Cost-effectiveness of Comprehensive screening of general population for hypertension: Can it save money and Life? Systematic review of Pharmacoeconomic Studies

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Abstract

Background: Hypertension is one of major modifiable risk factors contributing for development of ischemic heart disease, diabetes, kidney disease, cerebrovascular disease and peripheral arterial disease. Silent nature of the disease, delayed presentation of patients to health system after development of significant cardiovascular events and poor access to comprehensive health care are major challenge of hypertension control. Early screening, detection and treatment of hypertension is effective for control of the disease progression. However, there is no robust evidence on whether screening general population for hypertension is cost-effective or not. Therefore, this review was conducted t o generate evidence on cost effectiveness of population-based hypertension screening for asymptomatic individuals as early detection strategy for the primary prevention of cardiovascular diseases.

Methods: PubMed/Medline , Scopus, Web of sciences and Google Scholar were searched from January 2000 to 11 December 2019. Two investigators independently selected and reviewed fair and good-quality pharmacoeconomic studies for the cost-effectiveness of asymptomatic screening for hypertension in the community. Quality of selected literatures are evaluated by authors based on comprehensive tool developed for critical appraisal of pharmacoeconomic studies.

Results: Eleven included Pharmacoeconomic studies reported favorable results for screening asymptomatic adults for hypertension. Most of studies agreed on cost-effectiveness of screening adults aged 40 years and older. Screening of general adult population for hypertension is not-cost effective.

Conclusion: Screening population 40 years and older with or without additional risk factors is cost-effective in reducing hypertension and associated cardiovascular disease morbidity and mortality in developed and developing countries.

1. Background

Hypertension is one of major risk factors contributing for development of ischemic heart disease, diabetes, kidney disease, cerebrovascular disease and peripheral arterial disease. Global burden of the disease is increasing from time to time. The majority complications and deaths attributable by hypertension are now in developing countries where is lack of appropriate prevention and control mechanism due to overwhelming of the health system with infectious diseases. Silent nature of the disease and delayed presentation of patients to health system after development of significant cardiovascular events is the major challenge for prevention and control of hypertension. Early detection and treatment are believed to improve hypertension related patient outcomes. Opportunistic screening and treating population with high risk factors currently practiced for preventing and halting the disease progress after recommendations from World heart and health, World health organization and other national guidelines. Despite the introduction of this approach the disease incidence and prevalence in developing countries is increasing. This calls for action to increase the detection rate, prevention and treatment options (1, 2).

There are cost-effective pharmacological therapies to control blood pressure and prevent related cardiovascular disease morbidity and mortality. This requires early screening before development significant cardiovascular events. The burden of cardiovascular disease (CVD) has increasingly shifted toward low- and middle-income countries (3, 4). Studies indicated that there is insufficient Evidence to confirm the value of population screening for hypertension in low- and-middle-income settings. To save Limited resources and an evidence synthesis on cost-effectiveness and overall impact on the health system of screening strategies, especially in low- and middle-income settings (5). On the other hand, opportunistic screening program is ineffective due lack of access to basic health services and weak health insurance system in these countries. Early drug initiation of low-cost antihypertensive medicines and managing cardiovascular diseases as a single set of disease is cost-effective. Early initiation requires early detection of the cases. Therefore, this study was conducted to synthesize evidence on cost-effectiveness of screening general population for hypertension in the context of developing countries (6).

Prevention and management of raised blood pressure can significantly reduce the morbidity and mortality related to cardiovascular diseases (7). The question is how we can address these patients before development of cardiovascular events. Can we screen general population for raised blood pressure with available health budget which is already stressed with huge burden of infectious diseases and malnutrition in developing countries? Screening method so far applied by guidelines of different countries has not reduced the increasing burden of raised blood pressure and its consequences. Therefore, it is a time for searching a means for early detection and management of this disease. Can blanket screening be a solution for this?

2. Methods

2.1. Data sources and search strategy

We have searched the PubMed/Medline, Scopus, Web of Science and Google scholar with the following search query: PubMed: ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND ("population"[MeSH Terms] OR "population"[All Fields] OR "population groups"[MeSH Terms] OR ("population"[All Fields] AND "groups"[All Fields]) OR "population groups"[All Fields]) AND based[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND ("hypertension"[MeSH Terms] OR "hypertension"[All Fields]). Scopus: Cost-effectiveness AND of AND population AND based AND screening AND for AND hypertension. Web of Sciences: Cost-effectiveness of population-based hypertension Screening.

