

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Societal economic burden of hypertension at selected hospitals in southern Ethiopia; a patient-level analysis
AUTHORS	Sorato, Mende; Davari, Majid; Kebriaeezadeh, Abbas; Sarrafzadegan, Nizal; Shibru, Tamiru

VERSION 1 – REVIEW

REVIEWER	Joshi, Sushant University of Southern California, Sol Price School of Public Policy
REVIEW RETURNED	19-Oct-2021

GENERAL COMMENTS	<p>Thank you for the opportunity to review this manuscript.</p> <p>This paper contributes to the literature on the magnitude of economic burden due to hypertension in Ethiopia. Authors estimate the direct and indirect costs for the year 2021 using prevalence-based cost-of-illness. The underlying rationale to use the direct and indirect costs is that in addition to direct medical costs (e.g., costs of medicine, hospital stay) there are indirect costs (e.g., loss of forgone income through lack of employment, morbidity and mortality) due to hypertension. Their findings suggest that most of the costs are indirect. They estimate that of the total costs, 80 percent are due to indirect costs.</p> <p>Here are my comments on the paper.</p> <p>1. In several places is it difficult to understand the estimates given in the paper. For example, in the abstract, line 20 it is written 71 (18.5%) patients but 71/406 as a percent is not 18.5 but 17.5. Similarly, in the abstract, line 25 what is the denominator to get 44.6%? 7826 as a percentage of 11606 is around 67%. In the section 2.5.2 under sampling techniques, it is mentioned that sample from four general hospital were included (line 6). The sample from 3 hospitals sum to your total sample (line 9-12). Page 10 line 7 says that the authors estimate cost/patient-year but is not provided in the results section. Page 10 line 54 average monthly income is written as (97.00ETB) 34,931. Isn't 97 ETB too low for the income?</p> <p>2. On literature, there are couple of papers (A, B) that have estimated the direct and indirect cost of hypertension. The authors do not cite these papers. Given these are recent papers and also collect data from hospitals, it would have been beneficial to see how this paper differs from those papers. There are also papers that have estimated the direct medical costs of hypertension. Current paper does not compare the direct costs that have been estimated to earlier literature (C).</p> <p>A) Adane, Elsabet et al. "The Cost of Illness of Hypertension and Associated Factors at the</p>
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University of Gondar Comprehensive Specialized Hospital Northwest Ethiopia, 2018." ClinicoEconomics and outcomes research : CEOR vol. 12 133-140. 6 Mar. 2020.

B) Zawudie, Addisu Bogale et al. "Cost of Hypertension Illness and Associated Factors Among Patients Attending Hospitals in Southwest Shewa Zone, Oromia Regional State,

Ethiopia." ClinicoEconomics and outcomes research: CEOR vol. 12 201-211. 9 Apr. 2020, doi:10.2147/CEOR.S241591

C) Bedane S. Out of pocket expenditures among hypertensive patients and their households who visit public hospitals in Addis Ababa, Ethiopia, 2016. Health Econ Outcome Res Open Access Access. 2018; 4(147):2.).

3. In the strengths and limitations, the authors write that the estimates maybe an underestimate. We could imagine where being employed might be difficult even without hypertension if lack of employment exists. The exercise that the authors have done would provide an overestimate in this case.

4. Since this is a simulation-based exercise, it would greatly help to know which assumptions are critical to the overall estimate. Maybe generating few more estimates by changing assumptions would provide a range of estimates. This would provide evidence of sensitivity of the estimates as well as the range of values. For example, the paper assumes that the rate of hypertension for the persons aged 55+ is similar to the persons aged 50-54. Is this a reasonable assumption? This paper (A) has estimate of hypertension for different age groups for a individuals residing in a particular city.

A. Demisse, A.G., Greffie, E.S., Abebe, S.M. et al. High burden of hypertension across the age groups among residents of Gondar city in Ethiopia: a population based cross sectional study. BMC Public Health 17, 647 (2017)

5. Females are 2/3 of the sample. Assuming that females have lower(higher) rate of hypertension wouldn't your estimate underestimate(overestimate) the true estimate?

