CLINICAL RESEARCH STUDY

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Association of Optimism with Cardiovascular Events and All-Cause Mortality: Systematic Review and Meta-Analysis

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ABSTRACT

BACKGROUND: The effect of psychological health on cardiovascular disease is an underappreciated yet important area of study. Understanding the relationship between these two entities may allow for more comprehensive care of those with cardiovascular disease. The primary objective of this meta-analysis is to evaluate the relationship between optimism and risk of developing adverse events such as all-cause mortality or fatal and non-fatal cardiovascular disease in community-based populations.

METHOD: A systematic search of electronic databases was conducted from inception through November 2021 for prospective studies evaluating optimism and adverse outcomes. Two reviewers independently selected prospective cohort studies that evaluated optimism and either all-cause mortality or cardiovascular disease and reported hazard ratios of these outcomes between optimistic and non-optimistic groups. Studies that reported odds ratio or other risk assessments were excluded. Pooled hazard ratios were calculated in random-effects meta-analyses.

RESULTS: Pooled analysis of six studies (n = 181,709) showed a pooled hazard ratio of 0.87 (95% confidence interval [CI], 0.82-0.92) for all-cause mortality among those with more optimistic mindset. Analysis of seven studies (n = 201,210) showed a pooled hazard ratio of 0.59 (95% CI, 0.37-0.93) for cardiovascular disease and pooled hazard ratio of 0.57 (95% CI, 0.07-4.56) for stroke.

CONCLUSIONS: In this pooled meta-analysis, optimism was associated with a reduced risk of all-cause mortality and of cardiovascular disease. These results suggest an important relationship between psychological health and cardiovascular disease that may serve as an area for intervention by clinicians.

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INTRODUCTION

In early 2021, a Scientific Statement From the American Heart Association asserted that psychological health is an essential component of wellness/well-being for patients with, and at risk for, cardiovascular disease, and that there is high-quality data showing clear associations between psychological health and cardiovascular disease risk.[1] In addition, increasing evidence suggests that interventions to improve psychological health can have a beneficial impact on cardiovascular health as well. Simple screening measures can be employed by health care clinicians for patients with, or at risk for, cardiovascular disease to assess psychological health status. A previous meta-analysis that included 15 observational studies and 220,391 individuals found that higher levels of optimism were associated with a 35% decrease in risk of incident cardiovascular disease events (relative risk 0.65; 95% confidence interval [CI], 0.51-0.78) and a 14% decrease in risk of all-cause mortality (relative risk 0.86; 95% CI, 0.80-0.92).[2] This association was seen for both men and women and remained significant after adjusting for depression. Of note, the degree of association seen with optimism was similar to that of more traditional cardiovascular disease risk factors. To consider these findings more systematically, we conducted a meta-analysis of studies that have assessed the association between optimism and adverse cardiac outcomes. Our goals were to evaluate the magnitude of this association, the consistency of results among reported studies, the influence of potential confounders, and the quality of the reported literature.

CLINICAL SIGNIFICANCE

- Optimism is associated with a reduced risk of all-cause mortality.
- Optimism is associated with a reduced risk of cardiovascular disease.
- Positive psychological health can play a role in prevention and, possibly, reduction of cardiovascular disease.
- A comprehensive approach by clinicians that includes optimism may be beneficial.

METHODS

Data Sources and Searches

An experienced librarian (SF) developed search strategies for the literature review. We conducted a comprehensive search and extensive query of Ovid MEDLINE, Ovid Embase, Ovid Cochrane Database of Systematic Reviews, Scopus, and Web of Science from database inception in 1966 through November 2021 for all original studies that evaluated individuals with the following Medical Subject Heading terms: optimism, outcomes, endpoint, mortality, death, cardiovascular events, stroke, coronary artery disease, coronary heart disease, ischemic heart disease, and cardiovascular disease (Appendix). No language restrictions were imposed for the search. In addition, references from included studies and pertinent review articles were assessed to identify additional studies meeting the selection criteria. The definition of cardiovascular events as reported by studies is listed in the Table.[5-14] The present systematic review and meta-analysis was conducted and reported according to the recommendations of the PRISMA Reporting Guidelines.

Data Extraction and Quality Assessment

Two authors (CK and NSM) extracted and analyzed the data using a standard extraction form, which was then reviewed by other co-authors (HH and ZW). Conflicts were resolved through consensus. We extracted study characteristics (study name, authors, publication year, country of origin, sample size, study design, and follow-up duration), study sample characteristics (mean age, sex, and major comorbidities), main exposure (method of assessment of optimism), variables adjusted, and main outcomes (all-cause mortality, cardiovascular mortality, or cardiovascular events). Study quality was assessed by the Newcastle-Ottawa scale, with quality grades assigned based on selection of the study groups, comparability, and assessment of outcomes.