2.2. PICO for the systematic review

- **Population:** Adult Population age greater than or equal to 18 years
- **Intervention:** Population based screening for hypertension for adult's age greater than or equal to 18 years with no history of hypertension or cardiovascular diseases and diabetes
- **Comparison**: Opportunistic screening or screening patients visiting health facility for any for hypertension or Routine chronic care
- **Outcomes:** Quality of Life, Quality adjusted life years (QALY) gained or disability adjusted life years (DALY) averted

2.3. Study types

Cost-effectiveness analysis, Cost-benefit analysis, Cost-utility Analysis and budget impact analysis

2.4. Inclusion and exclusion criteria

- Population based screening (scheduled or opportunistic) for asymptomatic adults are included
- Population based screening (scheduled or opportunistic) for asymptomatic children are excluded
- Articles evaluating only high-risk population are excluded
- Articles that are not Pharmacoeconomic studies (CEA, CBA, CUA) are excluded
- Guidelines, Review articles, Short communications and Conference proceedings are excluded
- Articles that don't met quality evaluation criteria are excluded

2.5. Study selection

From total of 234 articles identified by literature search 44 potentially relevant articles were selected, after applying the inclusion exclusion criteria listed above only 17 articles were found to be relevant. With intention to have strong evidence we applied quality check for selected 17 articles and only 11 were found to meet our quality check and considered for review (8)(Figure 1). Two authors (MD, MM) independently reviewed each abstract based on pre-specified inclusion and exclusion criteria. In case of disagreement on quality of the article two authors discussed in presence of the third author (SN). We included good-quality Pharmacoeconomic studies written in English language since 2000 that assessed the effectiveness of population-based hypertension screening in asymptomatic general adult population without a history of CVD or diabetes.

2.6. Data Extraction and Quality Assessment

Two Authors collected baseline information, population characteristics, intervention details, disease incidence, mortality data and cost-effectiveness data from all included studies into a standardized evidence table. These authors independently assessed each study's quality as "good," or "poor" by using predefined quality criteria based on quality appraisal criteria of Pharmacoeconomic studies (9-11) (Table 1). We excluded all poor-quality Pharmacoeconomic studies. In general, a good-quality studies did not meet at most one pre-specified criteria. The study is labeled as having poor-quality if it did not meet at least two criterion. We used the Pharmacoeconomic studies quality appraisal criterial and Criteria for assessment of methodological quality of economic evaluations for quality evaluation and disagreements among us are managed through discussion in the presence of third author.

2.7. Data Synthesis and Analysis

The results were systematically analyzed, described and summarized qualitatively. We stratified results by method of (regular or opportunistic) screening, Perspective of Pharmacoeconomic evaluation, target population included, frequency of screening and method of

Pharmacoeconomic studies used and synthesized the results of included studies by examining outcomes and the respective recommendations.

2.8. Risk of bias assessment

We evaluated the risk of bias by using A critical appraisal tool to assess the quality of cross-sectional studies (AXIS) which is developed by experts (12). The AXIS tool contains 20 questions. Of which Seven (1, 4, 10, 11, 12, 16 and 18) of the questions related to quality of reporting, seven (2, 3, 5, 8, 17, 19 and 20) of the questions related to study design quality and six related to the possible introduction of biases in the study (6, 7, 9, 13, 14 and 15) (12). These six questions include: was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?, Were measures undertaken to address and categorize non responders?, Were the risk factor and outcome variables measured correctly using instruments/ measurements that had been trialled, piloted or published previously?, Does the response rate raise concerns about non-response bias?, If appropriate, was information about non-responders described? And were the results internally consistent? Respectively (12). All authors evaluated the risk of bias independently and rated the risk bias as high, intermediate or Low. High risk if the study has concerns for at least questions, intermediate if the study has concern to one question and low risk if the study has no risk of bias concern for all six questions. Based on the questions addressing possibility bias questions Pharmacoeconomic studies included in this review have low risk of bias (Table 3).

3. Results

We have screened 212 abstracts identified from search databases, reviewed 139 full-text of relevant articles, and included 11 articles in the final review. All studies involved modeling either markov's modeling or simulation modeling. The results were described by QALY gained or DALYs averted. Concerning the target populations four studies included people aged 40 years and above (13-16), three studies included people aged 50 years and above (17-19), two studies included age 30 years and above (20, 21) and two studies included age 15 years and above (Table 2) (22, 23).

Micro-simulation modeling study conducted in UK to predict lifetime CVD events, diabetes, and death in 259 146 asymptomatic UK Biobank participants aged 40–69 years showed that Periodic screening at 10-year CVD risk equivalent of 20% costed, £145/QALY gained and Periodic screening at CVD risk equivalent of 10% costed £11, 797/QALY gained. Periodic risk assessment using lower risk thresholds is not cost-effective (13).

Another study conducted in Australia showed that Screening and intensive treatment of hypertension resulted in ICER of $ 491/QALY gained. Primary care screening for hypertension, diabetes and protein urea between ages 50 and 69 years followed by ACEI therapy is cost effective (17).

Model-based economic evaluation conducted in Thailand (Bhutan) showed that screening people who are 40 years and above, are overweight, obese for diabetes and hypertension was cost-effective. Expanding opportunistic screening to the extent of universal coverage for target population is cost-effective (14).

