



Impact of one or two visits strategy on hypertension burden estimation in Yemen population aged 15 to 69: population based cross-sectional study.

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3 **Impact of one or two visits strategy on hypertension burden estimation in Yemen population**
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Contributorship Statement:

PAM, SR, MoB, and MaB drafted the manuscript. PAM, SR, MoB, MaB, LM, GFG, DAH, and HAG were involved in the conception and design of the study. DAH, and HAG were part of the project management team that coordinated data collection for the study. PAM, and MaB wrote the statistical analysis plan; PAM, SR, and LM conducted the main analyses and provided statistical advice; DZ provided substantial contributions to analysis and interpretation of data and revised the draft paper. All authors had access to all data sources, contributed to the interpretation of results, commented on the report, and approved the final version for publication. PAM is the guarantor.

Summary

1. Article Focus

To investigate the effect on hypertension prevalence estimation and on CV risk stratification of taking blood pressure at one or two visits in a cross-sectional national survey.

To identify the characteristics of subjects who are excluded from the final diagnosis when restricting the diagnostic criteria.

2. 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 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.

3. Strength and Limitations

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.

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 investigate the impact of one or two visits strategy on hypertension burden estimation and CV risk stratification.

Design. Population-based cross-sectional survey with triplicate blood pressure 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 to 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 blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or self-reported use of antihypertensive drugs.

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

Subject headings

hypertension (high blood pressure); hypertension diagnosis; cardiovascular disease risk factors; epidemiology; survey;

INTRODUCTION

The World Health Organization 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- and middle-income countries (2, 3). Surveys performed in developing countries are revealing that changing lifestyle and urbanization are associated with a 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 BP variability and episodic hypertension, with a final overestimation of a true 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 blood pressure readings performed during two separate home-visits as recommended by guidelines for the clinical diagnosis of hypertension (6,7). The aim of present study is 1) to compare the differences on prevalence, awareness, treatment, and control rates, and on 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) to identify 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 multi-stage 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 years; 15-24; 25-34; 35-44; 45-54; 55-69) to a total of twelve strata. All male and female subjects aged 6 through 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 study. One hundred and eighty-two subjects refused to participate, and 12257 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 health-care provider.

Data collection

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3 The survey was performed following the three different levels of the World Health Organization
4 Stepwise Approach to Chronic Disease Risk Factor Surveillance (STEPS)(12), which included
5 questionnaire, physical measurements, and biochemical measurements, using standardized methods.
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7 The burden of hypertension in the population was assessed by taking triplicate BP measurements on
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9 two visits, separated by few days. Data collection was conducted at home by centrally trained survey
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11 teams composed by two investigators of the opposite gender.
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14 Community sensitization activities preceded each survey round, including local council briefings
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16 with the chiefs and elders of the villages. During the first visit (visit 1) the head of the household or
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18 spouse and the participant were informed about the objectives, and procedural details of the survey.
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20 Privacy of information was assured. After obtaining consent, study questionnaire was administered.
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22 The study questionnaire included questions about demographics, lifestyle, and medical history (WHO
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24 STEPS-Instrument v2.0)(12). Participants were asked if they had been advised to change their diet
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26 (“special prescribed diet”), or to lose weight (“advice or treatment to lose weight”), or quit smoking
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28 (“advice or treatment to stop smoking”), or do exercise (“advice to start or do more exercise”),
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30 attributed to hypertension, by indication of a health professional. Close-ended questions were asked to
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32 find out if they had been seen by a traditional healer over the last year or if they had been using herbal
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34 or traditional remedies attributed to high blood pressure. “Known ischaemic heart disease” (IHD) was
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36 defined as a person with history of heart attack requiring hospitalization, or a person with physician-
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38 diagnosed IHD who was taking medication as confirmed by the survey team. “Known stroke” was
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40 defined as a person with a history of abrupt-onset weakness or paralysis on one side of the body, with
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42 or without a history of hospitalization, or a person with physician-diagnosed stroke and currently
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44 experiencing weakness or paralysis on one side of the body.
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47 The mid-arm circumference was measured to use the appropriate cuff size (small, medium, and
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49 large for mid-arm circumferences of 17-22 cm, 22-32 cm, and 32-42 cm respectively). Three
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51 measurements of BP and pulse rate were taken at 2-min intervals on the dominant arm after a rest of at
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53 least 15 min, in the seated position (7). Readings were obtained using a clinically validated
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55 semiautomatic sphygmomanometer (HEM 705 IT; Omron Matsusaka Co Ltd, Japan). The average of
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57 the last two readings for systolic and diastolic BP were defined as SBP1 and DBP1 respectively.
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59 Anthropometric measurements were taken on standing participants wearing light clothes and without
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61 shoes using standard techniques (13). Body weight was measured to the nearest 0.1 Kg using a spring
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63 balance and height to the nearest 0.5 cm using a stadiometer. Waist and hip circumference was
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65 measured to the nearest 0.1 cm. Finger prick blood samples were then obtained from fasting (>8h)

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3 subjects (aged ≥ 15 years) to measure glucose (Accutrend system, Roche Diagnostics, Mannheim,
4 Germany), cholesterol, and triglycerides blood values (MultiCare-in, HPS, Italy) using dry chemistry.
5 The subject was then asked to void. A midstream specimen of urine was collected and dipstick test
6 (Auction sticks, A.Menarini Diagnostics, Italy) was immediately performed and read manually to
7 semiquantitate the occult blood (trace, 1+ to 4+) and protein (trace, 1+ to 4+). A new appointment was
8 taken for non-fasting participants and for subjects who were menstruating. All subjects were then
9 visited again within the next ten days by the same survey team using the same measurement devices
10 and procedures for the second session of BP (SBP2 and DBP2) and fasting glucose (FG2)
11 measurements.
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21 **Diagnostic criteria**

22 Arterial hypertension was defined as 1) systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg
23 and/or 2) self-reported use of antihypertensive drugs at the time of the interview (7). More precisely the
24 prevalence of hypertension was based on values measured at the first visit (SBP1 and DBP1), at the
25 second visit (SBP2 and DBP2), and on fulfilling the same criteria for hypertension on both visits.
26 Awareness of hypertension was defined as self-report of any prior diagnosis of hypertension by a
27 health care professional among the population defined as having hypertension. Hypertension treatment
28 was defined as a self-reported use of antihypertensive drugs within the two weeks preceding the
29 interview. Hypertension control was defined as systolic BP < 140 mm Hg and diastolic BP < 90 mm Hg.
30 The proportion of hypertension control was relative to hypertensive treated with drugs.
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39 Diabetes mellitus (DM) was defined as 1) fasting glucose (FG) ≥ 7.0 mmol/L at the two visits or
40 2) self-reported use of hypoglycaemic medications at the time of the interview; impaired fasting
41 glucose (IFG) as $5.6 \leq \text{FG} < 7.0$ mmol/L in the absence of hypoglycaemic medications;
42 normal FG as $\text{FG} < 5.6$ mmol/L at the two visits (14). Overweight and obesity were defined as a body
43 mass index (BMI) 25.0 to 29.9 kg/m^2 , and ≥ 30 kg/m^2 respectively. Abdominal obesity was defined as
44 waist circumference > 102 cm in men or > 88 cm in women. Gender specific tertiles for BMI and waist-
45 to-hip (W/H) ratio, were calculated using data of adult subjects without hypertension, normal FG,
46 cholesterol < 5.0 mmol/L, triglycerides < 1.7 mmol/L, and no protein at urine dipstick test. Resulting
47 cut-offs were 20.0 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
48 0.907 in men and 0.815 and 0.887 in women for W/H ratio. On the basis of cholesterol and
49 triglycerides assessments subjects were classified as high cholesterol (> 5.0 mmol/l) or high
50 triglycerides (> 1.7 mmol/l) (7). Results of dipstick urinalysis were classified as no protein (0), protein
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3 trace (+/-), or proteinuria ($\geq+1$). A smoker was defined as one who smoked any form of tobacco on a
4 daily (daily smoker) or a non-daily (occasional smoker) basis. Those who had smoked but had quit
5 were designated as former smokers, and those who had never smoked at all were designated as never
6 smokers. On the basis of education level subjects were classified into six levels: 1) illiterate; 2) can
7 read and write; 3) primary school; 4) preparatory school; 5) secondary; 6) university or post. Fruit and
8 vegetable consumption were classified as 1) ≤ 1 day/week; 2) 2-4 day/week; 3) ≥ 5 days/week.
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10 Participants were categorized as sedentary if they walked or cycled for less than 10 min daily, if their
11 work did not involve intense physical activity, and they did not usually practice any sport or
12 recreational physical activities.
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19 According to the ESH/ESC chart (7) risk stratification (average, low, moderate, high, and very
20 high added risk categories) was based on the presence of risk factors (average of SBP1/SBP2 and
21 DBP1/DBP2 graded in five categories; age >55 years for men or >65 years for women; daily smoking;
22 waist circumference >102 cm in men or >88 cm in women; IFG; triglycerides >1.7 mmol/L; total
23 cholesterol >5.0 mmol/L), DM, subclinical organ damage (protein trace at dipstick test), and
24 established renal (proteinuria $\geq 1+$ at dipstick test) or CV disease (self-reported stroke, myocardial
25 infarction or peripheral artery disease). The cluster of three out of 4 risk factors among abdominal
26 obesity, altered fasting plasma glucose, BP $>130/85$ mmHg, and high triglycerides (as defined above),
27 was considered as the presence of metabolic syndrome.
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35 Measures have been taken to attain complete reliability and to reduce variation to reasonable
36 limits. All study personnel successfully completed the specific one-week training programme organized
37 in Sana'a (December 2007) on the aims of the study and the specific methods used to standardize the
38 procedure for sampling and contacting individuals, questionnaire administration and form filling, BP
39 measurements using electronic devices, performing blood biochemical assay, performing urine assay,
40 and data entry into computerized data base. The training program included a pilot testing performed on
41 a population sample of 400 individuals in urban and rural areas of Sana'a.
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49 **Statistical methods**

50 A sample size of at least 1,117 subjects was required to achieve a 1% precision around an
51 estimated prevalence of diabetes of 3% with 95% confidence level (CI). Estimated required sample size
52 for two-sample comparison of diabetes prevalence of 2.25% vs 3.75% with the assumption of 0.05
53 alpha (two-sided), 80% power, was 2,161 subjects for each group. Cleaning the data, handling missing
54 data, and outliers were done according to the guidelines of WHO for STEPS data management (12).
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3 Prevalence estimates were calculated for the five age groups in the overall population and by gender.
4 Data are expressed as mean±SD with 95% CI for continuous variables, and as rates with 95% CI for
5 categorical variables. Prevalence was also weighted to represent the total Yemen population aged 15-69
6 years (2008 estimated Yemen population) (11,16), and age-standardized for age ranges 15-69 years
7 using WHO World Standard Population (17). For hypertension awareness, and treatment the analysis
8 was done on the subpopulation of hypertensive patients; for hypertension control, analysis was done on
9 the subpopulation of treated people. As there were no national data available for these two
10 subpopulations for the purpose of weighting, at this stage of analysis, we did not weight the data.
11 Prevalence rates were compared using χ^2 analysis and Risk Ratio (RR) (16). When appropriate, test of
12 hypothesis was done at significance level 0.05 two sided. Associations between socio-demographic,
13 anthropometric, and clinical factors and the prevalence of hypertension were explored with logistic
14 regression analysis, the diagnosis of hypertension being entered as dependent dichotomic variable.
15 Results of regression analysis are expressed as RR with 95% CI for each independent variable (20). All
16 analyses were performed with SPSS software, version 17.0 (SPSS).
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RESULTS

Characteristics of study population

Characteristics of HYDY participants are reported in Table 1. Distribution among age decades and living location (urban, 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%CI 12.5 to 14.4; and 26.5%; 25.3 to 27.7) than in men (6.9%; 6.2 to 7.6; and 3.4%; 2.9 to 3.9).