6. Page 16 Line 21 has: 18,660,182.62 ETB (11,748,345.71 ETB, men; 96,911,836.90 ETB, women). The numbers in the parenthesis do not sum to the total amount. Also, why a large difference in male and female numbers?

7. Page 16 line 25 mentions that the 15,232 years lost due to premature mortality. Where did this number come from? In line 17 the authors write that total of 11,858 years were lost due to hypertension. Line 27, page 16 I would change one-half to four-fifths since 83% is closer to 4/5th than one-half.

8. Page 16 in the results, treated and uncontrolled hypertension accounts for more the years of life lost due to untreated hypertension. Is this a reasonable finding? Is there a reason to believe treated but uncontrolled hypertension account for more than untreated hypertension?

9. In Table 3, For men aged 45-49 compared to other age categories most of the deaths is in Treated and controlled group i.e. 1167 out of 1735. What is the reason for this?

	<p>10. Page 19 line 1, the authors write that they estimated the economic burden of hypertension among productive age group (15-64). The authors collected data for individuals who were 33 and older. How did they estimate the numbers for age categories they did not have data for?</p> <p>Other comments</p> <p>1. For convenience I would stick with a single monetary unit (US \$) after providing the exchange rate. Moving between the currencies within the text is difficult to follow.</p>
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REVIEWER	Xu, Xinpeng
REVIEW RETURNED	30-Jan-2022

GENERAL COMMENTS	<p>Comments: The study aims to determine the economic burden of hypertension at Selected Hospitals in Southern Ethiopia. The methods and conclusions are very clear and innovative.</p> <p>Minor issues:</p> <p>1. In the Results section of Abstract, the author stated “A total of 13,452,893.15 ETB (\$309,261.91) direct cost was incurred due to hypertension”, Are these costs cross-sectional or longitudinal here?</p> <p>2. In the section of Introduction, “according to a global health estimate in 2016, life years lost directly or indirectly due to hypertension was 42,781,885 in the African region. Regional productive healthy life year lost due to hypertension was estimated to be 19,395,946 (4, 5).” in which the numbers have no units, and the latter year should be plural.</p> <p>3. In the section of 2.1 study design, Area and Period, “A retrospective cohort study was conducted from September 2010-September 2020 in Southern Ethiopia to evaluate the economic burden of hypertension at selected three selected public hospitals.”, There are two selected in this sentence, and the previous one needs to be deleted.</p> <p>4. Table 1, Are these sociodemographic factors in the baseline? Or the characteristics of which year, not stated.</p> <p>5. Table 2, How is the direct non-medical cost calculated in the table? What items are included?</p> <p>6. Table 3, There are a lot of numbers in the table that don't add up to the total number of deaths, or one more, or one less, For example, for men aged 30 to 34, the deaths in those with to hypertension by treatment and control status was $487+654+294=1435$, and the corresponding deaths in hypertension cohort was 1436. Another example is for women aged 45 to 49, Deaths in those with to hypertension by treatment and control status was $265+400+168=833$, while the corresponding deaths in hypertension cohort was 832. There are a lot of other rows that don't match. Authors need to explain these discrepancies in the tables and examine the results.</p> <p>7. Too many abbreviations render readers to follow the story. Please try maintaining the number of abbreviations at the minimum level.</p>
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VERSION 1 – AUTHOR RESPONSE

Response to reviewers

Reviewer One

1. In the Results section of Abstract, the author stated “A total of 13,452,893.15 ETB (\$309,261.91) direct cost was incurred due to hypertension”, Are these costs cross-sectional or longitudinal here?

Answer: The costs are cross-sectional. We used 10 year retrospective data to generate average cost of hypertension. Since this is recommended to generate data for base case analysis by WHO choice.

2. In the section of Introduction, “according to a global health estimate in 2016, life years lost directly or indirectly due to hypertension was 42,781,885 in the African region. Regional productive healthy life year lost due to hypertension was estimated to be 19,395,946 (4, 5).” in which the numbers have no units, and the latter year should be plural.

