Published in final edited form as:

*JBI Database System Rev Implement Rep*. 2019 October ; 17(10): 2106–2114. doi:10.11124/JBISRIR-2017-003847.

# Impact of lifestyle modification on absolute cardiovascular disease risk: a systematic review protocol

**Jacob K. Kariuki**[1], **Cortes I. Yamnia**[2], **Christopher C. Imes**[1], **Patricia M. Weiss**[3], **Sandra J. Engberg**[1]

[1]School of Nursing, University of Pittsburgh, Pittsburgh, USA

[2]School of Nursing, University of North Carolina at Chapel Hill, Chapel Hill, USA

[3]Health Sciences Library System, University of Pittsburgh, Pittsburgh, USA

## Abstract

**Objective:** The objective of this review is to synthesize the available evidence on the effectiveness of lifestyle-based interventions for reducing absolute cardiovascular disease (CVD).

**Introduction:** Cardiovascular disease prevention guidelines recommend tailoring the choice and intensity of preventive interventions based on absolute CVD risk score. Several studies employing lifestyle-based interventions to mitigate CVD risk have reported heterogeneous outcomes, necessitating a systematic review to provide an exhaustive summary of current evidence.

**Inclusion criteria:** Eligible studies will include individuals at high-risk of CVD who are at least 18 years of age, with no history of CVD at baseline, regardless of sex, ethnicity and socio-economic status. Studies that compare lifestyle-based intervention to no intervention or usual care will be included. The outcome of interest is change in absolute CVD risk from baseline to post-intervention. Experimental and quasi-experimental study designs will be included.

**Methods:** Searches will be conducted in PubMed, EMBASE and CINAHL from the inception of each database. The search for gray literature will include ProQuest Dissertations and Theses Global, Grey Literature Report, Web of Science, BIOSIS Previews and the Proceedings database. Selected studies will be critically appraised by two independent reviewers at the study level for methodological quality. Extracted data will include details about the interventions, populations, study methods and outcomes of significance to the review question and objectives. Where possible, papers will be pooled in statistical meta-analysis. Effect sizes will be expressed as either odds ratios or standardized mean differences, and their 95% confidence intervals will be calculated for analysis.

**Systematic review registration number:** PROSPERO CRD42017073543

### Keywords

Absolute CVD risk assessment; cardiovascular disease; cardiovascular risk reduction; lifestyle modification

*Correspondence:* Jacob K. Kariuki, kigok@pitt.edu.

The authors declare no conflict of interest.

## Introduction

Cardiovascular disease (CVD), including coronary heart disease, stroke and peripheral vascular disease, continues to be the leading cause of death and disability globally,[1,2] with 70% of the mortality occurring in developing countries.[3] In the United States and other developed countries, significant gains in reducing CVD mortality rates have been made since the 1970s,[4] but the rate of decline has been disparate among groups, especially in racial and ethnic minorities.[1] In addition, most of the progress made in reducing preventable CVD mortality has largely benefited older adults, but more needs to be done in primary prevention of CVD, especially for individuals under 65 years.[5] Primary prevention of CVD entails screening for cardiovascular risk in asymptomatic individuals and initiating risk reduction interventions among those at high risk to prevent the first CVD event from occuring.[6,7]

To optimize primary prevention of CVD, current evidence-based guidelines recommend managing CVD risk based on absolute risk metrics rather than the traditional focus on individual risk factors.[8,9] This recommendation is based on the premise that whereas individual risk factors independently increase the likelihood of CVD events, clustering of multiple risk factors is known to compound the CVD risk.[10] Therefore, absolute CVD risk (also known as total or global CVD risk) denotes the probability that an individual will develop CVD within a certain time frame given the confluence of the risk factors present.[11] The absolute CVD risk approach employs risk assessment algorithms to compute absolute CVD risk scores for individuals based on the total impact of all risk factors present.[12] The scores range from 0%-100%, and they quantify the cumulative impact of multiple CVD risk factors present in the screened individual.[11,12] The absolute CVD risk scores are used to identify individuals at high risk for CVD. For instance, the American Heart Association guidelines consider individuals with absolute CVD risk score ≥7.5% to be at high risk for CVD.[8] In clinical settings, the metric helps in early detection of borderline elevation in multiple CVD risk factors, which leads to early detection and timely preventive interventions.[9] In some high-risk populations, such as African Americans, about 90% of CVD events are explained by elevated or borderline risk factors,[1] which can be easily missed when clinical assessments are focused on individual risk factors instead of absolute CVD risk scores.[11]