All subjects received two visits at home separated by a median interval of 5.36 days (95% CI 5.30 to 5.42; range 1 to 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% CI 18.3-19.8), being 15.9% (15.2-16.6) 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 (chi-squared 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%; 12.1-13.4). When data were standardized to the Yemen population (15-69 years) prevalence was 7.7% (95% CI 7.2 to 8.1). This value, considering both the two 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 11.0) are considered independently (Figure 1). Hypertension prevalence age-standardized 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 10.0) 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

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3 and estimating hypertension prevalence on BP measurements, the rate of hypertension among
4 participants was 17.2% (16.4-18.0) at visit 1 (n=1425), 12.8% (12.1-13.5) at visit 2 (n=1098), 8.7%
5 (8.1-9.3) of subjects (n=779) fulfilling the criteria at both visits.
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10 **Factors affecting misclassification of hypertension at visit one**

11 When considering untreated subjects, 53% out of the 1094 participants who had hypertension
12 Grade 1 at the first visit, and 24% out of the 239 subjects with hypertension Grade 2, did not fulfil the
13 criteria for hypertension at visit 2 reassessment. Conversely only 8% out of the 92 untreated
14 participants with Grade 3 hypertension had normal BP values at visit 2 reassessment. Misclassification
15 also varied by subject age. The younger the subjects were, the wider the difference was between
16 estimates based on one or two visits (Table 2). As a result only 43% of men, and 44% of women <35
17 years of age found to be hypertensive at visit one were hypertensive at both visits. These percentages
18 were 72% and 76% for men and women aged >45 years of age (Table 3).
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26 When characteristics of misclassified participants were compared to untreated subjects with
27 hypertension diagnosis confirmed at both visits (logistic regression analysis including 1396 subjects),
28 misclassification was found to be independent by gender, education level, BMI and W/H ratio tertiles.
29 The probability to have the diagnosis confirmed was directly associated with age decades, grade of
30 hypertension, provisional diagnosis of diabetes at visit 1 (FG ≥ 7.0 mmol/L or self-reported use of
31 hypoglycaemic medications), and proteinuria $\geq 1+$ at dipstick test.
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37 Rates of proteinuria ($\geq 1+$ at dipstick test), or the self-report of CV disease (MI,stroke,POAD) at
38 questionnaire, were comparable among subjects classified as hypertensive at the first, the second, or at
39 both visits (Table 3). However, the 959 participants found to be hypertensive at visit 1 or at visit 2 only
40 and thus excluded from the final diagnosis of hypertension (not confirmed), had rates of proteinuria and
41 self-reported CV disease comparable with normotensive subjects (at both visits) and the general
42 population (Table 4).
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49 **Cardiovascular risk stratification after one or two visits**

50 BP readings taken at the first visit (SBP1/DBP1) or average of BP readings taken at the first and
51 the second visits (SBP1-SBP2/DBP1-DBP2) were used to stratify HYDY participants in the five BP
52 categories according to ESH/ESC guidelines (7). As indicated by Figure 2 the different prevalence of
53 hypertension when the diagnosis rely on measurements taken at the first visit or at two visits is mainly
54 due to misclassification of subjects with Grade 1 hypertension.
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3 CV risk stratification according to the ESH/ESC chart (7) using average BP values at visit1 and
4 at both visits is reported in Table 5. Most people had average or low 10-year CV risk, and a large
5 fraction (84.3% after visit 1 and 86.2% after two visits) had CV risk <20% (average, low, or moderate).
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7 The age weighted percentage of the population with a CV risk $\geq 20\%$ (high, or very high CV risk) was
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9 13.8% after visit 1 and 12.0% after two visits (Table 5). Overall, only 1.9% of Yemen population
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11 classified at high or very high CV risk at visit 1 moved to average, low, or moderate CV risk categories
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13 after two visits (Figure 3).
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For peer review only

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 contribution is the information that a strategy based on two visits allows 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 programs.

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 (18). Therefore, guidelines for clinical practice commonly recommend that the diagnosis of hypertension rely on multiple measurements obtained at different visits (6,7). At 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 (19). 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 subjects aged 62 ± 11 years (9), being $>35\%$ in a cohort of subjects aged 39 ± 9 years (20). In particular, two thirds of men <30 years of age had normal BP values at the second visit (20). In both studies, the majority of subjects misclassified as hypertensive were in the less severe hypertensive grade (9,20). In a recent small surveys 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 programs might compete with other priorities. HYDY study participants were stratified by cardiovascular risk according to ESH/ESC criteria (7) thus allowing 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. Therefore when resources are limited the estimation of hypertension prevalence might be based

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3 on only one visit, while resources can be more efficiently used to target high-risk people who will
4 benefit the most.
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7 Heart attack and stroke are preventable either through conventional management of single risk
8 factors (hypertension), or by applying a total CV risk approach which could permit providers to
9 focalize drug treatment use only in high risk subjects. CV risk has a continuous relationship with BP
10 values. In particular, the present study clarify that although there is a large discrepancy (35%) in the
11 estimation of hypertension prevalence on the basis of one visit or two visits, only 1.9% of the Yemen
12 population classified at high or very high CV risk at visit 1 moved to average, low, or moderate CV
13 risk categories after two visits. Current treatment strategies are indeed based on CV risk stratification.
14 It is recommended that pharmacologic treatment should be provided for all people when their
15 calculated 10-year CV risk is at least 30% or more. The risk threshold can be lowered to 20% if and
16 when resources permit. More precisely, age weighted prevalence of subjects at very high CV risk
17 estimated after one visit did not differ vs the estimation based on the two visits strategy. A mild
18 difference is appreciable only when the 20% threshold is adopted, corresponding to an estimated
19 number of 227,000 Yemen patients aged 15-69 years.
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30 In conclusion, according to present data, the choice of one or two visits strategy is not relevant,
31 but it is important to implement a strategy that allows for a more comprehensive framework of CV risk.
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HYDY Study Group

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Disclosures

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Details of contributors

PAM, SR, MoB, and MaB drafted the manuscript. PAM, SR, MoB, MaB, LM, GFG, DAH, and HAG were involved in the conception and design of the study. DAH, and HAG were part of the project

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3 management team that coordinated data collection for the study. PAM, and MaB wrote the statistical
4 analysis plan; PAM, SR, and LM conducted the main analyses and provided statistical advice; DZ
5 revised the draft paper. All authors had access to all data sources, contributed to the interpretation of
6 results, commented on the report, and approved the final version for publication. PAM is the guarantor.
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8
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26 **Statements**

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42 All authors, external and internal, had full access to all of the data (including statistical reports
43 and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the
44 data analysis.
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47 **Data sharing**

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49 There is no additional data available.
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Table 1. Characteristics of HYDY 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)
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)
BMI (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 BP (mmHg)	123.0 (122.6 to 123.4)	122.7 (122.1 to 123.3)
Diastolic BP (mmHg)	76.9 (76.5 to 77.3)	76.9 (76.7 to 77.1)
Heart rate (mmHg)	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 (mmHg)	121.5 (121.1 to 121.9)	120.6 (120.2 to 121.0)
Diastolic BP (mmHg)	76.2 (76.0 to 76.4)	76.0 (75.8 to 76.2)
Heart rate (mmHg)	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)
Dipstick test $\geq 1+$, n (%)	339 (6.7)	270 (5.2)
Self report of MI,Stroke,POAD, n (%)	47 (0.9)	38 (0.7)

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 (16.9-19.1)	15.0 (14.0-16.0)	11.6 (10.8-12.5)	-35.3	26.4 (23.7-29.4)	31.3 (28.1-34.7)	39.9 (36.0-43.9)	54.5
Age standardized*	16.2 (15.1-17.3)	13.5 (12.5-14.4)	10.2 (9.4-11.0)	-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

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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 (19.1-21.2)	16.7 (15.7-17.8)	13.9 (12.9-14.8)	-31.2	33.8 (31.0-36.8)	39.8 (36.6-43.1)	46.9 (43.3-50.6)	45.3
Age standardized*	18.3 (17.2-19.4)	15.1 (14.1-16.1)	12.3 (11.4-13.2)	-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 10242 study participants.

	Current treatment among hypertensive subjects				BP 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 (20.9-26.5)	28.3 (25.2-31.6)	36.5 (32.7-40.5)	54.5	22.8 (17.7-28.8)	31.6 (25.8-38.1)	17.2 (12.8-22.6)	-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

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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 (27.3-32.9)	36.1 (33.0-39.4)	43.6 (40.0-47.2)	45.3	34.8 (29.7-40.2)	40.3 (35.0-45.7)	28.7 (24.0-34.0)	-17.4

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

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Table 4. Rates of proteinuria and self-reported CV disease in HYDY 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.

Diagnosis	Subjects	DIPSTIK test $\geq 1+$		Self-report of CV disease	
	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	10025	609	6.1 (5.6 to 6.6)	85	0.8 (0.7 to 1.0)

Table 5.

CV risk distribution among the 9926 adult subjects investigated in the HYDY study based on the results first visit (visit 1), or both visits.

