can be lowered to 20% if and when resources permit. More precisely, age-weighted prevalence of subjects at very high CV risk estimated after

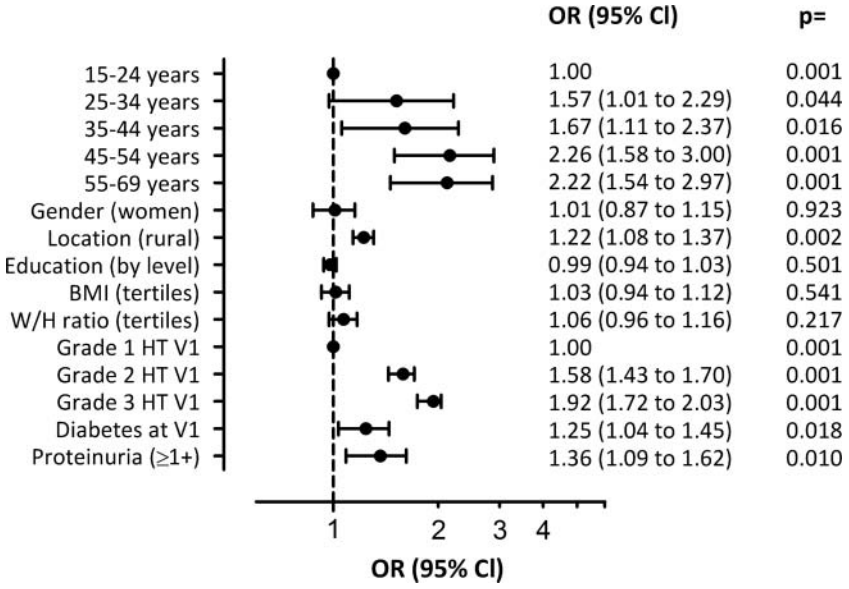

Figure 2 Factors associated with confirmation of hypertension diagnosis (systolic blood pressure (BP) ≥140 mm Hg and/or diastolic BP ≥90 mm Hg at both visits) at multiple logistic regression analysis including only non-treated subjects (n=1396). Results are expressed as OR with 95% CI.

Table 5 Cardiovascular risk distribution among the 9926 adult subjects investigated in the Hypertension and Diabetes in Yemen study based on the results first visit (visit 1), or both visits

	After visit 1			After two visits			Δ
Risk categories	n=	Crude (%)	Age weighted, % (95% CI)	n	Crude	Age weighted, % (95% CI)	n
Average	2246	22.6	30.3 (28.9 to 31.6)	2326	23.4	31.3 (29.9 to 32.7)	128 851
Low	3387	34.1	33.7 (32.4 to 35.0)	3495	35.2	34.1 (32.8 to 35.4)	48 207
Moderate	2234	22.5	20.3 (19.3 to 21.3)	2281	23.0	20.7 (19.7 to 21.7)	52 613
High	1206	12.1	8.2 (7.7 to 8.7)	1033	10.4	6.6 (6.1 to 7.1)	−190 741
Very high	853	8.6	7.5 (6.9 to 8.1)	792	8.0	7.2 (6.6 to 7.8)	−36 523

Δ=estimated difference between Yemen subjects attributed to the risk category on the basis of blood pressure (BP) measurements taken at the first visit and those attributed to the same class on the basis of average of BP measurements taken at both visits (subjects allocated at visit 1−subjects allocated after two visits).

one visit did not differ versus the estimation based on the two visits strategy. A mild difference is appreciable only when the 20% threshold is adopted, corresponding to an estimated number of 227 000 Yemen patients aged 15–69 years.

The age-standardised prevalence of hypertension at first visit for subjects aged 15–69 years (16.2%) is markedly lower than rates reported in economically developed countries for subjects older than 20 years (37.3%).[2] Most importantly, direct age standardisation to the 35–69 years WHO World Standard Population[17] (26.6%; 25.5% to 27.6%), allows comparison with Egypt (33.8%),[21] Iran (34.1%)[22] or Turkey (34.2%).[23] The low prevalence of hypertension, besides any methodological consideration, might thus be related to the possibility that Yemen is behind in the epidemiological transition currently ongoing in other countries of the Middle East Crescent area.

In conclusion, according to present data, the choice of one or two visits strategy is not relevant, but it is important to implement a strategy that allows for a more comprehensive framework of CV risk.

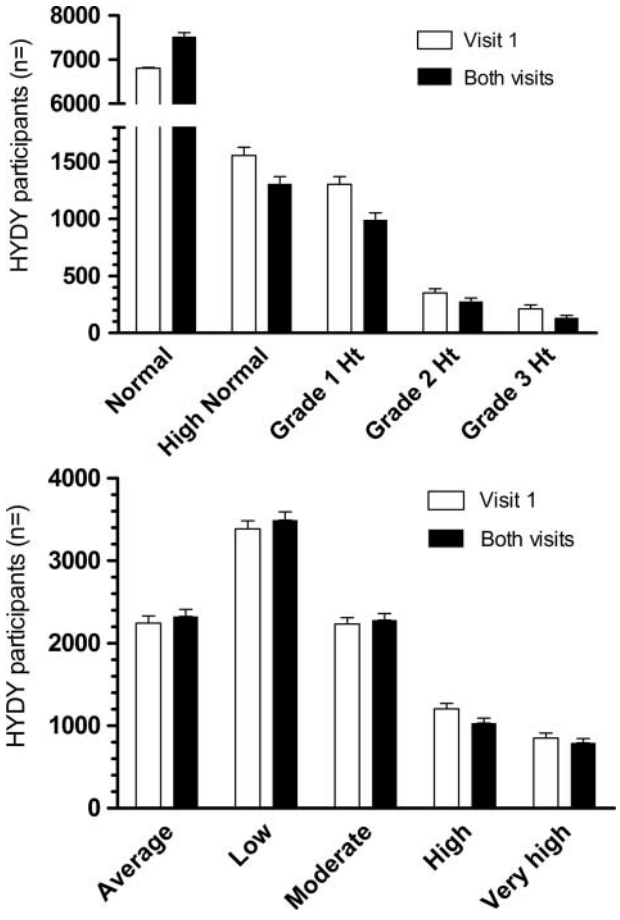

Figure 3 Blood pressure (BP) and cardiovascular risk stratification of Hypertension and Diabetes in Yemen participants according to the European Society of Hypertension/European Society of Cardiology chart using average BP values at visit1 and at both visits.

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