PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Cost of primary care approaches for hypertension management and risk-based cardiovascular disease prevention in Bangladesh: a HEARTS costing tool application
AUTHORS	Husain, Muhammad; Haider, Mohammad; Tarannum, Renesa; Jubayer, Shamim; Bhuiyan, Mahfuzur; Kostova, Deliana; Moran, Andrew; Choudhury, Sohel Reza

VERSION 1 – REVIEW

REVIEWER	Collins, Dylan University of British Columbia
REVIEW RETURNED	07-Mar-2022

GENERAL COMMENTS	This study describes the use of the HEARTS costing tool to estimate the cost of HEARTS implementation in Bangladesh. This study adds to the literature (1) by providing a worked example of the use of the HEARTS costing tool in a real world setting, which methodologically can assist other jurisdictions in their implementation and (2) provides the best current estimate of implementation costs for implementation of hypertension (i.e. single risk factor) prevention strategies and total risk based (i.e. integrated risk factor) prevention strategies in Bangladesh. Their findings suggest that considerable investment is required for broader implementation of this work, and like most health systems globally, face a significant primary care workforce shortage. I commend the authors on their work, clear and concise manuscript, and for prioritizing the publication of this work. I have several points for revision, some major and some minor, as follows. Major Comments 1. Section 2.1: please describe in detail the physician workforce that staff these “primary health care centres.” Are they general practitioners, residency trained family physicians, internal medicine specialists working in primary care? Other specialist? Etc. 2. Section 2.3: please further describe the training that was done for providers with respect to the use of treatment protocols, as well as the training of CHWs and nurses. Were each group of professionals (doctors, nurses, CHWs) trained together in one group or separately in cohorts? 3. Section 2.6: you state, “15% of the adult population was estimated to be at high risk for CVD.” Please define “high risk” and the risk calculator used for this definition. 4. In Table 2, please describe in the methods section how the distribution of CVD risk scores was calculated (i.e. did you have individual patient data for every patient in order to calculate their risk score? etc).

	5. Section 4. Discussion: regarding task sharing, while it may be more efficient, please discuss the in greater depths the barriers to task sharing and the recruitment of non-physician health workers (e.g. nurses). Also please discuss the local implementation climate with respect to the autonomy of nurses and the widening of their practice scope. In many jurisdictions trying to implement HEARTS and task sharing for NCDs, large cultural and professional barriers exist when trying to bolster the independence of nurses and increase their scope of practice. 6. Please include a conclusion section after the discussion Minor Comments 1. Typo in last bullet point of "Strengths and Limitations" section at the beginning of the manuscript -- "CDV" instead of "CVD" 2. In the background section, please provide more information on the overall health system of Bangladesh and please comment on the proportion of care that is provided publicly and privately 3. Background section, paragraph one, "An estimated 1.13 billion people (1 in 4 men and 1 in 5 women) worldwide has hypertension." Tense should be changed to "... have hypertension" and please add a citation 4. Section 4. Discussion – please define “NCD Corners” 5. Section 4. Discussion – limitations paragraph, typo “CDV” should be “CVD”

REVIEWER	Roque, David Hospital Professor Doutor Fernando Fonseca EPE
REVIEW RETURNED	12-Mar-2022

GENERAL COMMENTS	Dear authors, Congratulations on the massive effort undertaken on this project. Here are my comments to your article. Suggested corrections: PAGE 4 Line 13: Cardiac Failure -> Heart Failure Line 13: Blindness -> retinopathy Line 14: CVD deaths -> i believe the epidemiologic studies demonstrate that uncontrolled hypertension can be responsible for almost half of all CV EVENTS. Line 16: Raised blood pressure -> hypertension Line 21: global hypertension -> of all hypertension cases Line 37: only a less -> only less Line 39: This demonstrates the need for AN EFFECTIVE, LOW-COST AND EFFICIENT population-level APPROACH IN ADDRESSING HYPERTENSION Line 47: pharmaceutical -> pharmacological PAGE 5 Line 19: includes prevention, promotion, treatment… Lines 28-29: in the design, conduct, reporting or dissemination Line 39: programmatic -> programmed Line 50: procured -> obtained PAGE 6 Line 13: Metformin (1000mg), then Metformin (1000mg) -> Metformin (1000mg) PAGE 7 Line 17: where -> when