A case example for the utility of the absolute risk approach is a 64-year-old male, non-smoker, with no history of diabetes or hypertension, presenting with a blood pressure of 128/78 mmHg, body mass index of 29.5 kg/m$^2$, high-density lipoprotein cholesterol of 1.04mmol/L and total cholesterol of 5.62 mmol/L. Without considering the absolute CVD risk score, his major CVD risk factors, including blood pressure and lipids, do not meet their respective treatment thresholds. However, his estimated absolute risk for CVD, calculated using either the non-laboratory or laboratory-based Framingham algorithm,[13] is high at 21.7% and qualifies him for intensive preventive interventions.[8,9,11]

For many years, the absolute risk approach was primarily used as a strategy for predicting CVD risk,[10] with only a few randomized controlled trials examining changes in absolute CVD risk scores that were associated with risk-reduction interventions.[12] Over the last

decade, a growing number of investigators and clinicians have been using the metrics to evaluate the overall impact of cardiovascular risk-reduction interventions by comparing pre- and post-intervention absolute CVD risk scores. Interventions focusing on lifestyle modification to address major CVD risk factors such as physical inactivity, unhealthy diet, smoking and stress are considered first-line therapy in primary prevention of CVD and help reduce the need for drug interventions.[14,15] Interventions focusing on improving diet, physical activity, smoking cessation and stress management have been associated with significant reductions in absolute CVD risk scores among adults at high-risk for CVD.[16–19] Other studies have reported no significant differences between intervention and control groups.[20,21]

The heterogeneity of outcomes reported by the studies focusing on the impact of lifestyle modification on absolute CVD risk necessitate a systematic review to provide an exhaustive summary of current evidence. Such a review must appreciate the wide variation in the algorithms used to compute the absolute CVD risk scores. At present, more than 360 algorithms have been developed, with key differences in the number and type of risk factors included in the computation of absolute CVD risk scores.[22] In addition, the algorithms differ in the type of CVD events predicted (e.g., general versus hard coronary events) and the prediction horizon (5 year, 10 year and 30 years).[12] Currently, only 36% of these risk assessment algorithms have been externally validated.[22]

This systematic review seeks to synthesize the available research evidence on lifestyle-based cardiovascular risk reduction interventions that include a validated absolute CVD risk assessment metric as a study outcome. To make the review more informative and clinically relevant, studies employing comparable methodologies and risk assessment algorithms will be analyzed together before combining the outcomes of all the articles included in the review. For instance, all studies employing the Framingham algorithms[23] to assess absolute CVD risk will be analyzed together before the results are combined with studies employing other algorithms, such as the Reynolds Risk Score.[24] These data may help inform primary care providers on the most effective lifestyle interventions for patients at high risk of CVD. A preliminary search for existing systematic reviews was initially conducted in November 2016 and updated in October 2018. The databases searched were *JBI Database of Systematic Reviews and Implementation Reports*, Cochrane Library: Cochrane Reviews, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed, Embase and PROSPERO, which revealed no systematic reviews published or underway on this topic.

## Review question

What is the impact of lifestyle modification on absolute CVD risk in high-risk adult populations with no history of CVD?

## Inclusion criteria

### Participants

The systematic review will consider studies that include individuals at high risk for CVD, who are at least 18 years old, with no history of CVD at baseline, regardless of sex, ethnicity and socio-economic status.

### Intervention(s)

This review will consider original research focusing on lifestyle modification to reduce CVD risk as a single intervention or a combination of multiple lifestyle-based strategies. Types of lifestyle-based strategies will include, but are not limited to, physical activity, nutrition, stress management, patient education on CVD risk factors and smoking cessation. If other lifestyle-based interventions are identified during this systematic review, an assessment of these interventions will be made to consider for inclusion. The intensity, frequency and duration of the intervention will be considered when analyzing study outcomes and in the discussion of the results.