Risk Categories	After Visit 1			After two visits			Δ n=
	n=	Crude %	Age weighted % (95% CI)	n=	Crude %	Age weighted % (95% CI)	
Average risk	2246	22.6	30.3 (28.9 to 31.6)	2326	23.4	31.3 (29.9 to 32.7)	128851
Low risk	3387	34.1	33.7 (32.4 to 35.0)	3495	35.2	34.1 (32.8 to 35.4)	48207
Moderate risk	2234	22.5	20.3 (19.3 to 21.3)	2281	23.0	20.7 (19.7 to 21.7)	52613
High risk	1206	12.1	8.2 (7.7 to 8.7)	1033	10.4	6.6 (6.1 to 7.1)	-190741
Very high risk	853	8.6	7.5 (6.9 to 8.1)	792	8.0	7.2 (6.6 to 7.8)	-36523

Δ = estimated difference between Yemen subjects attributed to the risk category on the basis of 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).

Legends to Figures

Figure 1.

Diagnosis of hypertension (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 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.

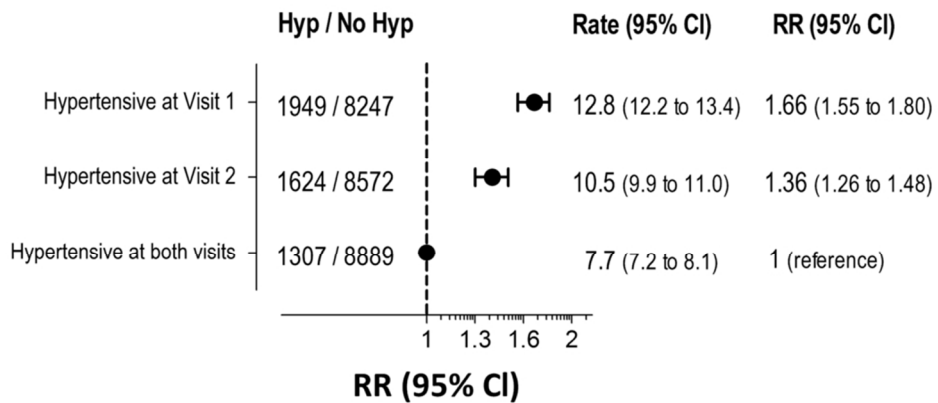
Figure 2.

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

Figure 3.

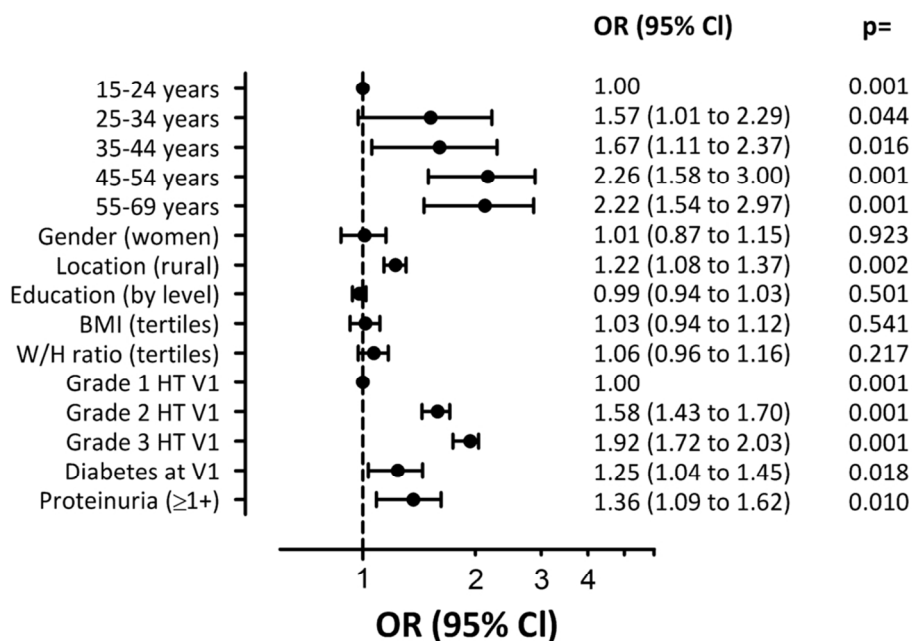
Blood pressure and CV risk stratification of HYDY participants according to the ESH/ESC chart using average blood pressure values at visit1 and at both visits.

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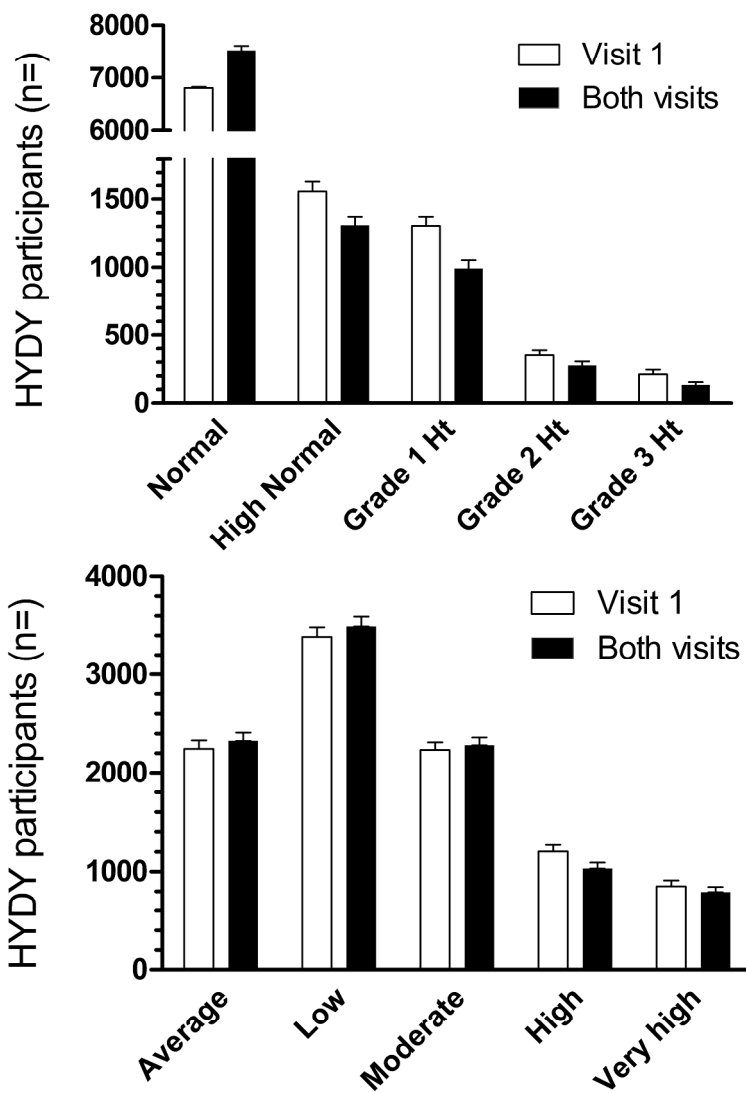
Diagnosis of hypertension (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg and/or self-reported use of antihypertensive drugs at the time of the interview) performed on the basis of measurements taken at the first visit (visit 1), at the second visit (visit 2), or both. The number of subjects with and without the condition and age-weighted rates (to the 15-69 years Yemen population) are reported.
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Factors associated with the misclassification of hypertension diagnosis (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg at both visits) at multiple logistic regression analysis including only non-treated subjects (n=1396). Results are expressed as odd ratio (OR) with 95% CI.
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Blood pressure and CV risk stratification of HYDY participants according to the ESH/ESC chart using average blood pressure values at visit1 and at both visits.
248x357mm (300 x 300 DPI)



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



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Overall comments

The authors thank the reviewers for their comments.

Responses to comments of Reviewer 1

Comment 1: The authors should more discuss the finding that microalbuminuria does not help in detecting real hypertensive patients.

Response 1: We did not screen subjects for microalbuminuria. Proteinuria (protein $\geq 1+$ at multiparametric conventional dipstick, MCD) was a significant predictor of hypertension confirmation at visit two. MCD at the score level of protein trace had 88% sensitivity and 81% specificity (AUC 88%) for microalbuminuria (urinary albumin concentration >20 mg/L) (Rapi et al. Saudi Med J. 2010; 31: 708-9). However, 95% CI for “protein trace” did not allow screening subjects fulfilling hypertension criteria at both visits. Data are reported in the following Table:

	All	Subjects with protein trace at DIPSTIK		
	n=	n=	%	(95% CI)
All	10025	1652	16.5	(15.8 to 17.2)
Hyp at Visit 1	1938	325	16.8	(15.2 to 18.5)
Hyp at Visit 2	1614	271	16.8	(15.0 to 18.7)
Hyp at both Visits	1296	225	17.4	(15.4 to 19.5)
Excluded	960	146	15.2	(13.1 to 17.6)
Normotensives	7769	1281	16.5	(15.7 to 17.3)

Probably this pattern is to be seen in the perspective of a developing country where the prevalence of hypertension is low and post-infectious diseases are still main etiology for kidney damage.

Comment 2: The authors should compare the prevalence of hypertension in Yemen as compared to developed countries, taking into consideration the difference in the age range.

Response 2: We have added the following paragraph in the last page (page 15) of the Discussion:

“The age-standardized 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 standardization 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.”

Comment 3: The manuscript is very interesting. It would be important to add some more information about the life style of the study population: alimentation, physical activity....

Response 3: Thank you for appreciating our study. We focused analysis on the impact of diagnostic criteria for resource allocation in developing countries. Information about the life style is however available so we added required data in Table 1.

Table 1. Characteristics of HYDY study participants.

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)

Responses to comments of Reviewer 2

Comment 1: *The authors aims to compare the differences on prevalence, awareness, treatment and control rates obtained on data collected at one vs, two visits, and to identify the characteristics of the subjects who have not high blood pressure in both visits. The authors seem to confuse the aims of a population-based survey where the objective is to estimate the prevalence of hypertension, usually in 3 measures within one visit, with the detection and diagnoses of hypertension at an individual level, which usually relies on more than one visit. Again, the overestimation of the prevalence of high BP when readings are based on a single visit is probably due to "regression to the mean", which is very important for the clinical diagnosis of HTN when just one BP check may overestimate this condition. On the other hand, if population-based prevalence data are based on two visits instead of one, the comparability assured by WHO-STEPS across the globe could be compromised and prevalence of HTN in Yemen could be underestimated.*

Response 1: We are aware of misinterpretations which may rise with our approach. To allow comparability with studies performed across the globe age specific and age standardized rates of HTN at visit 1 and at both visits were included in Table 2. However, as you correctly summarize, the aim of this approach was to identify the characteristics of the subjects who have not high blood pressure in both visits.