Answer: Modified

3. In the section of 2.1 study design, Area and Period, “A retrospective cohort study was conducted from September 2010-September 2020 in Southern Ethiopia to evaluate the economic burden of hypertension at selected three selected public hospitals.”, There are two selected in this sentence, and the previous one needs to be deleted.

Answer: Corrected

4. Table 1, Are these sociodemographic factors in the baseline? Or the characteristics of which year, not stated.

Answer: Corrected

5. Table 2, How is the direct non-medical cost calculated in the table? What items are included?

Answer: Direct non-medical costs include transportation costs and patient time costs due to care. The cost of patient time due to care was estimated by using the average daily wage of patients which was calculated from average monthly income (97.00 ETB) 34,931.00 annual income from our treatment effectiveness survey. Transportation cost was determined by using the cost of average traveling distance and local transportation tariff (42.00 ETB) in January 2021. According to EDHS 2016 survey showed that 33% of women and 88% of men are currently employed (13). This proportion was used to determine the patient time cost due to care for employed groups. For the unemployed proportion, the average daily wage of daily laborers workers working 8 hours per day for 6 days per week was used (26.53 ETB) from the monthly wage of 796.00 ETB.

6. Table3, There are a lot of numbers in the table that don't add up to the total number of deaths, or one more, or one less, For example, for men aged 30 to 34, the deaths in those with to hypertension by treatment and control status was $487+654+294=1435$, and the corresponding deaths in hypertension cohort was 1436. Another example is for women aged 45 to 49, Deaths in those with to hypertension by treatment and control status was $265+400+168=833$

, while the corresponding deaths in hypertension cohort was 832. There are a lot of other rows that don't match. Authors need to explain these discrepancies in the tables and examine the results.

Answer: Typographic discrepancies during coping and editing is modified. Thank you very much for this observation.

7. Too many abbreviations render readers to follow the story. Please try maintaining the number of abbreviations at the minimum level.

Answer: Accepted and done

Reviewer two

1. In several places is it difficult to understand the estimates given in the paper. For example, in the abstract, line 20 it is written 71 (18.5%) patients but 71/406 as a percent is not 18.5 but 17.5. Similarly, in the abstract, line 25 what is the denominator to get 44.6%? 7826 as a percentage of 11606 is around 67%. In the section 2.5.2 under sampling techniques, it is mentioned that sample from four general hospital were included (line 6). The sample from 3 hospitals sum to your total sample (line 9-12). Page 10 line 7 says that the authors estimate cost/patient-year but is not provided in the results section. Page 10 line 54 average monthly income is written as (97.00ETB) 34,931. Isn't 97 ETB too low for the income?

Answer: Modified, the figure is even higher than findings from national STEPS survey based on our effectiveness study. The article will be released soon.

2. On literature, there are couple of papers (A, B) that have estimated the direct and indirect cost of hypertension. The authors do not cite these papers. Given these are recent papers and also collect data from hospitals, it would have been beneficial to see how this paper differs from those papers. There are also papers that have estimated the direct medical costs of hypertension. Current paper does not compare the direct costs that have been estimated

to earlier literature (C).

A) Adane, Elsabet et al. "The Cost of Illness of Hypertension and Associated Factors at the University of Gondar Comprehensive Specialized Hospital Northwest Ethiopia,

2018." *ClinicoEconomics and outcomes research : CEOR* vol. 12 133-140. 6 Mar. 2020.

B) Zawudie, Addisu Bogale et al. "Cost of Hypertension Illness and Associated Factors Among Patients Attending Hospitals in Southwest Shewa Zone, Oromia Regional State, Ethiopia." *ClinicoEconomics and outcomes research: CEOR* vol. 12 201-211. 9 Apr. 2020, doi:10.2147/CEOR.S241591

C) Bedane S. Out of pocket expenditures among hypertensive patients and their households who visit public hospitals in Addis Ababa, Ethiopia, 2016. *Health Econ Outcome Res Open Access Access*. 2018; 4(147):2.).