### Comparator(s)

This review will consider studies that compare lifestyle-based interventions to usual care or no intervention. Usual care is delivered based on prevailing clinical practices and may include patient education materials such as a handout about the health benefits of physical activity.

### Outcomes

This review will consider studies that include the primary outcome of interest, which is change in absolute CVD risk from baseline to post-intervention. Studies that utilize validated absolute CVD risk assessment algorithms to calculate absolute CVD risk scores will be included. The outcomes will be categorized by the focus of the risk assessment tool employed (e.g., hard coronary events or general CVD) and the duration of risk prediction (e.g., 5-year or 10-year risk). Secondary outcomes will include changes in individual risk factors, which will be evaluated by comparing cardiovascular risk profiles at baseline and post-intervention.

### Types of studies

This review will consider both experimental and quasi-experimental study designs, including randomized controlled trials, non-randomized controlled trials, before and after studies and interrupted time-series studies. Only studies published in English will be included. No date limits will be employed to maximize the scope of the review. This systematic review will not include studies with participants who had CVD at baseline, or participants who received drug therapy in addition to lifestyle modification since the focus is on lifestyle-based interventions. Our review will also exclude systematic reviews, umbrella reviews, qualitative studies and observational studies because they do not allow for the rigorous evaluation of the intensity, frequency or duration of interventions.

## Methods

The proposed systematic review will be conducted in accordance with the JBI methodology for systematic reviews of effectiveness.[25] The title of the review has been registered in PROSPERO, registration number CRD42017073543.

### Search strategy

A three-step search strategy will be utilized in this review to identify published and unpublished studies. An initial limited search of PubMed and Embase databases has been undertaken, followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe articles. This informed the development of the second step of our search strategy that includes all identified keywords and index terms, which will be tailored for each of the databases included in the review. A full search strategy for PubMed and Embase databases is detailed in Appendix I. In the last step of our search strategy, the reference list of all studies selected for critical appraisal will be screened for more studies.

**Information sources—**Literature searches will be conducted in PubMed (National Library of Medicine), Embase (Elsevier B.V.) and CINAHL (EBSCO Industries, Inc.), covering all records from the inception of each database product. The search strategies will include both natural language and standardized terms taken from each source's native controlled vocabulary: Medical Subject Headings (MeSH) for PubMed, Emtree for Embase and CINAHL Headings. The trial registers to be searched include Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov. The search for unpublished studies/gray literature will include ProQuest Dissertations and Theses Global, Grey Literature Report, Web of Science, BIOSIS Previews and the Proceedings database.

### Study selection

Following the search, all identified citations will be collated and uploaded into DistillerSR (Evidence Partners, ON, Canada) and duplicates removed. Titles and abstracts will then be screened by two independent reviewers for assessment against the inclusion criteria for the review. Studies that may meet the inclusion criteria will be retrieved in full and their details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) (Joanna Briggs Institute, Adelaide, Australia). The full text of selected studies will be retrieved and assessed in detail against the inclusion criteria. Full-text studies that do not meet the inclusion criteria will be excluded, and reasons for exclusion will be provided in an appendix in the final systematic review report. The results of the search and the full process for selecting included studies will be reported in full in the final report and presented in a PRISMA flow diagram.[26] Any disagreements that arise between the reviewers will be resolved through discussion or with a third reviewer.

### Assessment of methodological quality

Selected studies will be critically appraised by two independent reviewers at the study level for methodological quality using the standardized critical appraisal instruments from JBI for the following study types: quasi-experimental studies and randomized controlled trials (RCT).[25] In this review, RCT criteria 3, 6, 7, 9, 10 and 11 and quasi-experimental criteria 1,

2, 3, 5, 7 and 8 are considered essential for methodological rigor of the appropriate studies. In that context, only studies meeting these criteria will be included in the review. Any disagreements that arise between reviewers will be resolved through discussion or with the help of a third reviewer. In cases where there is uncertainty on reliability of the data, we will contact the corresponding author for clarification. The results of the critical appraisal of the studies will be presented in a tabular or narrative form.