Microsimulation modelling study in NHS showed that, Screening and risk stratification resulted in ICER of 11,000/QALY gained. Screening and risk stratification of general population aged 40-74 years are dominated by healthy behavior interventions. Implementation of general screening for population aged 40-74 years is neither equitable nor cost-effective (15).

Cost-Effectiveness Analysis of Screening for and Managing Identified Hypertension for Cardiovascular Disease Prevention in Vietnam showed that screening for hypertension resulted in cost saving of $758,695 per QALY gained in ten year horizon. Screening at above 55 years and older with increasing treatment coverage by 20% is cost-effective (18).

An Economic Evaluation of the PEN Program in Indonesia showed that implementing screening targeted at high-risk groups of population aged 40 and above is cost-effective when compared with no screening. Screening will result in cost savings for the government and a possibility to reallocate resources to the country's priority health concerns, consequently leading to better health outcomes (16).

A Costs and cost-effectiveness of hypertension screening and treatment in adults with hypertension in rural Nigeria showed that the ICER for the first (hypertension and risk based) and second (risk based) strategy respectively ranged from US $1,406 to US $7,815 and US$ 732 to US$ 2,959 per DALY averted, depending on the assumptions on risk reduction after treatment and compared to no access to antihypertensive treatment. Cost-effectiveness of Screening for hypertension was sensitive to changes in underlying assumptions with a wide range of uncertainty (24).

Simulation study conducted in Holland showed that screening individuals 60 years or older with; diabetes, previous CHD, familial CVD, high cholesterol, history of hypertension is cost effective and lifesaving (increased healthy life expectancy). It is not cost-effective to measure the BP of all patients, regardless of age, who visit the general practitioner (19).

Introducing a model of cardiovascular prevention in Nairobi's slums by integrating a public health and private-sector approach study showed that a home-based screening service package resulted in 760 -1,200 USD/DALY averted. Home based screening for general population aged 35 years and older by using trained community health workers is cost-effective (21).

Microsimulation modeling study conducted to evaluate Health Benefits and Cost-Effectiveness of Asymptomatic Screening for Hypertension and High Cholesterol and Aspirin Counseling for Primary Prevention in US showed that Health impact is highest for hypertension screening and treatment (15,600 QALYs), but is closely followed by cholesterol screening and treatment (14,300 QALYs). Cost-effectiveness for cholesterol and hypertension screening and treatment is $33,800 per QALY and $48,500 per QALY, respectively (22).

Effectiveness and Cost-Effectiveness of Blood Pressure Screening in Adolescents in the United States showed that Hypertension screening and treatment ICER of $48,500/QALY gained. Routine Hypertension screening and treatment for adults 18 years and above is cost-effective was dominated by population-wide strategies such as salt reduction and increasing physical education (23).

4. Discussion

Globally only one out of seven (14.28%) people with high blood pressure have achieved good control (25, 26). Hypertension treatment and control in developing countries in poor. For example according to the household survey report, health system in Sub-Saharan Africa (SSA) has the worst performance with only 29.9% of participants received treatment, and 10.3% of participants achieved control of their hypertension (26).

Hypertension is probably the most researched modifiable risk factor for ischemic heart disease with poor control over the disease incidence and prevalence of the disease. Current studies indicated that mean blood pressure of the global adult population is in pre-hypertension stage. Control and management of hypertension is challenged by number of factors including silent nature of the disease, poor detection by the health system before development of major cardiovascular events, poor access to medicines and poor community awareness(27).

Delayed detection of hypertension after development of significant cardiovascular events is one of avoidable bottle necks for blood pressure control (28). Early identification of cardiovascular disease (CVD) risk is important to reach people in need of treatment (29). There is no clear evidence on cost effectiveness of population-based screening for hypertension as part of early detection in developing countries (5).

In response to this evidence gap we have reviewed Pharmacoeconomic studies addressing screening asymptomatic adult individuals for hypertension on December 11, 2019 to generate evidence on cost-effectiveness of hypertension screening in developing countries. We have identified 11 studies which met our inclusion criteria. Five out of 11 articles determined the cost-effectiveness from payer perspective, 3 studies from societal perspective and 3 from provider perspective. Only three studies are conducted in developing countries Vietnam (18), Nigeria (20) and Kenya (21).

Micro-simulation modeling study conducted in UK among 259,146 asymptomatic UK Biobank participants aged 40−69 years showed that Periodic screening at CVD risk equivalent of 10% costed £11, 797/QALY gained (13). Periodic screening for low risk population or adults aged below 40 years with no history cardiovascular disease or diabetes is not-effective. This is because people 40 years and above by default enter into risk category CVD risk equivalent of more than 10% (25).