Comment 2: *As BP values rise in a particular subject, so does the probability to remain hypertensive after a new measure. The same occurs when end-organ damage or other risk factors are present. This does not necessarily implies that these last individuals are "real" hypertensives but that they are higher risk hypertensives. This fact should be emphasized in the text.*

Response 2: Thank you for this observation. We added the following sentence in the Discussion (line two from the bottom, page 14):

"This does not necessarily imply that subjects with high blood pressure at both visits are "real" hypertensives but that they are higher risk hypertensives."

Comment 3: *The authors found that BP measured in two visits resulted in a 35% reduction in the prevalence of hypertension mostly based on excluding subjects with low risk. They highlight the importance of this issue as essential for estimating drug costs and budget allocation in prioritization of prevention program. This is relevant if the main research*

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3 *question of this approach is not just to estimate the prevalence of high BP in one or two*
4 *visits but to estimate more accurately the magnitude and extent of the resources that should*
5 *be allocated to the prevention of hypertension. In my opinion, the authors should reframe*
6 *the objectives of the study and highlight resource-allocation decision making rather than*
7 *prevalence.*

8
9 Response 3: You perfectly centered the goal of our study. Notwithstanding the progressive
10 reduction of BP values at repeated measurements, resource-allocation decision making is
11 usually based on data collected at a single visit, often on a single risk factor. To achieve our
12 objective we included strategies aimed at exploring risk of excluded subjects. According to
13 present data the integration of BP measurement with simple “low cost” diagnostic tests might
14 offer advantages in costs estimation. The importance for policy makers in the health care
15 resource allocation decision making process is now highlighted in the introduction section.
16 The objective was modified as follows:
17 “To investigate the effects on health care resource allocation decision making of taking blood
18 pressure at one or two visits with CV risk stratification.”
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20
21 We also modified the title as follows:

22 “Impact of one or two visits strategy on hypertension burden estimation in HYDY, a
23 population based cross-sectional study: implications for health care resource allocation
24 decision making.”
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3 **Impact of one or two visits strategy on hypertension burden estimation in HYDY, a population**
4 **based cross-sectional study: implications for health care resource allocation decision making.**
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Contributorship Statement:

PAM, SR, MoB, and MaB drafted the manuscript. PAM, SR, MoB, MaB, LM, GFG, DAH, and HAG were involved in the conception and design of the study. DAH, and HAG were part of the project management team that coordinated data collection for the study. PAM, and MaB wrote the statistical analysis plan; PAM, SR, and LM conducted the main analyses and provided statistical advice; DZ provided substantial contributions to analysis and interpretation of data and revised the draft paper. All authors had access to all data sources, contributed to the interpretation of results, commented on the report, and approved the final version for publication. PAM is the guarantor.

Summary

1. Article Focus

To investigate the effects on health care resource allocation decision making of taking blood pressure at one or two visits with CV risk stratification.

To identify the characteristics of subjects who are excluded from the final diagnosis when restricting the diagnostic criteria.

2. 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 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.

3. Strength and Limitations

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.

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 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 to 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 blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or self-reported use of antihypertensive drugs.

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

Subject headings

hypertension (high blood pressure); hypertension diagnosis; cardiovascular disease risk factors; epidemiology; survey;

INTRODUCTION

The World Health Organization 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- and middle-income countries (2, 3). Surveys performed in developing countries are revealing that changing lifestyle and urbanization are associated with a 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 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 blood pressure 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 ~~on~~ 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 multi-stage 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 years; 15-24; 25-34; 35-44; 45-54; 55-69) to a total of twelve strata. All male and female subjects aged 6 through 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 study. One hundred and eighty-two subjects refused to participate, and 12257 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 health-care provider.

Data collection

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3 The survey was performed following the three different levels of the World Health Organization
4 Stepwise Approach to Chronic Disease Risk Factor Surveillance (STEPS)(12), which included
5 questionnaire, physical measurements, and biochemical measurements, using standardized methods.
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7 The burden of hypertension in the population was assessed by taking triplicate BP measurements on
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9 two visits, separated by few days. Data collection was conducted at home by centrally trained survey
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11 teams composed by two investigators of the opposite gender.
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14 Community sensitization activities preceded each survey round, including local council briefings
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16 with the chiefs and elders of the villages. During the first visit (visit 1) the head of the household or
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18 spouse and the participant were informed about the objectives, and procedural details of the survey.
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20 Privacy of information was assured. After obtaining consent, study questionnaire was administered.
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22 The study questionnaire included questions about demographics, lifestyle, and medical history (WHO
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24 STEPS-Instrument v2.0)(12). Participants were asked if they had been advised to change their diet
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26 (“special prescribed diet”), or to lose weight (“advice or treatment to lose weight”), or quit smoking
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28 (“advice or treatment to stop smoking”), or do exercise (“advice to start or do more exercise”),
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30 attributed to hypertension, by indication of a health professional. Close-ended questions were asked to
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32 find out if they had been seen by a traditional healer over the last year or if they had been using herbal
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34 or traditional remedies attributed to high blood pressure. “Known ischaemic heart disease” (IHD) was
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36 defined as a person with history of heart attack requiring hospitalization, or a person with physician-
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38 diagnosed IHD who was taking medication as confirmed by the survey team. “Known stroke” was
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40 defined as a person with a history of abrupt-onset weakness or paralysis on one side of the body, with
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42 or without a history of hospitalization, or a person with physician-diagnosed stroke and currently
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44 experiencing weakness or paralysis on one side of the body.
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47 The mid-arm circumference was measured to use the appropriate cuff size (small, medium, and
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49 large for mid-arm circumferences of 17-22 cm, 22-32 cm, and 32-42 cm respectively). Three
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51 measurements of BP and pulse rate were taken at 2-min intervals on the dominant arm after a rest of at
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53 least 15 min, in the seated position (7). Readings were obtained using a clinically validated
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55 semiautomatic sphygmomanometer (HEM 705 IT; Omron Matsusaka Co Ltd, Japan). The average of
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57 the last two readings for systolic and diastolic BP were defined as SBP1 and DBP1 respectively.
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59 Anthropometric measurements were taken on standing participants wearing light clothes and without
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61 shoes using standard techniques (13). Body weight was measured to the nearest 0.1 Kg using a spring
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63 balance and height to the nearest 0.5 cm using a stadiometer. Waist and hip circumference was
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65 measured to the nearest 0.1 cm. Finger prick blood samples were then obtained from fasting (>8h)

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3 subjects (aged ≥ 15 years) to measure glucose (Accutrend system, Roche Diagnostics, Mannheim,
4 Germany), cholesterol, and triglycerides blood values (MultiCare-in, HPS, Italy) using dry chemistry.
5 The subject was then asked to void. A midstream specimen of urine was collected and dipstick test
6 (Auction sticks, A.Menarini Diagnostics, Italy) was immediately performed and read manually to
7 semiquantitate the occult blood (trace, 1+ to 4+) and protein (trace, 1+ to 4+). A new appointment was
8 taken for non-fasting participants and for subjects who were menstruating. All subjects were then
9 visited again within the next ten days by the same survey team using the same measurement devices
10 and procedures for the second session of BP (SBP2 and DBP2) and fasting glucose (FG2)
11 measurements.
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21 **Diagnostic criteria**

22 Arterial hypertension was defined as 1) systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg
23 and/or 2) self-reported use of antihypertensive drugs at the time of the interview (7). More precisely the
24 prevalence of hypertension was based on values measured at the first visit (SBP1 and DBP1), at the
25 second visit (SBP2 and DBP2), and on fulfilling the same criteria for hypertension on both visits.
26 Awareness of hypertension was defined as self-report of any prior diagnosis of hypertension by a
27 health care professional among the population defined as having hypertension. Hypertension treatment
28 was defined as a self-reported use of antihypertensive drugs within the two weeks preceding the
29 interview. Hypertension control was defined as systolic BP < 140 mm Hg and diastolic BP < 90 mm Hg.
30 The proportion of hypertension control was relative to hypertensive treated with drugs.
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39 Diabetes mellitus (DM) was defined as 1) fasting glucose (FG) ≥ 7.0 mmol/L at the two visits or
40 2) self-reported use of hypoglycaemic medications at the time of the interview; impaired fasting
41 glucose (IFG) as $5.6 \leq \text{FG} < 7.0$ mmol/L in the absence of hypoglycaemic medications;
42 normal FG as $\text{FG} < 5.6$ mmol/L at the two visits (14). Overweight and obesity were defined as a body
43 mass index (BMI) 25.0 to 29.9 kg/m^2 , and ≥ 30 kg/m^2 respectively. Abdominal obesity was defined as
44 waist circumference > 102 cm in men or > 88 cm in women. Gender specific tertiles for BMI and waist-
45 to-hip (W/H) ratio, were calculated using data of adult subjects without hypertension, normal FG,
46 cholesterol < 5.0 mmol/L, triglycerides < 1.7 mmol/L, and no protein at urine dipstick test. Resulting
47 cut-offs were 20.0 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
48 0.907 in men and 0.815 and 0.887 in women for W/H ratio. On the basis of cholesterol and
49 triglycerides assessments subjects were classified as high cholesterol (> 5.0 mmol/l) or high
50 triglycerides (> 1.7 mmol/l) (7). Results of dipstick urinalysis were classified as no protein (0), protein
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3 trace (+/-), or proteinuria ($\geq+1$). A smoker was defined as one who smoked any form of tobacco on a
4 daily (daily smoker) or a non-daily (occasional smoker) basis. Those who had smoked but had quit
5 were designated as former smokers, and those who had never smoked at all were designated as never
6 smokers. On the basis of education level subjects were classified into six levels: 1) illiterate; 2) can
7 read and write; 3) primary school; 4) preparatory school; 5) secondary; 6) university or post. Fruit and
8 vegetable consumption were classified as 1) ≤ 1 day/week; 2) 2-4 day/week; 3) ≥ 5 days/week.

14 Participants were categorized as: sedentary if they walked or cycled for less than 10 min daily, if
15 their work did not involve intense physical activity, and they did not usually practice any sport or
16 recreational physical activities; engaging in light to moderate physical activity if they performed work
17 or recreational physical activities one or two days/week; engaging in vigorous physical activity if they
18 performed work or recreational vigorous physical activities three days or more/week.

22 According to the ESH/ESC chart (7) risk stratification (average, low, moderate, high, and very
23 high added risk categories) was based on the presence of risk factors (average of SBP1/SBP2 and
24 DBP1/DBP2 graded in five categories; age >55 years for men or >65 years for women; daily smoking;
25 waist circumference >102 cm in men or >88 cm in women; IFG; triglycerides >1.7 mmol/L; total
26 cholesterol >5.0 mmol/L), DM, subclinical organ damage (protein trace at dipstick test), and
27 established renal (proteinuria $\geq 1+$ at dipstick test) or CV disease (self-reported stroke, myocardial
28 infarction or peripheral artery disease). The cluster of three out of 4 risk factors among abdominal
29 obesity, altered fasting plasma glucose, BP $>130/85$ mmHg, and high triglycerides (as defined above),
30 was considered as the presence of metabolic syndrome.