## Data extraction

Data will be extracted from papers included in the review using the standardized data extraction tool available in JBI SUMARI by two independent reviewers. The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives. Any disagreements that arise between the reviewers will be resolved through discussion or with a third reviewer. Authors of papers will be contacted to request missing or additional data where required.

## Data synthesis

Papers will, where possible, be pooled in statistical meta-analysis using JBI SUMARI. Effect sizes will be expressed as either odds ratios (for dichotomous outcomes) or standardized mean differences (for continuous data), and their 95% confidence intervals will be calculated for analysis. Heterogeneity will be assessed via the standard Cochran's Q statistic (chi-squared test).[27,28] The inconsistency index ($I^2$) will be computed to describe the percentage of the variability in effect estimates that is due to heterogeneity rather than random sampling error.[29] Since we have *a priori* knowledge about the heterogeneity among studies that will be included in this review, the random effects model will be employed in the analysis as recommended by Haidich.[27] The method for meta-analysis will be based on the guidance provided by Tufanaru and colleagues.[30] Subgroup analyses will be conducted where there are sufficient data to investigate the differential impact of lifestyle modification on absolute CVD risk by race and sex. Sensitivity analyses will be conducted to test the impact of decisions made during the review process (e.g., eligibility of studies for meta-analysis) on the overall results and conclusions of the systematic review. In cases where sensitivity analyses will reveal missing data or decisions that disproportionately skew the findings of the review, we will try to resolve the uncertainties by obtaining more information from the authors listed in the articles as recommended by Higgins and colleagues.[28] Where statistical pooling is not possible due to limitations such as substantial heterogeneity among studies ($I^2$ ≥50%),[29] the findings will be presented in narrative form, including tables and figures, to aid in data presentation where appropriate. A funnel plot will be generated to assess publication bias if there are 10 or more studies included in a meta-analysis. Statistical tests for funnel plot asymmetry (Egger test, Begg test, Harbord test) will be performed where appropriate.[31,32]

## Assessing certainty in the findings

A summary of findings table will be created using GRADEpro software (McMaster University, ON, Canada).[33] The GRADE approach for grading the quality of evidence will be followed.[34,35] The Summary of Findings will present the following information where appropriate: absolute risks for treatment and control, estimates of relative risk and a ranking

of the quality of the evidence based on study limitations (risk of bias), indirectness, inconsistency, imprecision and publication bias. The following outcomes will be included in the summary of findings table: pre- and post-intervention absolute CVD risk scores, and changes in the CVD risk factors associated with the intervention.

## Acknowledgments

Funding

This work was supported by the University of Pittsburgh Central Research Development Fund awarded to JKK. The funders played no role in the review process.