An economic evaluation conducted in Thailand (Bhutan) showed that screening people who are 40 years or older with overweight, obesity for diabetes and hypertension is cost effective. Expanding opportunistic screening to universal screening for target population is cost-effective (14). This is in line with world heart health recommendation (7). However, this screening in developing countries is challenged by limited access to health care, in adequate health task force, poor financial protection and low health literacy of the population (2). Integrating multiple interventions together, shifting screening task to low level trained professionals and using local opportunities for addressing the target population are important possibilities to decreasing burden of hypertension and associated morbidity and mortality (28-32).

Study conducted to determine Future cost-effectiveness and equity of the NHS Health Checkup program showed that, screening and risk stratification of general population aged 40-74 years is neither equitable nor cost-effective (15). This could be explained by that professionals are providing only screening and stratification of patients without providing counseling services on health-related behavior and life style. As NHS system involves Universal financing system and internal privatization, service providers usually take a great deal of their time in stratification and categorizing them to different diagnostic related groups to make profit (33).

An Economic Evaluation of the PEN Program in Indonesia showed that targeted screening of high-risk groups of population aged 40 and above is cost-effective. Screening will result in cost savings for the government and a possibility to reallocate resources to the country's priority health concerns, consequently leading to better health outcomes (16). This study directly addresses our basic question screening at developing countries with limited health budget and screening adults above 40 years of age can be done without casing significant change in health budget with good return in investment.

Modeling study conducted in Australia showed that Screening and intensive treatment of hypertension resulted in ICER of $ 491/QALY gained. Primary care screening for hypertension, diabetes and protein urea between ages 50 and 69 years followed by ACEI therapy is cost effective (17). Cost-Effectiveness Analysis of Screening for and Managing Identified Hypertension for Cardiovascular Disease Prevention in Vietnam showed that screening at age 55 years and above with or without increase treatment coverage by 20% cost-effective (18). Theses may not be such important in developing countries in which life expectancy is rarely greater than 60 years.

A Markov model-based Costs and cost-effectiveness of hypertension screening and treatment in adults with hypertension in rural Nigeria showed that Screening and treatment for hypertension was potentially cost-effective with a wide range of uncertainty (24). This is in line with other studies that screening for adults below age 40 years is not-cost effective.

Modeling study conducted in Holland showed that, screening individuals above 60 years with; diabetes, previous CHD, familial CVD is cost effective. It is not cost-effective to measure the BP of all patients, regardless of age, who visit the general practitioner (19). This is in line with other studies that screening for adults below age 40 years is not-cost effective.

Introducing a model of cardiovascular prevention in Nairobi's slums by integrating a public health and private-sector approach: the SCALE-UP study showed that home based screening for general population aged 35 years and older by using trained community health workers is cost-effective (21). This because the program integrated community awareness creation with screening service.

Modeling study conducted to evaluate Health Benefits and Cost-Effectiveness of Asymptomatic Screening for Hypertension and High Cholesterol in US showed that Health impact is highest for hypertension screening and treatment (15,600 QALYs), but is closely followed by cholesterol screening and treatment (14,300 QALYs) (22). Another study USA showed that in the United States showed that screening Adolescents for Hypertension and treatment resulted in ICER = $48,500/QALY gained. Routine Hypertension screening and treatment for adults 18 years and above is cost-effective was dominated by population-wide strategies such as salt reduction and increasing physical education (23).

There is no enough evidence to recommend screening asymptomatic adults with no risk factor for hypertension. All studies form developed and developing countries revealed that screening adults aged 40 years with one or more risk factor is cost-effective (13-23). This is in line with WHO PEN package interventions for primary health care in developing countries (34). The recent Cochrane review on general health check which showed that Health checks have little or probably no effect on cardiovascular mortality (RR 1.05, 95% CI 0.94 to 1.16), Health checks have little or no effect on fatal and non-fatal ischemic heart disease (RR 0.98, 95% CI 0.94 to 1.03), and probably have little or no effect on fatal and non-fatal stroke (RR 1.05 95% CI 0.95 to 1.17) (35).

World health organization (34) and World heart health association (7) recommended opportunistic screening of patients attending health facility for any reason for hypertension. Universal Access to health care in developing countries is yet not ensured and health facility-based screening hypertension will not bear expected fruit in controlling the alarmingly rising disease and associated cardiovascular morbidity and mortality. This supported by rising prevalence of the disease and shift of the burden from developed to developing countries (36). Out of an estimated 1.13 billion people worldwide living with hypertension, two-thirds are living in low- and middle-income countries and 80% of CVD related premature deaths are in also in low and middle-income countries (21, 30, 31, 36, 37).

It is important for developing countries to devise ways to increase opportunities for adult's aged 40 years and older to extent that all of these population screened for hypertension by using less trained community health workers. It is also important to consider the associated change in demand for drugs and laboratory facilities to determine the extent screening to ensure the availability of recommended treatment for patients. We have handful of evidence that early initiation of non-pharmacologic and pharmacologic therapy of hypertension is cost-effective. Early initiation requires early detection of the disease. Incorporating adult screening programs with community awareness programs or providing set of integrated programs can improve hypertension management and control (7, 30).

