

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

### ARTICLE DETAILS

|                            |  |
|----------------------------|--|
| <b>TITLE (PROVISIONAL)</b> | 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 |
| <b>AUTHORS</b>             | Modesti, Pietro ; Rapi, Stefano; Bamoshmoosh, Mohamed; Baldereschi, Marzia; Massetti, Luciano; Gensini, Gian Franco; Zhao, Dong; Al-Hidabi, Dawood; Al Goshae, Husni                       |

### VERSION 1 - REVIEW

|                        |  |
|------------------------|--|
| <b>REVIEWER</b>        | Stefano Taddei<br>Professor of Internal Medicine<br>Department of Internal Medicine<br>University of Pisa<br>Pisa - Italy<br><br>My research and clinical interest concern the diagnosis and treatment of primary and secondary of hypertension. |
| <b>REVIEW RETURNED</b> | 22-Mar-2012  |

|                                  |   |
|----------------------------------|---|
| <b>RESULTS &amp; CONCLUSIONS</b> | The authors should more discuss the finding that microalbuminuria does not help in detecting real hypertensive patients.<br><br>The authors should compare the prevalence of hypertension in Yemen as compared to developed countries, taking into consideration the difference in the age range. |
| <b>GENERAL COMMENTS</b>          | The manuscript is very interesting.<br>It would be important to add some more information about the life style of the study population: alimentation, physical activity....   |

|                        |   |
|------------------------|---|
| <b>REVIEWER</b>        | Adolfo Rubinstein MD, MSc, PhD<br>Institute for Clinical effectiveness and Health Policy. Buenos Aires. Argentina |
| <b>REVIEW RETURNED</b> | 22-May-2012   |

|                                  |  |
|----------------------------------|--|
| <b>THE STUDY</b>                 | 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.<br><br>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. |
| <b>RESULTS &amp; CONCLUSIONS</b> | Again, the overestimation of the prevalence of high BP when  |

|  |  |
|--|--|
|  | <p>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 in stead of one, the comparability assured by WHO-STEPS across the globe could be compromised and prevalence of HTN in Yemen could be underestimated.</p> <p>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.</p> <p>The authors found that BP measured in two visits resulted in a 35% reduction in the prevalence of hypertension. mostlybased 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 question of this approach is not just to estimate the prevalence of high BP in one or two visits but to estimate more accurately the magnitude and extent of the resources that should be allocated to the prevention of hypertension.</p> <p>In my opinion, the authors should reframe the objectives of the study and highlight resource-allocation decision making rather than prevalence.</p> |
|--|--|

### VERSION 1 – AUTHOR RESPONSE

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

Response 3: You perfectly centered the goal of our study. Notwithstanding the progressive reduction of BP values at repeated measurements, resource-allocation decision making is usually based on data collected at a single visit, often on a single risk factor. To achieve our objective we included strategies aimed at exploring risk of excluded subjects. According to present data the integration of BP measurement with simple "low cost" diagnostic tests might offer advantages in costs estimation. The importance for policy makers in the health care resource allocation decision making process is now highlighted in the introduction section. The objective was modified as follows:

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

We also modified the title as follows:

"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."

#### VERSION 2 – REVIEW

|                        |   |
|------------------------|---|
| <b>REVIEWER</b>        | Adolfo Rubinstein M.D, MSC, PhD<br>I have no conflict of interest |
| <b>REVIEW RETURNED</b> | 15-Jun-2012   |

|                         |  |
|-------------------------|--|
| <b>GENERAL COMMENTS</b> | The authors responded to my concerns and suggestions. I accept this manuscript for publication<br>Thanks |
|-------------------------|--|