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

52 53 **Statistical methods**

54 A sample size of at least 1,117 subjects was required to achieve a 1% precision around an
55 estimated prevalence of diabetes of 3% with 95% confidence level (CI). Estimated required sample size
56 for two-sample comparison of diabetes prevalence of 2.25% vs 3.75% with the assumption of 0.05
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3 alpha (two-sided), 80% power, was 2,161 subjects for each group. Cleaning the data, handling missing
4 data, and outliers were done according to the guidelines of WHO for STEPS data management (12).
5 Prevalence estimates were calculated for the five age groups in the overall population and by gender.
6 Data are expressed as mean±SD with 95% CI for continuous variables, and as rates with 95% CI for
7 categorical variables. Prevalence was also weighted to represent the total Yemen population aged 15-69
8 years (2008 estimated Yemen population) (11,16), and age-standardized for age ranges 15-69 years
9 using WHO World Standard Population (17). For hypertension awareness, and treatment the analysis
10 was done on the subpopulation of hypertensive patients; for hypertension control, analysis was done on
11 the subpopulation of treated people. As there were no national data available for these two
12 subpopulations for the purpose of weighting, at this stage of analysis, we did not weight the data.
13 Prevalence rates were compared using χ^2 analysis and Risk Ratio (RR) (16). When appropriate, test of
14 hypothesis was done at significance level 0.05 two sided. Associations between socio-demographic,
15 anthropometric, and clinical factors and the prevalence of hypertension were explored with logistic
16 regression analysis, the diagnosis of hypertension being entered as dependent dichotomic variable.
17 Results of regression analysis are expressed as RR with 95% CI for each independent variable (20). All
18 analyses were performed with SPSS software, version 17.0 (SPSS).
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RESULTS

Characteristics of study population

Characteristics of HYDY participants are reported in Table 1. Distribution among age decades and living location (urban, 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%CI 12.5 to 14.4; and 26.5%; 25.3 to 27.7) than in men (6.9%; 6.2 to 7.6; and 3.4%; 2.9 to 3.9).

All subjects received two visits at home separated by a median interval of 5.36 days (95% CI 5.30 to 5.42; range 1 to 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% CI 18.3-19.8), being 15.9% (15.2-16.6) 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 (chi-squared 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%; 12.1-13.4). When data were standardized to the Yemen population (15-69 years) prevalence was 7.7% (95% CI 7.2 to 8.1). This value, considering both the two 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 11.0) are considered independently (Figure 1). Hypertension prevalence age-standardized 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 10.0) 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

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3 and estimating hypertension prevalence on BP measurements, the rate of hypertension among
4 participants was 17.2% (16.4-18.0) at visit 1 (n=1425), 12.8% (12.1-13.5) at visit 2 (n=1098), 8.7%
5 (8.1-9.3) of subjects (n=779) fulfilling the criteria at both visits.
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10 **Factors affecting misclassification of hypertension at visit one**

11 When considering untreated subjects, 53% out of the 1094 participants who had hypertension
12 Grade 1 at the first visit, and 24% out of the 239 subjects with hypertension Grade 2, did not fulfil the
13 criteria for hypertension at visit 2 reassessment. Conversely only 8% out of the 92 untreated
14 participants with Grade 3 hypertension had normal BP values at visit 2 reassessment. Misclassification
15 also varied by subject age. The younger the subjects were, the wider the difference was between
16 estimates based on one or two visits (Table 2). As a result only 43% of men, and 44% of women <35
17 years of age found to be hypertensive at visit one were hypertensive at both visits. These percentages
18 were 72% and 76% for men and women aged >45 years of age (Table 3).
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26 When characteristics of misclassified participants were compared to untreated subjects with
27 hypertension diagnosis confirmed at both visits (logistic regression analysis including 1396 subjects),
28 misclassification was found to be independent by gender, education level, BMI and W/H ratio tertiles.
29 The probability to have the diagnosis confirmed was directly associated with age decades, grade of
30 hypertension, provisional diagnosis of diabetes at visit 1 (FG ≥ 7.0 mmol/L or self-reported use of
31 hypoglycaemic medications), and proteinuria $\geq 1+$ at dipstick test.
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37 Rates of proteinuria ($\geq 1+$ at dipstick test), or the self-report of CV disease (MI,stroke,POAD) at
38 questionnaire, were comparable among subjects classified as hypertensive at the first, the second, or at
39 both visits (Table 3). However, the 959 participants found to be hypertensive at visit 1 or at visit 2 only
40 and thus excluded from the final diagnosis of hypertension (not confirmed), had rates of proteinuria and
41 self-reported CV disease comparable with normotensive subjects (at both visits) and the general
42 population (Table 4).
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49 **Cardiovascular risk stratification after one or two visits**

50 BP readings taken at the first visit (SBP1/DBP1) or average of BP readings taken at the first and
51 the second visits (SBP1-SBP2/DBP1-DBP2) were used to stratify HYDY participants in the five BP
52 categories according to ESH/ESC guidelines (7). As indicated by Figure 2 the different prevalence of
53 hypertension when the diagnosis rely on measurements taken at the first visit or at two visits is mainly
54 due to misclassification of subjects with Grade 1 hypertension.
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3 CV risk stratification according to the ESH/ESC chart (7) using average BP values at visit1 and
4 at both visits is reported in Table 5. Most people had average or low 10-year CV risk, and a large
5 fraction (84.3% after visit 1 and 86.2% after two visits) had CV risk <20% (average, low, or moderate).
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7 The age weighted percentage of the population with a CV risk $\geq 20\%$ (high, or very high CV risk) was
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9 13.8% after visit 1 and 12.0% after two visits (Table 5). Overall, only 1.9% of Yemen population
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11 classified at high or very high CV risk at visit 1 moved to average, low, or moderate CV risk categories
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13 after two visits (Figure 3).
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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 contribution is the information that a strategy based on two visits allows 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 programs.

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 (18). Therefore, guidelines for clinical practice commonly recommend that the diagnosis of hypertension rely on multiple measurements obtained at different visits (6,7). At 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 (19). 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 subjects aged 62 ± 11 years (9), being $>35\%$ in a cohort of subjects aged 39 ± 9 years (20). In particular, two thirds of men <30 years of age had normal BP values at the second visit (20). In both studies, the majority of subjects misclassified as hypertensive were in the less severe hypertensive grade (9,20). In a recent small surveys 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 programs might compete with other priorities. HYDY study participants were stratified by cardiovascular risk according to ESH/ESC criteria (7) thus allowing 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 blood pressure at both visits are "real" hypertensives but that they are higher risk hypertensives. Therefore when resources are limited the

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3 estimation of hypertension prevalence might be based on only one visit, while resources can be more
4 efficiently used to target high-risk people who will benefit the most.
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7 Heart attack and stroke are preventable either through conventional management of single risk
8 factors (hypertension), or by applying a total CV risk approach which could permit providers to
9 focalize drug treatment use only in high risk subjects. CV risk has a continuous relationship with BP
10 values. In particular, the present study clarify that although there is a large discrepancy (35%) in the
11 estimation of hypertension prevalence on the basis of one visit or two visits, only 1.9% of the Yemen
12 population classified at high or very high CV risk at visit 1 moved to average, low, or moderate CV
13 risk categories after two visits. Current treatment strategies are indeed based on CV risk stratification.
14 It is recommended that pharmacologic treatment should be provided for all people when their
15 calculated 10-year CV risk is at least 30% or more. The risk threshold can be lowered to 20% if and
16 when resources permit. More precisely, age weighted prevalence of subjects at very high CV risk
17 estimated after one visit did not differ vs the estimation based on the two visits strategy. A mild
18 difference is appreciable only when the 20% threshold is adopted, corresponding to an estimated
19 number of 227,000 Yemen patients aged 15-69 years.
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22 The age-standardized prevalence of hypertension at first visit for subjects aged 15-69 years
23 (16.2%) is markedly lower than rates reported in economically developed countries for subjects older
24 than 20 years (37.3%) (2). Most importantly, direct age standardization to the 35-69 years WHO World
25 Standard Population (17) (26.6%; 25.5 to 27.6), allows comparison with Egypt (33.8%) (21), Iran
26 (34.1%) (22), or Turkey (34.2%) (23). The low prevalence of hypertension, besides any methodological
27 consideration, might thus be related to the possibility that Yemen is behind in the epidemiological
28 transition currently ongoing in other countries of the Middle East Crescent area.
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31 In conclusion, according to present data, the choice of one or two visits strategy is not relevant,
32 but it is important to implement a strategy that allows for a more comprehensive framework of CV risk.
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Details of contributors

PAM, SR, MoB, and MaB drafted the manuscript. PAM, SR, MoB, MaB, LM, GFG, DAH, and HAG were involved in the conception and design of the study. DAH, and HAG were part of the project

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3 management team that coordinated data collection for the study. PAM, and MaB wrote the statistical
4 analysis plan; PAM, SR, and LM conducted the main analyses and provided statistical advice; DZ
5 revised the draft paper. All authors had access to all data sources, contributed to the interpretation of
6 results, commented on the report, and approved the final version for publication. PAM is the guarantor.
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26 **Statements**

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42 All authors, external and internal, had full access to all of the data (including statistical reports
43 and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the
44 data analysis.
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47 **Data sharing**

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49 There is no additional data available.
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Table 1. Characteristics of HYDY 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)
BMI (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 BP (mmHg)	123.0 (122.6 to 123.4)	122.7 (122.1 to 123.3)
Diastolic BP (mmHg)	76.9 (76.5 to 77.3)	76.9 (76.7 to 77.1)
Heart rate (mmHg)	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 (mmHg)	121.5 (121.1 to 121.9)	120.6 (120.2 to 121.0)
Diastolic BP (mmHg)	76.2 (76.0 to 76.4)	76.0 (75.8 to 76.2)
Heart rate (mmHg)	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)
Dipstick test ≥1+, n (%)	339 (6.7)	270 (5.2)
Self report of MI,Stroke,POAD, n (%)	47 (0.9)	38 (0.7)

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 (16.9-19.1)	15.0 (14.0-16.0)	11.6 (10.8-12.5)	-35.3	26.4 (23.7-29.4)	31.3 (28.1-34.7)	39.9 (36.0-43.9)	54.5
Age standardized*	16.2 (15.1-17.3)	13.5 (12.5-14.4)	10.2 (9.4-11.0)	-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 (19.1-21.2)	16.7 (15.7-17.8)	13.9 (12.9-14.8)	-31.2	33.8 (31.0-36.8)	39.8 (36.6-43.1)	46.9 (43.3-50.6)	45.3
Age standardized*	18.3 (17.2-19.4)	15.1 (14.1-16.1)	12.3 (11.4-13.2)	-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 10242 study participants.