Limitations

The findings of this review should be considered in light of its limitations. The quality of Pharmacoeconomic studies included was low. We have only included articles published in English language. Articles published in other languages could have significant contribution in evidence synthesis.

Conclusion

There is no sufficient evidence to suggest general screening of adult populations for hypertension. Our review further strengthened the available evidence on opportunistic screening of adults aged 40 years and above with or without history of cardiovascular disease and diabetes for hypertension at least annually. Extending opportunistic screening of target population (i.e. population 40 years and above) to ensure universal screening, will yield good return on investment without casing significant change on health care budget for both developed and developing countries. Integrating screening services with other community services like education and counseling on salt reduction and physical activity will further improve cost-effectiveness of program for developing countries. In addition to this developing countries should design strategies to increase access availability essential medicines to address increased demand secondary to screening and take step to conduct health system research to develop cost-effective screening strategies for hypertension for their specific population.

Abbreviations

CEA: Cost Effectiveness Analysis

CBA: Cost Benefit Analysis

CUA: Cost Utility Analysis

CVD: Cardiovascular Diseases

QALY: Quality Adjusted Life Years

ICER: Incremental Cost Effectiveness Ratio

RR: Relative Risk

CI: Confidence Interval

DALY: Disability Adjusted Life Years

MeSH: Medical Subject Heading

SSA: Sub-Saharan Africa

WHO: World Health Organization

PEN: Package of Essential Non-communicable Diseases

CHD: Coronary Heart Disease

ACEIs: Angiotensin Converting Enzyme Inhibitors

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not Applicable. This is systematic review and we have used only published articles

Competing interests

Authors' contributions

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References

1. Bhatt H, Ghazi L, Calhoun D, Oparil S. BP Targets in Hypertension: What Should We Do Now That SPRINT Is Out? Current cardiology reports. 2016;18(10):98.

2. Brand M, Woodiwiss AJ, Michel F, Booysens HL, Majane OH, Maseko MJ, et al. Chronic diseases are not being managed effectively in either high-risk or low-risk populations in South Africa. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde. 2013;103(12):938-41.

3. Margaret A. Piper, Corinne V. Evans, Brittany U. Burda, Karen L. Margolis, Elizabeth O'Connor, Ning Smith, et al. Screening for High Blood Pressure in Adults: A Systematic Evidence Review for the U.S. Preventive Services Task Force: Evidence Synthesis. In: AHRQ Publication No. 13-05194-EF-1. Rockville MAfHRaQ, editor. US: AHRQ Publication; 2014. p. 1-305.

4. Davidson PM, Reid C. Population screening an important step in identifying and increasing awareness of cardiovascular disease in developing countries. Heart Lung and Circulation. 2012;21(2):61-2.

5. Durao S, Ajumobi O, Kredo T, Naude C, Levitt NS, Steyn K, et al. Evidence insufficient to confirm the value of population screening for diabetes and hypertension in low- and-middle-income settings. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde. 2015;105(2):98-102.

6. Correia JC, Lachat S, Lagger G, Chappuis F, Golay A, Beran D. Interventions targeting hypertension and diabetes mellitus at community and primary healthcare level in low- and middle-income countries:a scoping review. BMC public health. 2019;19(1):1542.

7. Adler AJ, Prabhakaran D, Bovet P, Kazi DS, Mancia G, Mungal-Singh V, et al. Reducing cardiovascular mortality through prevention and management of raised blood pressure. Glob Heart. 2015;10(2):111-22.

8. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev.[Internet]. 2015; 4: 1.

9. Rascati K. Essentials of pharmacoeconomics: Lippincott Williams & Wilkins; 2013.

10. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. International journal of technology assessment in health care. 2005;21(2):240-5.

11. Jefferson T, Demicheli V, Vale L. Quality of systematic reviews of economic evaluations in health care. Jama. 2002;287(21):2809-12.

12. Downes MJ, Brennan ML, Williams HC, Dean RS. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). BMJ open. 2016;6(12):e011458.

13. Ferket BS, Hunink MG, Khanji M, Agarwal I, Fleischmann KE, Petersen SE. Cost-effectiveness of the polypill versus risk assessment for prevention of cardiovascular disease. Heart (British Cardiac Society). 2017;103(7):483-91.

14. Dukpa W, Teerawattananon Y, Rattanavipapong W, Srinonprasert V, Tongsri W, Kingkaew P, et al. Is diabetes and hypertension screening worthwhile in resource-limited settings? An economic evaluation based on a pilot of a Package of Essential Non-communicable disease interventions in Bhutan. Health policy and planning. 2015;30(8):1032-43.