	Line 42: procured -> obtained Comments: 1) What where the risk charts used to estimate CVD risk and are they validated in that population? 2) Where patients stratified according to the severity of the arterial hypertension? Since the authors followed a three-step protocol how was that organized? All patients, regardless of the basal hypertension level started in step 1 and then progress if they were not controlled? How was that assessed? 3) Same question for dyslipidemia: what where the labs used in the screening? >190mg/dl is total cholesterol or LDL cholesterol? And were the cut-offs and the need for treatment stratified according to global CVD risk? How was the protocol implemented? 4) Same questions for diabetes: how do authors estimated the need for step 1,2 or 3 drugs? Is it not clear for me how the authors estimated the stratification of patients: if we look at Table 1, 65% of patients were in low CVD risk, which is the exact same % that received step 1 of the hypertension protocol, diabetes protocol and hyperlipidemia protocol. The same can be said regarding the % of patients in medium and high CVD risk and the step 2 and 3 of each protocol. This can lead to two different interpretations: is a coincidence that the % of patients with low, medium and high CVD risk estimate are the same that were allocated to the first, second and third step of all treatment protocols? Or if one is estimated, for example, to be at low CVD risk is considered to be controlled on the step 1 of the treatment protocol?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1 (Dr. Dylan Collins, University of British Columbia)

Comments to the Author: *This study describes the use of the HEARTS costing tool to estimate the cost of HEARTS implementation in Bangladesh. This study adds to the literature (1) by providing a worked example of the use of the HEARTS costing tool in a real world setting, which methodologically can assist other jurisdictions in their implementation and (2) provides the best current estimate of implementation costs for implementation of hypertension (i.e. single risk factor) prevention strategies and total risk based (i.e. integrated risk factor) prevention strategies in Bangladesh. Their findings suggest that considerable investment is required for broader implementation of this work, and like most health systems globally, face a significant primary care workforce shortage. I commend the authors on their work, clear and concise manuscript, and for prioritizing the publication of this work. I have several points for revision, some major and some minor, as follows.*

Author Response: Many thanks for summarizing the contributions of our paper so aptly. We are very thankful for your comments and recommendations.

Reviewer Comment: (1) Section 2.1: please describe in detail the physician workforce that staff these “primary health care centres.” Are they general practitioners, residency trained family physicians, internal medicine specialists working in primary care? Other specialist? Etc.

Author Response: The outpatient service is usually staffed with 5 outpatient general practitioners including 1 resident medical officer, 2 medical officers, and 2 medical assistants. An 'NCD corner' was set-up in the outpatient with necessary logistics and personnel for screening and treatment. We amended section 2.1 (Settings) of the manuscript.

Reviewer Comment: (2) Section 2.3: please further describe the training that was done for providers with respect to the use of treatment protocols, as well as the training of CHWs and nurses. Were each group of professionals (doctors, nurses, CHWs) trained together in one group or separately in cohorts?

Author Response: We amended section 2.1 (Settings) of the manuscript. The healthcare providers were trained to acquire the necessary skills to provide brief interventions to encourage behavior change, to assess CVD risk, or initiate treatment protocol. The training sessions were conducted in one set-up with a pool of selected doctors, nurses, and community health workers trained with relevant modules.

Reviewer Comment: (3) Section 2.6: you state, "15% of the adult population was estimated to be at high risk for CVD." Please define "high risk" and the risk calculator used for this definition.

Author Response: The risk-stratification is based on WHO and International Society of Hypertension cardiovascular risk prediction charts and expressed as the probability of developing CVD over 10 years: low CVD risk (0 to <10%); medium CVD risk (10 to 20%); and high CVD risk (>=20%). Citation: HEARTS technical package for cardiovascular disease management in primary health care: risk based CVD management. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.

Additionally, we revised the population (patient) distribution parameters upon further review and expert consultation. We revised the distribution as: 85.1% low CVD-risk, 14.4% medium CVD-risk, and 0.5% high CVD-risk patients. This distribution of patients by CVD risks is adopted from Islam, J. Y., Zaman, M. M., Moniruzzaman, M., Shakoor, S. A., & Hossain, A. E. (2020). Estimation of total cardiovascular risk using the 2019 WHO CVD prediction charts and comparison of population-level costs based on alternative drug therapy guidelines: a population-based study of adults in Bangladesh. BMJ open, 10(7), e035842.

Reviewer Comment: (4) In Table 2, please describe in the methods section how the distribution of CVD risk scores was calculated (i.e. did you have individual patient data for every patient in order to calculate their risk score? etc).

Author Response: The program entails assessment of target population by total CVD risk estimation to categorize their risk for CVD. The risk-stratification is based on WHO and International Society of Hypertension cardiovascular risk prediction charts and expressed as the probability of developing CVD over 10 years: low CVD risk (0 to <10%); medium CVD risk (10 to 20%); and high CVD risk (>=20%).

Reviewer Comment: (5) Section 4. Discussion: regarding task sharing, while it may be more efficient, please discuss the in greater depths the barriers to task sharing and the recruitment of non-physician health workers (e.g. nurses). Also please discuss the local implementation climate with respect to the autonomy of nurses and the widening of their practice scope. In many jurisdictions trying to implement HEARTS and task sharing for NCDs, large cultural and professional barriers exist when trying to

bolster the independence of nurses and increase their scope of practice.