## Appendix I:: Search strategies

| **PubMed** | |
|---|---|
| **Search** | **Query** |
| #1 | Cardiovascular Diseases[mh] OR cardiovascular disease*[tiab] OR cardiovascular disease*[ot] OR CVD[tiab] OR CVD[ot] OR coronary disease[tiab] OR coronary disease[ot] OR coronary heart disease[tiab] OR coronary heart disease[ot] OR MI[tiab] OR MI[ot] OR myocardial infarction[tiab] OR myocardial infarction[ot] OR myocardial ischemia[tiab] OR myocardial ischemia[ot] OR myocardial ischaemia[tiab] OR myocardial ischaemia[ot] |
| #2 | Risk[mh] OR risk[tiab] OR risk[ot] |
| #3 | absolute[tiab] OR absolute[ot] OR global[tiab] OR global[ot] OR total[tiab] OR total[ot] OR Framingham[tiab] OR Framingham[ot] OR office based[tiab] OR office based[ot] OR office-based[tiab] OR office-based[ot] OR non-laboratory[tiab] OR non-laboratory[ot] OR non-laboratory[tiab] OR non-laboratory[ot] OR IDEAL[tiab] OR IDEAL[ot] OR SCORE[tiab] OR SCORE[ot] |
| #4 | #2 AND #3 |
| #5 | FR-10[tiab] OR FR-10[ot] OR FRS[tiab] OR FRS[ot] OR ACC/AHA [tiab] OR ACC/AHA [ot] OR American College of Cardiology/American Heart Association[tiab] OR American College of Cardiology/American Heart Association[ot] OR QRISK[tiab] OR QRISK[ot] OR PROCAM[tiab] OR PROCAM[ot] OR REYNOLDS[tiab] OR REY-NOLDS[ot] OR WHO/ISH[tiab] OR WHO/ISH[ot] |
| #6 | (American College of Cardiology[tiab] OR American College of Cardiology[ot]) AND (American Heart Association[tiab] OR American Heart Association[ot]) |
| #7 | #5 OR #6 |
| #8 | #4 OR #7 |
| #9 | Primary Health Care[mh] OR primary care[tiab] OR primary care[ot] OR Primary Prevention[mh] OR prevention and control[sh] OR prevent*[tiab] OR prevent*[ot] OR Health Promotion[mh] OR Health Education[mh] OR Urban Health Services[mh] OR Community Networks[mh] OR Community Medicine[mh] OR community[tiab] OR community[ot] OR Mass Screening[mh] OR screening[tiab] OR screening[ot] OR neighborhood[tiab] OR neighborhood[ot] OR program[tiab] OR program[ot] |
| #10 | Risk Assessment[mh] OR Risk Management[mh] OR Risk Reduction Behavior[mh] OR risk appraisal[tiab] OR risk appraisal[ot] OR Exercise[mh] OR exercise[tiab] OR exercise[ot] OR physical activit*[tiab] OR physical activit*[ot] OR Walking[mh] OR walking[tiab] OR walking[ot] OR Smoking Cessation[mh] OR Smoking[mh] OR smoking[tiab] OR smoking[ot] OR Weight Loss[mh] OR weight loss[tiab] OR weight loss[ot] OR Body Weight[mh] OR Diet[mh] OR Diet Therapy[mh] OR diet therapy[sh] OR diet[tiab] OR diet[ot] OR dietary[tiab] OR dietary[ot] OR Health Behavior[mh] OR behavior[tiab] OR behavior[ot] OR behavioral[tiab] OR behavioral[ot] OR behaviour[tiab] OR behaviour[ot] OR behavioural[tiab] OR behavioural[ot] OR Life Style[mh] OR life style[tiab] OR life style[ot] OR lifestyle[tiab] OR lifestyle[ot] |
| #11 | Outcome Assessment[mh] OR Patient Outcome Assessment[mh] OR outcome* [tiab] OR outcome* [ot] OR Exercise[mh] OR exercise[tiab] OR exercise[ot] OR physical activit*[tiab] OR physical activit*[ot] OR Walking[mh] OR walking[tiab] OR walking[ot] OR Smoking Cessation[mh] OR Smoking[mh] OR smoking[tiab] OR smoking[ot] OR Weight Loss[mh] OR weight loss[tiab] OR weight loss[ot] OR Body Weight[mh] OR Diet[mh] OR Diet Therapy[mh] OR diet therapy[sh] OR diet[tiab] OR diet[ot] OR dietary[tiab] OR dietary[ot] OR Life Style[mh] OR life style[tiab] OR life style[ot] OR lifestyle[tiab] OR lifestyle[ot] |
| #12 | #1 AND #8 AND #9 AND #10 AND #11 |