	Current treatment among hypertensive subjects				BP 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 (20.9-26.5)	28.3 (25.2-31.6)	36.5 (32.7-40.5)	54.5	22.8 (17.7-28.8)	31.6 (25.8-38.1)	17.2 (12.8-22.6)	-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 (27.3-32.9)	36.1 (33.0-39.4)	43.6 (40.0-47.2)	45.3	34.8 (29.7-40.2)	40.3 (35.0-45.7)	28.7 (24.0-34.0)	-17.4

$\Delta = (\text{percentage based on visit 1} - \text{percentage based on both visits}) / \text{percentage based on visit 1}$

Table 4. Rates of proteinuria and self-reported CV disease in HYDY 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.

Diagnosis	Subjects	DIPSTIK test $\geq 1+$		Self-report of CV disease	
	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	10025	609	6.1 (5.6 to 6.6)	85	0.8 (0.7 to 1.0)

Table 5.

CV risk distribution among the 9926 adult subjects investigated in the HYDY study based on the results first visit (visit 1), or both visits.

Risk Categories	After Visit 1			After two visits			Δ n=
	n=	Crude %	Age weighted % (95% CI)	n=	Crude %	Age weighted % (95% CI)	
Average risk	2246	22.6	30.3 (28.9 to 31.6)	2326	23.4	31.3 (29.9 to 32.7)	128851
Low risk	3387	34.1	33.7 (32.4 to 35.0)	3495	35.2	34.1 (32.8 to 35.4)	48207
Moderate risk	2234	22.5	20.3 (19.3 to 21.3)	2281	23.0	20.7 (19.7 to 21.7)	52613
High risk	1206	12.1	8.2 (7.7 to 8.7)	1033	10.4	6.6 (6.1 to 7.1)	-190741
Very high risk	853	8.6	7.5 (6.9 to 8.1)	792	8.0	7.2 (6.6 to 7.8)	-36523

Δ = estimated difference between Yemen subjects attributed to the risk category on the basis of 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).

Legends to Figures

Figure 1.

Diagnosis of hypertension (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 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.

Figure 2.

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

Figure 3.

Blood pressure and CV risk stratification of HYDY participants according to the ESH/ESC chart using average blood pressure values at visit1 and at both visits.

~~Impact of one or two visits strategy on hypertension burden estimation in Yemen population aged 15 to 69: a population based cross-sectional study.~~

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

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Contributorship Statement:

PAM, SR, MoB, and MaB drafted the manuscript. PAM, SR, MoB, MaB, LM, GFG, DAH, and HAG were involved in the conception and design of the study. DAH, and HAG were part of the project management team that coordinated data collection for the study. PAM, and MaB wrote the statistical analysis plan; PAM, SR, and LM conducted the main analyses and provided statistical advice; DZ provided substantial contributions to analysis and interpretation of data and revised the draft paper. All authors had access to all data sources, contributed to the interpretation of results, commented on the report, and approved the final version for publication. PAM is the guarantor.

Summary

1. Article Focus

~~To investigate the effect on hypertension prevalence estimation and on CV risk stratification of taking blood pressure at one or two visits in a cross-sectional national survey.~~

To investigate the effects on health care resource allocation decision making of taking blood pressure at one or two visits with CV risk stratification.

To identify the characteristics of subjects who are excluded from the final diagnosis when restricting the diagnostic criteria.

2. 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 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.

3. Strength and Limitations

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.

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 investigate the impact of one or two visits strategy on hypertension burden estimation and CV risk stratification.~~ **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 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 to 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 blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or self-reported use of antihypertensive drugs.

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

Subject headings

hypertension (high blood pressure); hypertension diagnosis; cardiovascular disease risk factors; epidemiology; survey;

INTRODUCTION

The World Health Organization 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- and middle-income countries (2, 3). Surveys performed in developing countries are revealing that changing lifestyle and urbanization are associated with a 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 BP variability and episodic hypertension, with a final overestimation of ~~a true~~ 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 blood pressure 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) ~~to compared the differences on~~ prevalence, awareness, treatment, and control rates, and ~~on~~ 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) ~~to identify~~ **ied** 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 multi-stage 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 years; 15-24; 25-34; 35-44; 45-54; 55-69) to a total of twelve strata. All male and female subjects aged 6 through 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 study. One hundred and eighty-two subjects refused to participate, and 12257 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 health-care provider.

Data collection

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3 The survey was performed following the three different levels of the World Health Organization
4 Stepwise Approach to Chronic Disease Risk Factor Surveillance (STEPS)(12), which included
5 questionnaire, physical measurements, and biochemical measurements, using standardized methods.
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7 The burden of hypertension in the population was assessed by taking triplicate BP measurements on
8
9 two visits, separated by few days. Data collection was conducted at home by centrally trained survey
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11 teams composed by two investigators of the opposite gender.
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14 Community sensitization activities preceded each survey round, including local council briefings
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16 with the chiefs and elders of the villages. During the first visit (visit 1) the head of the household or
17
18 spouse and the participant were informed about the objectives, and procedural details of the survey.
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20 Privacy of information was assured. After obtaining consent, study questionnaire was administered.
21
22 The study questionnaire included questions about demographics, lifestyle, and medical history (WHO
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24 STEPS-Instrument v2.0)(12). Participants were asked if they had been advised to change their diet
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26 (“special prescribed diet”), or to lose weight (“advice or treatment to lose weight”), or quit smoking
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28 (“advice or treatment to stop smoking”), or do exercise (“advice to start or do more exercise”),
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30 attributed to hypertension, by indication of a health professional. Close-ended questions were asked to
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32 find out if they had been seen by a traditional healer over the last year or if they had been using herbal
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34 or traditional remedies attributed to high blood pressure. “Known ischaemic heart disease” (IHD) was
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36 defined as a person with history of heart attack requiring hospitalization, or a person with physician-
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38 diagnosed IHD who was taking medication as confirmed by the survey team. “Known stroke” was
39
40 defined as a person with a history of abrupt-onset weakness or paralysis on one side of the body, with
41
42 or without a history of hospitalization, or a person with physician-diagnosed stroke and currently
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44 experiencing weakness or paralysis on one side of the body.
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47 The mid-arm circumference was measured to use the appropriate cuff size (small, medium, and
48
49 large for mid-arm circumferences of 17-22 cm, 22-32 cm, and 32-42 cm respectively). Three
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51 measurements of BP and pulse rate were taken at 2-min intervals on the dominant arm after a rest of at
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53 least 15 min, in the seated position (7). Readings were obtained using a clinically validated
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55 semiautomatic sphygmomanometer (HEM 705 IT; Omron Matsusaka Co Ltd, Japan). The average of
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57 the last two readings for systolic and diastolic BP were defined as SBP1 and DBP1 respectively.
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59 Anthropometric measurements were taken on standing participants wearing light clothes and without
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61 shoes using standard techniques (13). Body weight was measured to the nearest 0.1 Kg using a spring
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63 balance and height to the nearest 0.5 cm using a stadiometer. Waist and hip circumference was
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65 measured to the nearest 0.1 cm. Finger prick blood samples were then obtained from fasting (>8h)

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3 subjects (aged ≥ 15 years) to measure glucose (Accutrend system, Roche Diagnostics, Mannheim,
4 Germany), cholesterol, and triglycerides blood values (MultiCare-in, HPS, Italy) using dry chemistry.
5 The subject was then asked to void. A midstream specimen of urine was collected and dipstick test
6 (Auction sticks, A.Menarini Diagnostics, Italy) was immediately performed and read manually to
7 semiquantitate the occult blood (trace, 1+ to 4+) and protein (trace, 1+ to 4+). A new appointment was
8 taken for non-fasting participants and for subjects who were menstruating. All subjects were then
9 visited again within the next ten days by the same survey team using the same measurement devices
10 and procedures for the second session of BP (SBP2 and DBP2) and fasting glucose (FG2)
11 measurements.
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21 **Diagnostic criteria**

22 Arterial hypertension was defined as 1) systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg
23 and/or 2) self-reported use of antihypertensive drugs at the time of the interview (7). More precisely the
24 prevalence of hypertension was based on values measured at the first visit (SBP1 and DBP1), at the
25 second visit (SBP2 and DBP2), and on fulfilling the same criteria for hypertension on both visits.
26 Awareness of hypertension was defined as self-report of any prior diagnosis of hypertension by a
27 health care professional among the population defined as having hypertension. Hypertension treatment
28 was defined as a self-reported use of antihypertensive drugs within the two weeks preceding the
29 interview. Hypertension control was defined as systolic BP < 140 mm Hg and diastolic BP < 90 mm Hg.
30 The proportion of hypertension control was relative to hypertensive treated with drugs.
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39 Diabetes mellitus (DM) was defined as 1) fasting glucose (FG) ≥ 7.0 mmol/L at the two visits or
40 2) self-reported use of hypoglycaemic medications at the time of the interview; impaired fasting
41 glucose (IFG) as FG ≥ 5.6 mmol/L and < 7.0 mmol/L in the absence of hypoglycaemic medications;
42 normal FG as FG < 5.6 mmol/L at the two visits (14). Overweight and obesity were defined as a body
43 mass index (BMI) 25.0 to 29.9 kg/m², and ≥ 30 kg/m² respectively. Abdominal obesity was defined as
44 waist circumference > 102 cm in men or > 88 cm in women. Gender specific tertiles for BMI and waist-
45 to-hip (W/H) ratio, were calculated using data of adult subjects without hypertension, normal FG,
46 cholesterol < 5.0 mmol/L, triglycerides < 1.7 mmol/L, and no protein at urine dipstick test. Resulting
47 cut-offs were 20.0 and 23.2 kg/m² for men and 20.5 and 24.3 kg/m² for women for BMI and 0.849 and
48 0.907 in men and 0.815 and 0.887 in women for W/H ratio. On the basis of cholesterol and
49 triglycerides assessments subjects were classified as high cholesterol (> 5.0 mmol/l) or high
50 triglycerides (> 1.7 mmol/l) (7). Results of dipstick urinalysis were classified as no protein (0), protein
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3 trace (+/-), or proteinuria ($\geq+1$). A smoker was defined as one who smoked any form of tobacco on a
4 daily (daily smoker) or a non-daily (occasional smoker) basis. Those who had smoked but had quit
5 were designated as former smokers, and those who had never smoked at all were designated as never
6 smokers. On the basis of education level subjects were classified into six levels: 1) illiterate; 2) can
7 read and write; 3) primary school; 4) preparatory school; 5) secondary; 6) university or post. Fruit and
8 vegetable consumption were classified as 1) ≤ 1 day/week; 2) 2-4 day/week; 3) ≥ 5 days/week.