Author Response: We revised the discussion section stating that there are several barriers to team-based care with task sharing, including staff attrition and turnover, retention of training, patient perception and acceptance toward non-physician health workers, lack of delegation of work by physicians, legislation and policy etc. Citation: HEARTS Technical package for cardiovascular disease management in primary health care: team-based care. Geneva: World Health Organization; 2018 (WHO/NMH/ NVI/18.4). Licence: CC BY-NC-SA 3.0 IGO

Reviewer Comment: (6) Please include a conclusion section after the discussion

Author Response: We added the following content: “Expanding the HEARTS hypertension management and CVD prevention program to provide services to the entire eligible population in the catchment area may face constraints in physician capacity. A task-sharing model involving shifting of select tasks from doctors to nurses and local community health workers would be essential for the eventual scale-up of primary care services to prevent CVD in Bangladesh.”

Reviewer Comment: (7) Typo in last bullet point of "Strengths and Limitations" section at the beginning of the manuscript -- "CDV" instead of "CVD"

Author Response: Thanks for pointing to this typo.

Reviewer Comment: (8) In the background section, please provide more information on the overall health system of Bangladesh and please comment on the proportion of care that is provided publicly and privately

Author Response: We discussed the health system in the realm of primary health care delivery and NCDs in the discussion section. We also made few amendments. Kindly see below relevant manuscript content from the discussion section:

In Bangladesh, of the four entities (i.e., the government, for-profit private sector, non-profit nongovernmental organization, and donor agencies) involved in the primary healthcare provision, the government plays the leading role, mainly in rural areas. There are six tiers of public healthcare infrastructure: national, divisional, district, upazila (sub-district), union, and ward levels. To tackle NCDs, the government of Bangladesh introduced ‘NCD Corners’ initiative in 2012 dedicated to providing prevention and care services for common NCDs and related conditions. The government has plans to expand ‘NCD corners’ at the upazila level, and the upazila primary care setting is well-positioned to bridge the link the health care providers down to the union, ward (and community) levels by harnessing community support and delegating suitable activities under task-sharing principles.[17, 38, 39] This will enhance healthcare access among disadvantaged populations and mitigate health disparities. Further, in Bangladesh, according to the 2016 Household Income Expenditure Survey and 2014 Health and Morbidity Status Survey, one in three patients received treatment from a pharmacy or medical shop, while about one in five received treatment from public health providers.[40, 41] This emphasizes the need for partnerships with various types of public-private health providers.

The models of care introduced in the Bangladesh national hypertension guidelines and NCD operational plan are encouraging; however, there are capacity challenges to the scaling-up of NCD

care in Bangladesh.[42, 43] The fiscal year 2021 budget allocation to the health sector stands just above 5%, which is less than 1% of GDP. Further, less than 5% of public sector funding for health covers NCDs, despite NCDs being responsible for almost two-thirds (63% in 2016) of disability-adjusted life years (DALYs) in Bangladesh.[17] The per capita NCD allocation is only USD 0.08.[17] There is a need for better coordination of non-state stakeholders in NCD control with the public sector with a stronger focus of the public sector on NCD prevention and health promotion.[17] The health sector in Bangladesh is financed 93% from domestic sources (74% out-of-pocket, 17% government health expenditure, and 3% other private sources) and 7% from external health expenditures. Domestic general government health expenditure per capita is only USD 7 (0.4% of GDP per capita).[44] Due to insufficient public sector funding, out-of-pocket expenditure for NCD care is large in Bangladesh, contributing to the impoverishment of patients and their families. Moreover, a recent policy review by Biswas et al (2017) highlights the lack of proper planning, implementation, and monitoring of NCD health initiatives.[45]

Reviewer Comment: (9) Background section, paragraph one, "An estimated 1.13 billion people (1 in 4 men and 1 in 5 women) worldwide has hypertension." Tense should be changed to "... have hypertension" and please add a citation

Author Response: Thank you. Citation included.

Reviewer Comment: (10) Section 4. Discussion – please define "NCD Corners"

Author Response: We added a sentence and a reference to describe NCD Corner. **"**To tackle NCDs, the government of Bangladesh introduced 'NCD Corners' initiative in 2012 dedicated to providing prevention and care services for common NCDs and related conditions."

Reviewer Comment: (11) Section 4. Discussion – limitations paragraph, typo "CDV" should be "CVD"

Author Response: Thanks for pointing out the typo.

Reviewer: 2 (Dr. David Roque, Hospital Professor Doutor Fernando Fonseca EPE)

Comments to the Author: *Dear authors, Congratulations on the massive effort undertaken on this project.*

Author Response: We are grateful for your review comments.