15. Kypridemos C, Collins B, McHale P, Bromley H, Parvulescu P, Capewell S, et al. Future cost-effectiveness and equity of the NHS Health Check cardiovascular disease prevention programme: Microsimulation modelling using data from Liverpool, UK. PLoS medicine. 2018;15(5):e1002573.

16. Rattanavipapong W, Luz ACG, Kumluang S, Kusumawardani N, Teerawattananon Y, Indriani D, et al. One Step Back, Two Steps Forward: An Economic Evaluation of the PEN Program in Indonesia. Health Systems & Reform. 2016;2(1):84-98.

17. Howard K, White S, Salkeld G, McDonald S, Craig JC, Chadban S, et al. Cost-effectiveness of screening and optimal management for diabetes, hypertension, and chronic kidney disease: a modeled analysis. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2010;13(2):196-208.

18. Nguyen TPL, Wright EP, Nguyen TT, Schuiling-Veninga CCM, Bijlsma MJ, Nguyen TBY, et al. Cost-Effectiveness Analysis of Screening for and Managing Identified Hypertension for Cardiovascular Disease Prevention in Vietnam. PloS one. 2016;11(5).

19. Van Buuren S, Boshuizen HC, Reijneveld SA. Toward targeted hypertension screening guidelines. Medical decision making : an international journal of the Society for Medical Decision Making. 2006 26(2):145-53.

20. Rosendaal NTA, Hendriks ME, Verhagen MD, Bolarinwa OA, Sanya EO, Kolo PM, et al. Costs and cost-effectiveness of hypertension screening and treatment in adults with hypertension in rural Nigeria in the context of a health insurance program. PloS one. 2016;11(6).

21. van de Vijver S, Oti S, Tervaert TC, Hankins C, Kyobutungi C, Gomez GB, et al. Introducing a model of cardiovascular prevention in Nairobi's slums by integrating a public health and private-sector approach: the SCALE-UP study. Global health action. 2013;6:22510.

22. Dehmer SP, Maciosek MV, LaFrance AB, Flottemesch TJ. Health Benefits and Cost-Effectiveness of Asymptomatic Screening for Hypertension and High Cholesterol and Aspirin Counseling for Primary Prevention. Annals of family medicine. 2017;15(1):23-36.

23. Wang YC, Cheung AM, Bibbins-Domingo K, Prosser LA, Cook NR, Goldman L, et al. Effectiveness and Cost-Effectiveness of Blood Pressure Screening in Adolescents in the United States. The Journal of pediatrics. 2011;158(2):257-64.e7.

24. Rosendaal NTA HM, Verhagen MD, Bolarinwa OA, Sanya EO, Kolo PM, et al. Costs and Cost-Effectiveness of Hypertension Screening and Treatment in Adults with Hypertension in Rural Nigeria in the Context of a Health Insurance Program. . PLoS ONE 2016;11(6):e0157925.

25. Whelton PK CR, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018;71:e13-e115.

26. Geldsetzer P, Manne-Goehler J, Marcus M-E, Ebert C, Zhumadilov Z, Wesseh CS, et al. The state of hypertension care in 44 low-income and middle-income countries: a cross-sectional study of nationally representative individual-level data from 1·1 million adults. The Lancet. 2019;394(10199):652-62.

27. Mohan V, Seedat Y. The Rising Burden of Diabetes and Hypertension in Southeast Asian and African Regions: Need for Effective Strategies for Prevention and Control in Primary Health Care Settings. International Journal of Hypertension. 2013.

28. Proia KK, Thota AB, Njie GJ, Finnie RKC, Hopkins DP, Mukhtar Q, et al. Team-Based Care and Improved Blood Pressure Control: A Community Guide Systematic Review. American journal of preventive medicine. 2014;47(1):86-99.

29. Shlay JC, Barber B, Mickiewicz T, Maravi M, Drisko J, Estacio R, et al. Peer Reviewed: Reducing Cardiovascular Disease Risk Using Patient Navigators, Denver, Colorado, 2007-2009. Preventing chronic disease. 2011;8(6).

30. Jeet G, Thakur JS, Prinja S, Singh M. Community health workers for non-communicable diseases prevention and control in developing countries: Evidence and implications. PloS one. 2017;12(7).

31. Ciapponi A, Lewin S, Herrera CA, Opiyo N, Pantoja T, Paulsen E, et al. Delivery arrangements for health systems in low-income countries: an overview of systematic reviews. Cochrane Database of Systematic Reviews. 2017(9).

32. McBrien KA, Ivers N, Barnieh L, Bailey JJ, Lorenzetti DL, Nicholas D, et al. Patient navigators for people with chronic disease: a systematic review. PloS one. 2018;13(2):e0191980.

33. Florin D, Dixon J. Public involvement in health care. BMJ (Clinical research ed). 2004;328(7432):159-61.

34. WHO. Package of Essential Noncommunicable (PEN) Disease Interventions for Primary Health Care in Low-Resource Settings. 2013.