Statistical Analysis

We extracted hazard ratio and related 95% CIs from the studies that compared the highest level of optimism to the lowest level of optimism at the longest follow-up. Adjusted hazard ratio was preferred over unadjusted hazard ratio to reduce potential confounding factors on outcomes. The DerSimonian and Laird random-effects model with the Hartung-Knapp-Sidik-Jonkman variance correction was used to pool the estimates.[3,4] Heterogeneity across trials was estimated with I^2 statistics (I^2 <25% suggests low heterogeneity). We were unable to evaluate statistical publication bias due to the small number of studies included in the meta-analyses. A 2-tailed $P < .05$ was considered to be statistically significant. All analyses were performed using Stata statistical software, version 16 (StataCorp LLC, College Station, Texas).

RESULTS

A flow diagram of the literature search and related screening process is shown in Figure 1. A total of 10 studies published between November 2001 and October 2021 met our inclusion criteria, for a total of 215,151 individuals. Of the 10 studies, 7 reported data pertaining to cardiovascular events (n = 201,210), while 6 studies provided data about all-cause mortality (n = 181,709). The characteristics of the studies reviewed are shown in the Table. Of the included

Table Characteristics of Included Studies

Study	Cohort Studied	Study Period	n	Male %	Mean Age (Years)	Follow-Up Duration (Years)	Assessment of Optimism	Endpoint	CVD Definition
Weiss-Faratci (2017)	Israeli MI age <65 y	1992-1993	664	85.2	52.4	22.4	LOT-R	All-cause mortality	N/A
Kim (2017)	Female nurses (Nurses' Health Study cohort)	2004-2014	70,021	0	70	10	LOT-R	All-cause mortality, CVD mortality	"Heart disease" evaluated by study physicians who reviewed death certificates and medical records
Boehm (2011)	Community Cohort	1991-1994	7942	69.1	49.5	5.4	1-item questionnaire	CHD (fatal and nonfatal)	Fatal coronary disease, first nonfatal MI, or first definite angina
Hansen (2010)	Community cohort	1995	1739	49.6	46.2	10	2 items from LOT-R	CVD mortality	Fatal or nonfatal ischemic heart disease, ICD-9 codes (410-414) and ICD-10 codes (I21-I25)
Nabi (2010)	Community cohort	1998-2005	23,216	41	NR	7	LOT-R	Stroke	Fatal or nonfatal stroke
Grossardt (2009)	Ambulatory patients	1962-1965	7080	48.7	48.1	32.4	CoNeg	All-cause mortality	N/A
Tindle (2009)	Post-menopausal women	1994-1998	97,253	0	NR	8	LOT-R	All-cause mortality, CHD Mortality	Mortality related to MI, angina, PCI, or CABG
Brummett (2006)	Community cohort	1964-1966	5750	82.6	18.5	40	PSM	All-cause mortality	N/A
Giltay (2006)	Elderly individuals	1985-1990	545	100	71.7	15	4-item questionnaire	CVD mortality	ICD-9 codes 390-459
Giltay (2004)	Elderly individuals	1991	941 (494 CVD)	49.5	74.5	9.1	7-item questionnaire	All-cause mortality, CVD mortality	ICD-10 codes I00-I96

CABG = coronary artery bypass graft surgery; CHD = coronary heart disease; CVD = cardiovascular disease; ICD = International Classification of Diseases; LOT-R = Revised Life Orientation Test; MI = myocardial infarction; PCI = percutaneous coronary intervention; PSM = paradoxical septal motion.