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14 ~~Participants were categorized as sedentary if they walked or cycled for less than 10 min daily, if~~
15 ~~their work did not involve intense physical activity, and they did not usually practice any sport or~~
16 ~~recreational physical activities.~~

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20 Participants were categorized as: sedentary if they walked or cycled for less than 10 min daily, if
21 their work did not involve intense physical activity, and they did not usually practice any sport or
22 recreational physical activities; engaging in light to moderate physical activity if they performed work
23 or recreational physical activities one or two days/week; engaging in vigorous physical activity if they
24 performed work or recreational vigorous physical activities three days or more/week.

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28 According to the ESH/ESC chart (7) risk stratification (average, low, moderate, high, and very
29 high added risk categories) was based on the presence of risk factors (average of SBP1/SBP2 and
30 DBP1/DBP2 graded in five categories; age >55 years for men or >65 years for women; daily smoking;
31 waist circumference >102 cm in men or >88 cm in women; IFG; triglycerides >1.7 mmol/L; total
32 cholesterol >5.0 mmol/L), DM, subclinical organ damage (protein trace at dipstick test), and
33 established renal (proteinuria $\geq 1+$ at dipstick test) or CV disease (self-reported stroke, myocardial
34 infarction or peripheral artery disease). The cluster of three out of 4 risk factors among abdominal
35 obesity, altered fasting plasma glucose, BP $>130/85$ mmHg, and high triglycerides (as defined above),
36 was considered as the presence of metabolic syndrome.

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

51 52 53 54 55 56 57 58 **Statistical methods**

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3 A sample size of at least 1,117 subjects was required to achieve a 1% precision around an
4 estimated prevalence of diabetes of 3% with 95% confidence level (CI). Estimated required sample size
5 for two-sample comparison of diabetes prevalence of 2.25% vs 3.75% with the assumption of 0.05
6 alpha (two-sided), 80% power, was 2,161 subjects for each group. Cleaning the data, handling missing
7 data, and outliers were done according to the guidelines of WHO for STEPS data management (12).
8 Prevalence estimates were calculated for the five age groups in the overall population and by gender.
9 Data are expressed as mean±SD with 95% CI for continuous variables, and as rates with 95% CI for
10 categorical variables. Prevalence was also weighted to represent the total Yemen population aged 15-69
11 years (2008 estimated Yemen population) (11,16), and age-standardized for age ranges 15-69 years
12 using WHO World Standard Population (17). For hypertension awareness, and treatment the analysis
13 was done on the subpopulation of hypertensive patients; for hypertension control, analysis was done on
14 the subpopulation of treated people. As there were no national data available for these two
15 subpopulations for the purpose of weighting, at this stage of analysis, we did not weight the data.
16 Prevalence rates were compared using χ^2 analysis and Risk Ratio (RR) (16). When appropriate, test of
17 hypothesis was done at significance level 0.05 two sided. Associations between socio-demographic,
18 anthropometric, and clinical factors and the prevalence of hypertension were explored with logistic
19 regression analysis, the diagnosis of hypertension being entered as dependent dichotomic variable.
20 Results of regression analysis are expressed as RR with 95% CI for each independent variable (20). All
21 analyses were performed with SPSS software, version 17.0 (SPSS).
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RESULTS

Characteristics of study population

Characteristics of HYDY participants are reported in Table 1. Distribution among age decades and living location (urban, 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%CI 12.5 to 14.4; and 26.5%; 25.3 to 27.7) than in men (6.9%; 6.2 to 7.6; and 3.4%; 2.9 to 3.9).

All subjects received two visits at home separated by a median interval of 5.36 days (95% CI 5.30 to 5.42; range 1 to 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% CI 18.3-19.8), being 15.9% (15.2-16.6) 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 (chi-squared 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%; 12.1-13.4). When data were standardized to the Yemen population (15-69 years) prevalence was 7.7% (95% CI 7.2 to 8.1). This value, considering both the two 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 11.0) are considered independently (Figure 1). Hypertension prevalence age-standardized 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 10.0) 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

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3 and estimating hypertension prevalence on BP measurements, the rate of hypertension among
4 participants was 17.2% (16.4-18.0) at visit 1 (n=1425), 12.8% (12.1-13.5) at visit 2 (n=1098), 8.7%
5 (8.1-9.3) of subjects (n=779) fulfilling the criteria at both visits.
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10 **Factors affecting misclassification of hypertension at visit one**

11 When considering untreated subjects, 53% out of the 1094 participants who had hypertension
12 Grade 1 at the first visit, and 24% out of the 239 subjects with hypertension Grade 2, did not fulfil the
13 criteria for hypertension at visit 2 reassessment. Conversely only 8% out of the 92 untreated
14 participants with Grade 3 hypertension had normal BP values at visit 2 reassessment. Misclassification
15 also varied by subject age. The younger the subjects were, the wider the difference was between
16 estimates based on one or two visits (Table 2). As a result only 43% of men, and 44% of women <35
17 years of age found to be hypertensive at visit one were hypertensive at both visits. These percentages
18 were 72% and 76% for men and women aged >45 years of age (Table 3).
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26 When characteristics of misclassified participants were compared to untreated subjects with
27 hypertension diagnosis confirmed at both visits (logistic regression analysis including 1396 subjects),
28 misclassification was found to be independent by gender, education level, BMI and W/H ratio tertiles.
29 The probability to have the diagnosis confirmed was directly associated with age decades, grade of
30 hypertension, provisional diagnosis of diabetes at visit 1 (FG \geq 7.0 mmol/L or self-reported use of
31 hypoglycaemic medications), and proteinuria \geq 1+ at dipstick test.
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37 Rates of proteinuria (\geq 1+ at dipstick test), or the self-report of CV disease (MI,stroke,POAD) at
38 questionnaire, were comparable among subjects classified as hypertensive at the first, the second, or at
39 both visits (Table 3). However, the 959 participants found to be hypertensive at visit 1 or at visit 2 only
40 and thus excluded from the final diagnosis of hypertension (not confirmed), had rates of proteinuria and
41 self-reported CV disease comparable with normotensive subjects (at both visits) and the general
42 population (Table 4).
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49 **Cardiovascular risk stratification after one or two visits**

50 BP readings taken at the first visit (SBP1/DBP1) or average of BP readings taken at the first and
51 the second visits (SBP1-SBP2/DBP1-DBP2) were used to stratify HYDY participants in the five BP
52 categories according to ESH/ESC guidelines (7). As indicated by Figure 2 the different prevalence of
53 hypertension when the diagnosis rely on measurements taken at the first visit or at two visits is mainly
54 due to misclassification of subjects with Grade 1 hypertension.
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3 CV risk stratification according to the ESH/ESC chart (7) using average BP values at visit1 and
4 at both visits is reported in Table 5. Most people had average or low 10-year CV risk, and a large
5 fraction (84.3% after visit 1 and 86.2% after two visits) had CV risk <20% (average, low, or moderate).
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7 The age weighted percentage of the population with a CV risk $\geq 20\%$ (high, or very high CV risk) was
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9 13.8% after visit 1 and 12.0% after two visits (Table 5). Overall, only 1.9% of Yemen population
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11 classified at high or very high CV risk at visit 1 moved to average, low, or moderate CV risk categories
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13 after two visits (Figure 3).
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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 contribution is the information that a strategy based on two visits allows 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 programs.

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 (18). Therefore, guidelines for clinical practice commonly recommend that the diagnosis of hypertension rely on multiple measurements obtained at different visits (6,7). At 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 (19). 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 subjects aged 62 ± 11 years (9), being $>35\%$ in a cohort of subjects aged 39 ± 9 years (20). In particular, two thirds of men <30 years of age had normal BP values at the second visit (20). In both studies, the majority of subjects misclassified as hypertensive were in the less severe hypertensive grade (9,20). In a recent small surveys 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 programs might compete with other priorities. HYDY study participants were stratified by cardiovascular risk according to ESH/ESC criteria (7) thus allowing 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 blood pressure at both visits are "real" hypertensives but that they are higher risk hypertensives.** Therefore when resources are limited the

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3 estimation of hypertension prevalence might be based on only one visit, while resources can be more
4 efficiently used to target high-risk people who will benefit the most.
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7 Heart attack and stroke are preventable either through conventional management of single risk
8 factors (hypertension), or by applying a total CV risk approach which could permit providers to
9 focalize drug treatment use only in high risk subjects. CV risk has a continuous relationship with BP
10 values. In particular, the present study clarify that although there is a large discrepancy (35%) in the
11 estimation of hypertension prevalence on the basis of one visit or two visits, only 1.9% of the Yemen
12 population classified at high or very high CV risk at visit 1 moved to average, low, or moderate CV
13 risk categories after two visits. Current treatment strategies are indeed based on CV risk stratification.
14 It is recommended that pharmacologic treatment should be provided for all people when their
15 calculated 10-year CV risk is at least 30% or more. The risk threshold can be lowered to 20% if and
16 when resources permit. More precisely, age weighted prevalence of subjects at very high CV risk
17 estimated after one visit did not differ vs the estimation based on the two visits strategy. A mild
18 difference is appreciable only when the 20% threshold is adopted, corresponding to an estimated
19 number of 227,000 Yemen patients aged 15-69 years.
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22 The age-standardized prevalence of hypertension at first visit for subjects aged 15-69 years
23 (16.2%) is markedly lower than rates reported in economically developed countries for subjects older
24 than 20 years (37.3%) (2). Most importantly, direct age standardization to the 35-69 years WHO World
25 Standard Population (17) (26.6%; 25.5 to 27.6), allows comparison with Egypt (33.8%) (21), Iran
26 (34.1%) (22), or Turkey (34.2%) (23). The low prevalence of hypertension, besides any methodological
27 consideration, might thus be related to the possibility that Yemen is behind in the epidemiological
28 transition currently ongoing in other countries of the Middle East Crescent area.
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31 In conclusion, according to present data, the choice of one or two visits strategy is not relevant,
32 but it is important to implement a strategy that allows for a more comprehensive framework of CV risk.
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All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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PAM, SR, MoB, and MaB drafted the manuscript. PAM, SR, MoB, MaB, LM, GFG, DAH, and HAG were involved in the conception and design of the study. DAH, and HAG were part of the project