35. Krogsbøll LT, Jørgensen KJ, Gøtzsche PC. General health checks in adults for reducing morbidity and mortality from disease. Cochrane Database of Systematic Reviews. 2019(1).

36. Mende Mensa Sorato, Majid Davari, Kebriaeezadeh A. Health Care System Response to Cardiovascular Diseases, Trends from 2010-2018: Can Ethiopia Achieve 2025 Global Voluntary Targets for Non-Communicable Diseases from Cardiovascular Diseases Perspective? Explanatory Review of Available Literatures. Research & Reviews: Journal of Medical and Health Sciences. 2019;9(1):1-13.

37. Gaziano TA, Bertram M, Tollman SM, Hofman KJ. Hypertension education and adherence in South Africa: a cost-effectiveness analysis of community health workers. BMC public health. 2014;14:240.

Tables

Table 1: Rating Quality of included Pharmacoeconomic studies based on quality appraisal criteria of pharmacoeconomic studies

o	Criteria	Reference										
		Ferket, BS. et al. 2016 (13)	Dukpa W. et al. 2015 (14)	Kypridemos C. et al, 2018 (15)	Rattanavipapong W, et al, 2016 (16)	Howard K, et al, 2010 (17)	Nguyen TPL. et al, 2016 (18)	Van Buuren S.et al, 2006 (19)	Rosendaal NTA, et al, 2016 (20)	Van de Vijver S. et al, 2013 (21)	Dehmer SP. et al, 2017 (22)	Wang YC., et al, 2011 (23)
	Is the title complete (answer, What, Where, How, in Whom)?	N	Y	Y	Y	N	Y	N	Y	N	N	Y
	Is the study population clearly described?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are competing alternatives clearly described?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Is a well-defined research question posed in answerable form?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Is the economic study design appropriate to the stated objective?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Is the chosen time horizon appropriate to include relevant costs and consequences?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Is the actual perspective chosen appropriate?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are all important and relevant costs for each alternative identified?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are all costs measured appropriately in physical units?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are costs valued appropriately?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are all important and relevant outcomes for each alternative identified?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are all outcomes measured appropriately?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are outcomes valued appropriately?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Is an incremental analysis of costs and outcomes of alternatives performed?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are all future costs and outcomes discounted appropriately?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are Limitations addressed?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Do the conclusions follow from the data reported?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Does the study discuss the generalizability of the results to other settings and patient/client groups?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Are ethical and distributional issues discussed appropriately?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Total quality score	95.2%	100%	100%	100%	95.2%	100%	95.2%	100%	95.2%	95.2%	100%

Table 2: Summery analytic approaches and major outcome measures in Studies conducted to evaluate cost-effectiveness of screening general population for hypertension, form 2000- December 11/2019 years.

S.No	Study reference	Country	Study design	Perspective	Participants	Measured outcome	frequency of screening	Findings	Recommendations
1	Ferket, BS. et al., 2016 (13)	UK	Microsimulation model	Payer	40-69 years	ICER/QALY gained	Every 5 years	Periodic screening at 10-year CVD risk equivalent of 20% costed, £145/QALY gained AND Periodic screening at CVD risk equivalent of 10% costed £11, 797/QALY gained	Periodic risk assessment with lower risk thresholds to initiate preventive drugs is unlikely to be cost-effective
2	Dukpa W. et al, 2015 (14)	Thailand	Model-based economic evaluation	Societal	40 years and older	ICER/DALY averted	annual	Universal screening for 40 years and older ICER = 112,906/DALY averted (BTN)= Bhutanese Ngultrum	Universal screening for 40 years and older is cost-effective
3	Kypridemos C. et al, 2018 (15)	UK	Dynamic stochastic microsimulation policy model,	Payer	40-74 years	ICER/QALY gained	every 5 years	Screening and risk stratification ICER = 11,000/QALY gained	Screening and risk stratification are dominated by healthy behavior interventions
4	Rattanavipapong W, et al, 2016 (16)	Indonesia	A decision tree and Markov model combined	Societal	40 years and older	ICER/QALY gained	Annual	Screening for diabetes and hypertension is cost-saving at the ICER of 14.22 million IDR per DALY averted	Screening for diabetes and hypertension is cost-saving compared to no screening
5	Howard K, et al, 2010 (17)	Australia	Markov modeling study	Payer (Funder)	50-69 Years	ICER/QALY gained	annual	Screening and intensive treatment of hypertension = $ 491/QALY	Screening for hypertension, diabetes and protein urea followed by ACEI therapy is cost effective
6	Nguyen TPL. et al, 2016 (18)	Vietnam	Decision tree and Markov model combined	Health service provider	55 years and above	ICER/QALY gained	Biannually	Screening is cost effective= $ 758,695 per QALY gained over ten years	Screening and increasing treatment coverage by 20% cost-effective
7	Van Buuren S.et al, 2006 (19)	Holland	Simulation study	Provider	60 years and older	ICER/QALY gained	Annual	Screening individuals with; diabetes, previous CHD, age > 60, familial CVD, high cholesterol, history of hypertension is cost effective	It is not cost-effective to measure the BP of all patients, regardless of age, who visit the general practitioner