| **PubMed** | |
|---|---|
| **Search** | **Query** |
| #13 | (("Infant"[Mesh] OR "Child"[Mesh] OR "Adolescent"[Mesh]) NOT "Adult"[Mesh]) |
| #14 | #12 NOT #13 |
| #15 | Animals[mh] NOT Humans[mh] |
| #16 | #14 NOT #15 |
| #17 | rat[tiab] OR rats[tiab] OR mouse[tiab] OR mice[tiab] OR murine[tiab] OR monkey[-tiab] OR monkeys[tiab] OR primate[tiab] OR primates[tiab] OR rabbit[tiab] OR rabbits[tiab] OR pig[tiab] OR pigs[tiab] OR swine[tiab] |
| #18 | #16 NOT #17 |
| **Embase** | |
| **Search** | **Query** |
| #1 | 'cardiovascular disease'/exp OR 'cardiovascular disease*':ti,ab OR 'coronary disease':-ti,ab OR 'coronary heart disease':ti,ab OR 'CVD':ti,ab OR 'MI':ti,ab OR 'myocardial infarction':ti,ab OR 'myocardial ischaemia':ti,ab OR 'myocardial ischemia':ti,ab |
| #2 | 'Framingham risk score'/de OR 'IDEAL score'/de |
| #3 | 'risk'/de OR 'risk':ti,ab |
| #4 | 'absolute':ti,ab OR 'global':ti,ab OR 'total':ti,ab OR 'Framingham':ti,ab OR 'office based':ti,ab OR 'office-based':ti,ab OR 'non-laboratory':ti,ab OR 'non-laboratory':-ti,ab OR 'IDEAL':ti,ab OR 'SCORE':ti,ab |
| #5 | 'American College of Cardiology':ti,ab AND 'American Heart Association':ti,ab |
| #6 | #4 OR #5 |
| #7 | #3 AND #6 |
| #8 | 'FR-10':ti,ab OR 'FRS':ti,ab OR 'ACC/AHA':ti,ab OR 'QRISK':ti,ab OR 'PROCAM':-ti,ab OR 'REYNOLDS':ti,ab OR 'WHO/ISH':ti,ab |
| #9 | #2 OR #7 OR #8 |
| #10 | 'community program'/de OR 'health promotion'/de OR 'health service'/de OR 'primary medical care'/de OR 'primary prevention'/de OR 'screening'/de OR 'community':ti,ab OR 'primary care':ti,ab OR 'prevent*':ti,ab OR 'screening':ti,ab OR 'neighborhood':ti,ab OR 'program':ti,ab OR 'intervention':ti,ab |
| #11 | 'aerobic exercise'/de OR 'behavior modification'/de OR 'caloric intake'/de OR 'diet restriction'/de OR 'exercise'/de OR 'exercise':ti,ab OR 'feeding behavior'/de OR 'group therapy'/de OR 'lifestyle'/de OR 'lifestyle':ti,ab OR 'life style':ti,ab OR 'lifestyle':ti,ab OR 'lifestyle modification'/de OR 'Mediterranean diet'/de OR 'patient counseling'/de OR 'patient education'/de OR 'personalized medicine'/de OR 'physical activity'/exp OR 'risk assessment'/de OR 'screening':ti,ab OR 'smoking':ti,ab OR 'smoking cessation'/de OR 'smoking cessation program'/de OR 'smoking':ti,ab OR 'smoking'/de OR 'walking'/de OR 'walking':ti,ab OR 'weight reduction'/de OR 'weight loss':ti,ab OR 'weight loss program'/de OR 'diet':ti,ab OR 'dietary':ti,ab OR 'yoga'/de OR 'yoga':ti,ab |
| #12 | 'outcome assessment'/de OR 'outcome*':ti,ab OR 'cardiorespiratory fitness'/de OR 'smoking cessation'/de OR 'smoking cessation':ti,ab OR 'smoking':ti,ab OR 'smoking '/de OR 'weight reduction'/de OR 'weight loss':ti,ab OR 'risk reduction'/de OR 'risk management'/de |
| #13 | #1 AND #9 AND #10 AND #11 AND #12 |
| #14 | #13 AND ([adolescent]/lim OR [child]/lim OR [embryo]/lim OR [fetus]/lim OR [infant]/lim OR [newborn]/lim OR [preschool]/lim OR [school]/lim) |
| #15 | #13 AND ([adult]/lim OR [aged]/lim OR [middle aged]/lim OR [very elderly]/lim OR [young adult]/lim) |
| #16 | #14 NOT #15 |
| #17 | #13 NOT #16 |
| #18 | #17 AND [animals]/lim |
| #19 | #17 AND [humans]/lim |
| #20 | #18 NOT #19 |
| #21 | #17 NOT #20 |