Answer: Updated references are cited and compared under discussion

3. In the strengths and limitations, the authors write that the estimates maybe an underestimate. We could imagine where being employed might be difficult even without hypertension if lack of employment exists. The exercise that the authors have done would provide an overestimate in this case. **Answer:** Modified
4. Since this is a simulation-based exercise, it would greatly help to know which assumptions are critical to the overall estimate. Maybe generating few more estimates by changing assumptions would provide a range of estimates. This would provide evidence of sensitivity of the estimates as well as the range of values. For example, the paper assumes that the rate of hypertension for the persons aged 55+ is similar to the persons aged 50-54.

Is this a reasonable assumption? This paper (A) has estimate of hypertension for different age groups for a individuals residing in a particular city.

A. Demisse, A.G., Greffie, E.S., Abebe, S.M. *et al.* High burden of hypertension across the age groups among residents of Gondar city in Ethiopia: a population based cross sectional study. *BMC Public Health* **17**, 647 (2017)

Answer: Even the above study mentioned similar rate for age group $\geq 35-64$ years as **36.1 %** and 46.3% in 65 years and above. This is in line with our assumption

5. Females are 2/3 of the sample. Assuming that females have lower (higher) rate of hypertension wouldn't your estimate underestimate (overestimate) the true estimate?

Answer: Rate of hypertension has no significant difference among men and women in Ethiopia based on different studies including National STEPS Survey.

6. Page 16 Line 21 has: 18,660,182.62 ETB (11,748,345.71 ETB, men; 96,911,836.90 ETB, women). The numbers in the parenthesis do not sum to the total amount. Also, why a large difference in male and female numbers?

Answer: Modified

7. Page 16 line 25 mentions that the 15,232 years lost due to premature mortality. Where did this number come from? In line 17 the authors write that total of 11,858 years were lost due to hypertension. Line 27, page 16 I would change one-half to four-fifths since 83% is closer to 4/5th than one-half.

Answer: The numbers are based on Mortality rate in the total population, Mortality rate among people without hypertension, Mortality rate among people with treated and controlled hypertension, Mortality rate among people with treated but uncontrolled hypertension, Mortality rate among people with untreated hypertension of Ethiopian population from systematic review and meta-analysis RCTs and cohort studies

8. Page 16 in the results, treated and uncontrolled hypertension accounts for more the years of life lost due to untreated hypertension. Is this a reasonable finding? Is there a reason to believe treated but uncontrolled hypertension account for more than untreated hypertension?

Answer: This is based on relative risk of death findings from other studies. Based on simple observation it seems not, however, we look into the details it is reasonable. This is because: (1) Untreated hypertension cases may be hypertension responsive antihypertensive drug therapy or may be resistant (10-15%). (2) Treated but uncontrolled hypertension is usually apparent treatment resistant (pseudo resistant and true resistant). Because of difference in severity and probability to die or develop other cardiac complications. Life years lost due to treated uncontrolled hypertension could be greater than untreated hypertension.

9. In Table 3, for men aged 45-49 compared to other age categories most of the deaths is in Treated and controlled group i.e. 1167 out of 1735. What is the reason for this?

Answer: Typographic discrepancies during coping and editing is modified. Thank you very much for this observation.

10. Page 19 line 1, the authors write that they estimated the economic burden of hypertension among productive age group (15-64). The authors collected data for individuals who were 33 and older. How did they estimate the numbers for age categories they did not have data for?

Answer: Our intension was to measure economic burden of hypertension in productive age population of Ethiopia (15-64). However, during our information retrieval from data sources we could not find hypertension patient below 33 years. Therefore, our analysis is based on the population aged (33-64 years) for estimating premature mortality and morbidity associated with hypertension. Thank you very much for this question.

Other comments

1. For convenience I would stick with a single monetary unit (US \$) after providing the exchange rate. Moving between the currencies within the text is difficult to follow.

Answer: Accepted

VERSION 2 – REVIEW

REVIEWER	Xu, Xinpeng
REVIEW RETURNED	26-Feb-2022
GENERAL COMMENTS	None