Reviewer Comment: *Here are my comments to your article.*
Suggested corrections:
PAGE 4
Line 13: Cardiac Failure -> Heart Failure
Line 13: Blindness -> retinopathy
Line 14: CVD deaths -> i believe the epidemiologic studies demonstrate that uncontrolled

hypertension can be responsible for almost half of all CV EVENTS.
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Author Response: We incorporated the edits; thanks so much.

Reviewer Comment: (1) What where the risk charts used to estimate CVD risk and are they validated in that population?

Author Response: The program entails assessment of target population by total CVD risk estimation to categorize their risk for CVD. The risk-stratification is based on WHO and International Society of Hypertension cardiovascular risk prediction charts and expressed as the probability of developing CVD over 10 years: low CVD risk (0 to <10%); medium CVD risk (10 to 20%); and high CVD risk (>=20%).

Reviewer Comment: (2) Where patients stratified according to the severity of the arterial hypertension? Since the authors followed a three-step protocol how was that organized? All patients, regardless of the basal hypertension level started in step 1 and then progress if they were not controlled? How was that assessed?

Author Response: We added the detailed hypertension management protocol for primary care setting as an appendix (appendix 1). Hypertension medication distribution among patients by treatment line has been revised to 62%, 34%, and 4% for treatment line 1, 2, and 3, respectively. The distribution of patients for the pharmacological treatment for hypertension by different treatment lines are adopted from Hasan, M. J. (2016). Pattern of drugs prescribed for treatment of hypertensive patients: Bangladesh. African Journal of Pharmacy and Pharmacology, 10(25), 521-525.

Reviewer Comment: (3) Same question for dyslipidemia: what where the labs used in the screening? >190mg/dl is total cholesterol or LDL cholesterol? And were the cut-offs and the need for treatment stratified according to global CVD risk? How was the protocol implemented? (4) Same questions for diabetes: how do authors estimated the need for step 1,2 or 3 drugs? Is it not clear for me how the

authors estimated the stratification of patients: if we look at Table 1, 65% of patients were in low CVD risk, which is the exact same % that received step 1 of the hypertension protocol, diabetes protocol and hyperlipidemia protocol. The same can be said regarding the % of patients in medium and high CVD risk and the step 2 and 3 of each protocol. This can lead to two different interpretations: is a coincidence that the % of patients with low, medium and high CVD risk estimate are the same that were allocated to the first, second and third step of all treatment protocols? Or if one is estimated, for example, to be at low CVD risk is considered to be controlled on the step 1 of the treatment protocol?

Author Response: Thanks so much for your comment. The protocols for the planned expansion of the hypertension management program into a risk-based integrated hypertension, diabetes, and hyperlipidemia management program are yet to be finalized. This costing exercise in this study is based on local expert consensus and the costing parameters were informed by context-specific literature and assumptions. Costs for lab diagnostic tests for diabetes and cholesterol (Fasting glucose and blood lipid panel) were considered. Upon further review of literature and consultation with local experts we revised the prescription distribution by line of treatment for each conditions as follows:

- The treatment protocol for patients with uncomplicated type 2 diabetes (defined as fasting plasma glucose (FPG) ≥ 7.0 mmol/l or routine plasma glucose (RPG) ≥ 11.1 mmol/l or HbA1C ≥ 6.5%) managed at the primary care level included Metformin (500 mg), Metformin (1000 mg), then Metformin (1000 mg) and Gliclazide (80 mg) as the first, second, and third lines of treatments, respectively. Assumed diabetes medication distribution was 75%, 15%, and 10% for treatment line 1, 2, and 3, respectively. The distribution of patients by treatment lines is based on consensus among local consultants and Chowdhury, A., Niloy, S. E. N., & Banik, S. (2017). Prescribing pattern of antidiabetic drugs in type 2 diabetic patients of Noakhali city in Bangladesh. Marmara Pharmaceutical Journal, 21(4), 1010-1014.
- The study assumes the World Health Organization (WHO) definition of elevated cholesterol of total cholesterol greater than 5.0 mmol/L (190 mg/dl) and very high cholesterol of total cholesterol greater than 6.2 mmol/L (240 mg/dl). Cholesterol medication (85%, 15%, and 10% for treatment line 1, 2, and 3, respectively): The distribution of patients by high Cholesterol treatment lines is based on consensus estimates of local experts and partly informed by Elnaem, M. H., Mohamed, M. H. N., Huri, H. Z., & Shah, A. S. M. (2019). Effectiveness and prescription pattern of lipid-lowering therapy and its associated factors among patients with type 2 diabetes mellitus in Malaysian primary care settings. Therapeutics and Clinical Risk Management, 15, 137.