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3 management team that coordinated data collection for the study. PAM, and MaB wrote the statistical
4 analysis plan; PAM, SR, and LM conducted the main analyses and provided statistical advice; DZ
5 revised the draft paper. All authors had access to all data sources, contributed to the interpretation of
6 results, commented on the report, and approved the final version for publication. PAM is the guarantor.
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26 **Statements**

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42 All authors, external and internal, had full access to all of the data (including statistical reports
43 and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the
44 data analysis.
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47 **Data sharing**

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49 There is no additional data available.
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Table 1. Characteristics of HYDY 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 (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)
BMI (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 BP (mmHg)		123.0 (122.6 to 123.4)	122.7 (122.1 to 123.3)
Diastolic BP (mmHg)		76.9 (76.5 to 77.3)	76.9 (76.7 to 77.1)
Heart rate (mmHg)		79.3 (79.1 to 79.5)	82.2 (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 (mmHg)		121.5 (121.1 to 121.9)	120.6 (120.2 to 121.0)
Diastolic BP (mmHg)		76.2 (76.0 to 76.4)	76.0 (75.8 to 76.2)
Heart rate (mmHg)		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)
Dipstick test $\geq 1+$, n (%)		339 (6.7)	270 (5.2)
Self report of MI, Stroke, POAD, n (%)		47 (0.9)	38 (0.7)

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 (16.9-19.1)	15.0 (14.0-16.0)	11.6 (10.8-12.5)	-35.3	26.4 (23.7-29.4)	31.3 (28.1-34.7)	39.9 (36.0-43.9)	54.5
Age standardized*	16.2 (15.1-17.3)	13.5 (12.5-14.4)	10.2 (9.4-11.0)	-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

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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 (19.1-21.2)	16.7 (15.7-17.8)	13.9 (12.9-14.8)	-31.2	33.8 (31.0-36.8)	39.8 (36.6-43.1)	46.9 (43.3-50.6)	45.3
Age standardized*	18.3 (17.2-19.4)	15.1 (14.1-16.1)	12.3 (11.4-13.2)	-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 10242 study participants.

	Current treatment among hypertensive subjects				BP 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 (20.9-26.5)	28.3 (25.2-31.6)	36.5 (32.7-40.5)	54.5	22.8 (17.7-28.8)	31.6 (25.8-38.1)	17.2 (12.8-22.6)	-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

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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 (27.3-32.9)	36.1 (33.0-39.4)	43.6 (40.0-47.2)	45.3	34.8 (29.7-40.2)	40.3 (35.0-45.7)	28.7 (24.0-34.0)	-17.4

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

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Table 4. Rates of proteinuria and self-reported CV disease in HYDY 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.

Diagnosis	Subjects	DIPSTIK test $\geq 1+$		Self-report of CV disease	
	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	10025	609	6.1 (5.6 to 6.6)	85	0.8 (0.7 to 1.0)

Table 5.

CV risk distribution among the 9926 adult subjects investigated in the HYDY study based on the results first visit (visit 1), or both visits.

Risk Categories	After Visit 1			After two visits			Δ n=
	n=	Crude %	Age weighted % (95% CI)	n=	Crude %	Age weighted % (95% CI)	
Average risk	2246	22.6	30.3 (28.9 to 31.6)	2326	23.4	31.3 (29.9 to 32.7)	128851
Low risk	3387	34.1	33.7 (32.4 to 35.0)	3495	35.2	34.1 (32.8 to 35.4)	48207
Moderate risk	2234	22.5	20.3 (19.3 to 21.3)	2281	23.0	20.7 (19.7 to 21.7)	52613
High risk	1206	12.1	8.2 (7.7 to 8.7)	1033	10.4	6.6 (6.1 to 7.1)	-190741
Very high risk	853	8.6	7.5 (6.9 to 8.1)	792	8.0	7.2 (6.6 to 7.8)	-36523

Δ = estimated difference between Yemen subjects attributed to the risk category on the basis of 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).

Legends to Figures

Figure 1.

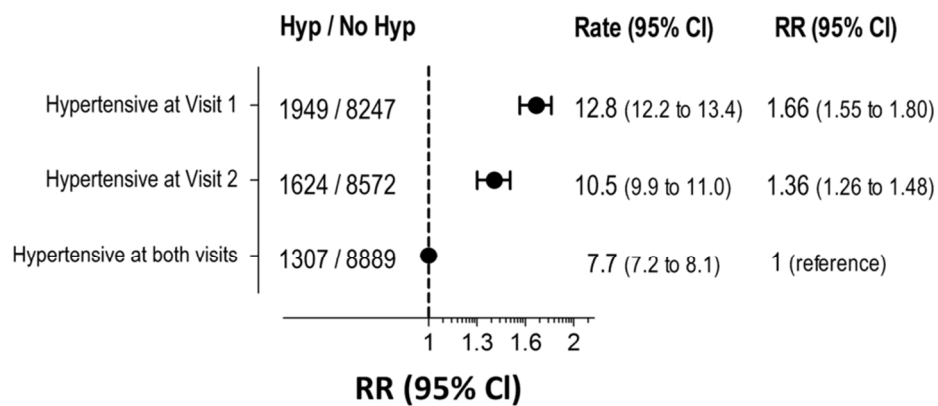
Diagnosis of hypertension (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg and/or self-reported use of antihypertensive drugs at the time of the interview) performed on the basis of measurements taken at the first visit (visit 1), at the second visit (visit 2), or both.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

Figure 2.

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

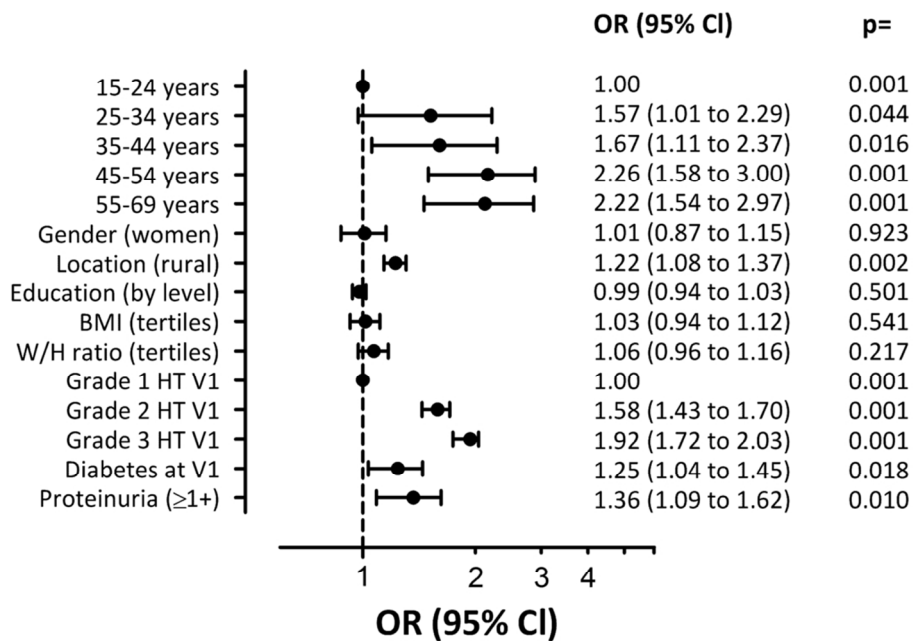
Figure 3.

Blood pressure and CV risk stratification of HYDY participants according to the ESH/ESC chart using average blood pressure values at visit1 and at both visits.



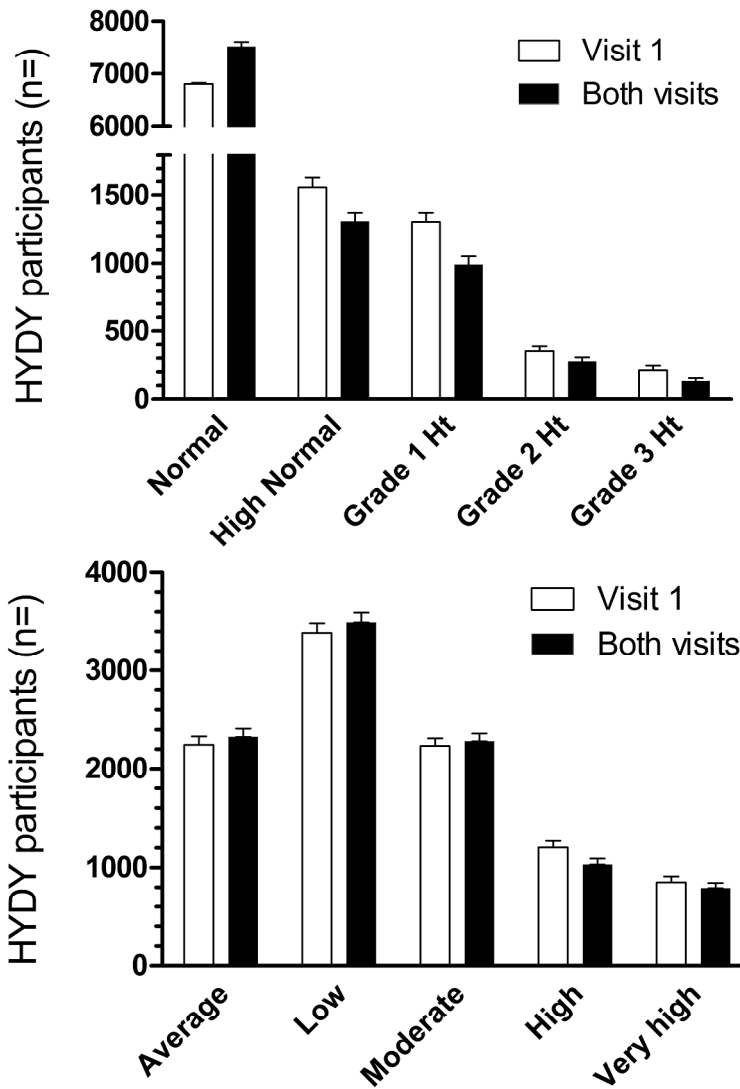
Diagnosis of hypertension (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg and/or self-reported use of antihypertensive drugs at the time of the interview) performed on the basis of measurements taken at the first visit (visit 1), at the second visit (visit 2), or both. The number of subjects with and without the condition and age-weighted rates (to the 15-69 years Yemen population) are reported.
87x41mm (300 x 300 DPI)

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Factors associated with the misclassification of hypertension diagnosis (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg at both visits) at multiple logistic regression analysis including only non-treated subjects (n=1396). Results are expressed as odd ratio (OR) with 95% CI.
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Blood pressure and CV risk stratification of HYDY participants according to the ESH/ESC chart using average blood pressure values at visit1 and at both visits.
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