| PubMed | |
|---|---|
| **Search** | **Query** |
| #22 | 'rat':ti,ab OR 'rats':ti,ab OR 'mouse':ti,ab OR 'mice':ti,ab OR 'murine':ti,ab OR 'monkey':ti,ab OR 'monkeys':ti,ab OR 'primate':ti,ab OR 'primates':ti,ab OR 'rabbit':ti,ab OR 'rabbits':ti,ab OR 'pig':ti,ab OR 'pigs':ti,ab OR 'swine':ti,ab |
| #23 | #21 NOT #22 |

## References


1. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart disease and stroke statistics—2017 update: a report from the American Heart Association. Circulation 2017;135:e146–603. [PubMed: 28122885]
2. Bloom DE, Cafiero EE, Jané-Llopis E, Abrahams-Gessel S, Bloom LR, Fathima S, et al. The global economic burden of noncommunicable diseases. PGDA Working Papers 8712, Program on the Global Demography of Aging [Internet] 2012 [cited 2018 Mar 23]. Available from: http://ideas.repec.org/p/gdm/wpaper/8712.html.
3. World Health Organization Global status report on noncommunicable diseases [Internet] Geneva; World Health Organization; 2014 [cited 2018 Mar 23]. Available from: http://apps.who.int/iris/bitstream/handle/10665/148114/9789241564854_eng.pdf.
4. Pearson-Stuttard J, Guzman-Castillo M, Penalvo JL, Rehm CD, Afshin A, Danaei G, et al. Modelling future cardiovascular disease mortality in the United States: national trends and racial and ethnic disparities. Circulation 2016;133(10): 967–78. [PubMed: 26846769]
5. Centers for Disease Control and Prevention. Preventable deaths from heart disease & stroke. 2013 [cited 2018 Mar 27]. Available from: https://www.cdc.gov/vitalsigns/heart-disease-stroke/.
6. Weintraub WS, Daniels SR, Burke LE, Franklin BA, Goff DC, Hayman LL, et al. Value of primordial and primary prevention for cardiovascular disease: a policy statement from the American Heart Association. Circulation 2011;124(8): 967–90. [PubMed: 21788592]
7. Hennekens C, Lopez-Sendon J. Overview of the prevention of cardiovascular disease events in those with established disease (secondary prevention) or at high risk [Internet]. UpToDate 2017 [cited 2018 March 16]. Available from: https://www.uptodate.com/contents/overview-of-the-prevention-of-cardiovascular-disease-events-in-those-with-established-disease-secondary-prevention-or-at-high-risk?-search=prevention-of-cardiovascular-disease-events-in-those-with-established-disease-&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.
8. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;129(25 suppl 2):S49–73. [PubMed: 24222018]
9. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. Atherosclerosis 2016;252:207–74. [PubMed: 27664503]
10. Beswick AD, Brindle P, Fahey T, Ebrahim S. A systematic review of risk scoring methods and clinical decision aids used in the primary prevention of coronary heart disease [Internet] London: Royal College of General Practitioners 2008 [cited 2018 April 18]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK55818/pdf/Bookshelf_NBK55818.pdf.
11. World Health Organization. Prevention of cardiovascular disease: pocket guidelines for assessment and management of cardiovascular risk. Geneva: World Health Organization; 2007.
12. Cooney MT, Dudina AL, Graham IM. Value and limitations of existing scores for the assessment of cardiovascular risk: a review for clinicians. J Am Coll Cardiol 2009;54(14): 1209–27. [PubMed: 19778661]

13. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. Framingham heart study: cardiovascular disease (10-year risk) [Internet] 2015 [cited 2018 May 2]. Available from: https://www.framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk/.
14. Eckel RH, Jakicic JM, Ard JD, Hubbard VS, de Jesus JM, Lee I, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;129(25 suppl 2):S76–99. [PubMed: 24222015]
15. Masana L, Ros E, Sudano I, Angoulvant D. Lifestyle Expert Working Group. Is there a role for lifestyle changes in cardiovascular prevention? What, when and how? Atheroscler Suppl 2017;26:2–15. [PubMed: 28434481]
16. Soares TS, Piovesan CH, Gustavo Ada S, Macagnan FE, Bodanese LC, Feoli AM. Alimentary habits, physical activity, and Framingham global risk score in metabolic syndrome. Arq Bras Cardiol 2014;102(4):374–82. [PubMed: 24652053]
17. Márquez-Celedonio FG, Téxon-Fernández O, Chávez-Negrete A, Hernández-López S, Marín-Rendón S, Berlín-Lascurain S. Clinical effect of lifestyle modification on cardiovascular risk in prehypertensives: PREHIPER I Study. Rev Esp Cariol 2009;62(1):86–90.
18. Edelman D, Oddone EZ, Liebowitz RS, Yancy WS Jr, Olsen MK, Jeffreys AS, et al. A multidimensional integrative medicine intervention to improve cardiovascular risk. J Gen Intern Med 2006;21(7):728–34. [PubMed: 16808774]
19. Wister A, Loewen N, Kennedy-Symonds H, McGowan B, McCoy B, Singer J. One-year follow-up of a therapeutic lifestyle intervention targeting cardiovascular disease risk. CMAJ 2007;177(8):859–65. [PubMed: 17923653]
20. Ketola E, Mäkelä M, Klockars M. Individualised multifactorial lifestyle intervention trial for high-risk cardiovascular patients in primary care. Br J Gen Pract 2001;51(465):291–4. [PubMed: 11458482]
21. Gibbs BB, King WC, Belle SH, Jakicic JM. Six-month changes in ideal cardiovascular health vs. Framingham 10-year coronary heart disease risk among young adults enrolled in a weight loss intervention. Prev Med 2016;86:123–9. [PubMed: 26923555]
22. Damen JA, Hooft L, Schuit E, Debray TP, Collins GS, Tzoulaki I, et al. Prediction models for cardiovascular disease risk in the general population: systematic review. BMJ 2016;353:i2416. [PubMed: 27184143]
23. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: The Framingham heart study. Circulation 2008;117(6):743–53. [PubMed: 18212285]
24. Ridker PM, Buring JE, Rifai N, Cook NR. Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds Risk Score. JAMA 2007;297(6):611. [PubMed: 17299196]
25. Tufanaru C, Munn Z, Aromataris E, Campbell J, Hopp L. Chapter 3: Systematic reviews of effectiveness In: Aromataris E, Munn Z, editors. Joanna Briggs Institute Reviewer's Manual [Internet] Adelaide: Joanna Briggs Institute, 2017 [cited 2018 May 10]. Available from: https://reviewersmanual.joannabriggs.org/.
26. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. Open Med 2009;3(3):e123–30. [PubMed: 21603045]
27. Haidich AB. Meta-analysis in medical research. Hippokratia 2010;14(Suppl 1):29–37. [PubMed: 21487488]
28. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327(7414):557–60. [PubMed: 12958120]
29. Green S, Otesph O. Cochrane handbook for systematic reviews of interventions [Internet] 2008 [cited 2018 May 4]. Available from: https://pdfs.semanticscholar.org/4b43/91c08c45ebfcd046a53106c97ca09fcdf9fa.pdf.
30. Tufanaru C, Munn Z, Stephenson M, Aromataris E. Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. Int J Evid Based Healthc 2015;13(3):196–207. [PubMed: 26355603]

31. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315(7109):629–34. [PubMed: 9310563]

32. Sterne JAC, Sutton AJ, Ioannidis JPA, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ 2011;342:d4002.

33. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, et al. Going from evidence to recommendations. BMJ 2008;336(7652):1049–51. [PubMed: 18467413]

34. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction - GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64(4):383–94. [PubMed: 21195583]

35. Jaeschke R, Guyatt GH, Dellinger P, Schünemann H, Levy MM, Kunz R, et al. Use of GRADE grid to reach decisions on clinical practice guidelines when consensus is elusive. BMJ 2008;337:a744. [PubMed: 18669566]