8	Rosendaal NTA, et al, 2016 (20)	Nigeria	Markov modeling	Provider	30-79 years	ICER/DALY averted	Single	Presence of hypertension in combination with a CVD risk of >20% (risk-based strategy is cost effective with $ 1406-7815/DALY averted	Screening may be cost-effective with wide range of uncertainty
9	Van de Vijver S. et al, 2013 (21)	Kenya	Theoretical Modeling study	Payer	35 years and older	ICER/DALY averted	Annual	The service delivery package is cost-effective with of 760 -1,200 USD/DALY averted	Home based screening by using trained community health workers is cost-effective
10	Dehmer SP. et al, 2017 (22)	US	Integrated, microsimulation model	Societal	18 Years and older	ICER/QALY gained	annual	Hypertension screening and treatment ICER = $48,500/QALY gained	Hypertension screening and treatment is cost-effective
11	Wang YC., et al, 2011 (23)	US	Simulation modeling study	Payer	15 years and older	ICER/QALY gained	Variable	Screen and treat strategy is moderately cost-effective with mean cost = $32500/QALY gained	The strategy is dominated by population measures like physical education and salt reduction

Table 3:Rating risk bias of Pharmacoeconomic studies included based on a critical appraisal tool to assess the quality of cross-sectional studies (AXIS)

S.No	References	Risk of bias score	Percent of authors agreed
1	Ferket, BS. et al., 2016 (13)	Low	100%
2	Dukpa W. et al, 2015 (14)	Low	100%
3	Kypridemos C. et al, 2018 (15)	Low	100%
4	Rattanavipapong W, et al, 2016 (16)	Low	100%
5	Howard K, et al, 2010 (17)	Low	100%
6	Nguyen TPL. et al, 2016 (18)	Low	100%
7	Van Buuren S.et al, 2006 (19)	Low	100%
8	Rosendaal NTA, et al, 2016 (20)	Low	100%
9	Van de Vijver S. et al, 2013 (21)	Low	100%
10	Dehmer SP. et al, 2017 (22)	Low	100%
11	Wang YC., et al, 2011 (23)	Low	100%

Note: Low risk means the study has no concerns of bias asper the AXIS risk of bias assessment questions, Intermediate means, there is one concern among six questions of AXIS tool regarding the given study.
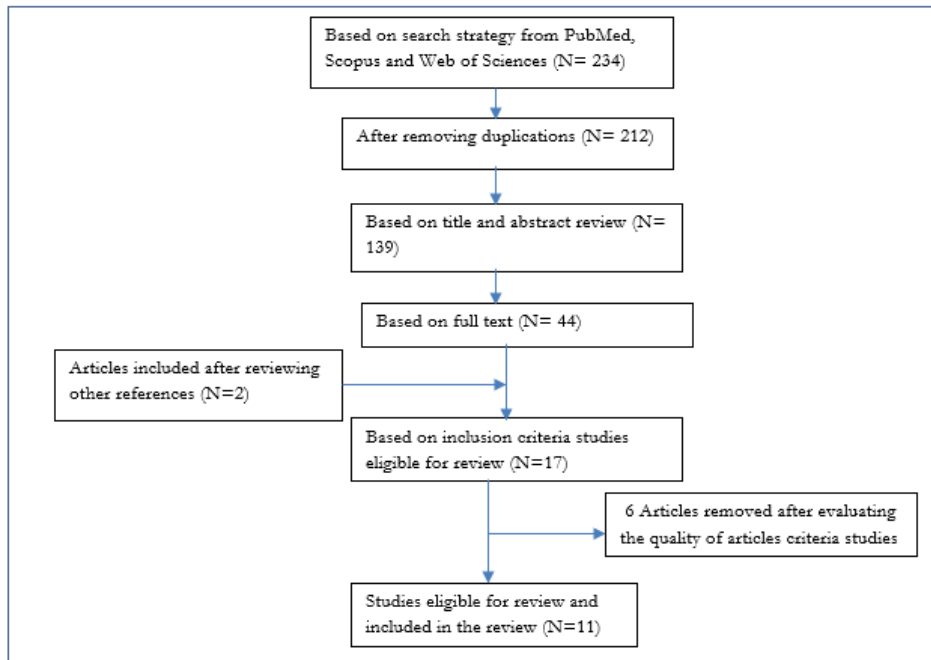
Figures

Figure 1

PRISMA Flowchart representing the result of search and the number of articles excluded and eligible for review

Supplementary Files

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