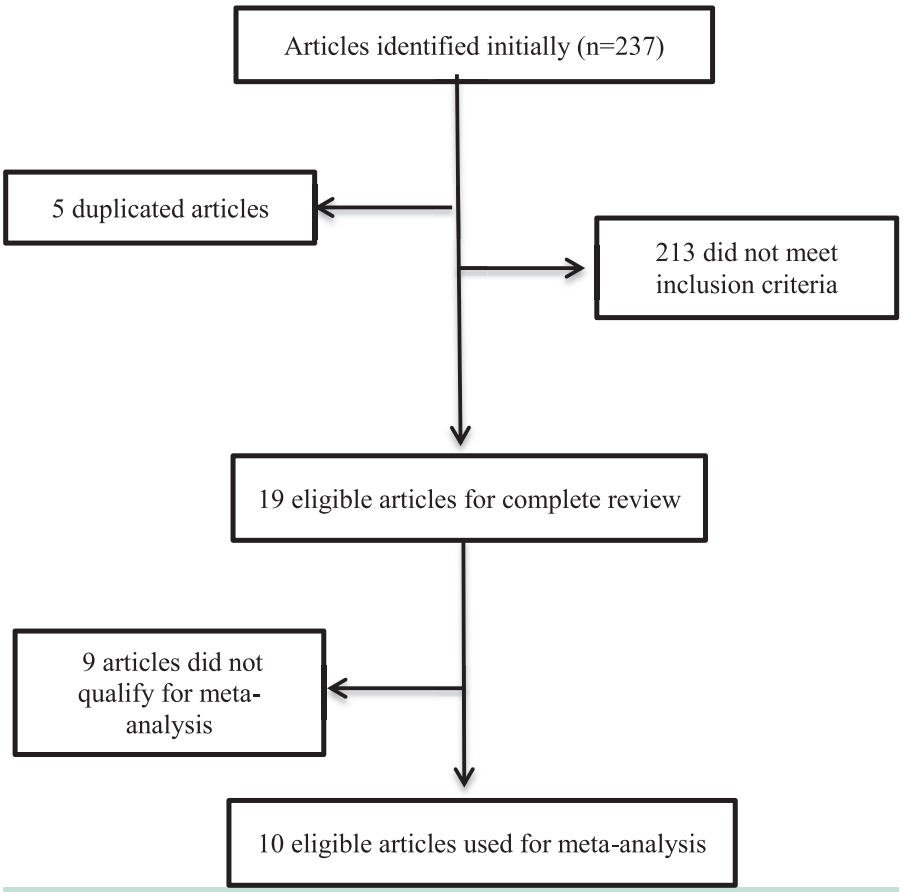

Figure 1 Study design. This flow chart illustrates the selection process for published reports.

studies, one study investigated post-myocardial infarction patients, one study investigated ambulatory patients, one study investigated a cohort of female nurses, and the remainder investigated community-based cohorts.

The age of individuals at baseline assessment ranged between 19 and 75 years, and the follow-up period ranged between 7 and 40 years. Methods of assessing optimism included the Revised Life Orientation Test, the Revised Optimism-Pessimism score derived from the Minnesota Multiphasic Personality Inventory, or 1- to 7-item questionnaires assessing optimism. All studies had a low risk for bias using the Modified Newcastle-Ottawa Scale (Supplementary Table[5-14]).

Based on pooled analysis of adjusted hazard ratios, all-cause mortality was assessed in 181,709 participants derived from data of 6 studies. Optimism was associated with a statistically significant reduction of all-cause mortality (pooled hazard ratio 0.87; 95% CI, 0.82-0.92, I^2 = 0.0%). The reported hazard ratio of each study is depicted in Figure 2.[5,6,10-13]

Based on pooled analysis of adjusted hazard ratios, cardiovascular events were assessed in 201,210 participants derived from data of 7 studies. Optimism was associated with a significant reduction of cardiovascular mortality (pooled hazard ratio 0.59; 95% CI, 0.37-0.93, I^2 = 65.8%). Stroke was assessed in 93,237 participants derived from the data of 2 studies. Optimism was associated with a non-significant reduction of stroke (pooled hazard ratio 0.57; 95% CI, 0.07-4.56; I^2 = 0.0%). The reported hazard ratio of each study is depicted in Figure 3.[6-9,11,13,14]

Additional studies could not be quantified with our meta-analytic approach. The findings of these studies are consistent with our meta-analytic results. For example, Lee and colleagues[15] reported that optimism was associated with a reduction of all-cause mortality (odds ratio 0.91; 95% CI, 0.83-0.91). Engberg and colleagues[16] found that optimism to be associated with a reduction of all-cause mortality in both males and females by comparing with a neutral scoring cohort. Other studies also reported beneficial effects of optimism on cardiovascular disease mortality and all-cause mortality.[17-19] However, these studies used different outcome measures (eg, odds ratio, or continuous optimism score), or a comparison group; therefore, they could not be quantified with our meta-analytic methods.[15-19]

DISCUSSION

In the present study, we found that optimism was associated with lower rates of all-cause mortality and cardiovascular events. Using entirely separate literature, our results are

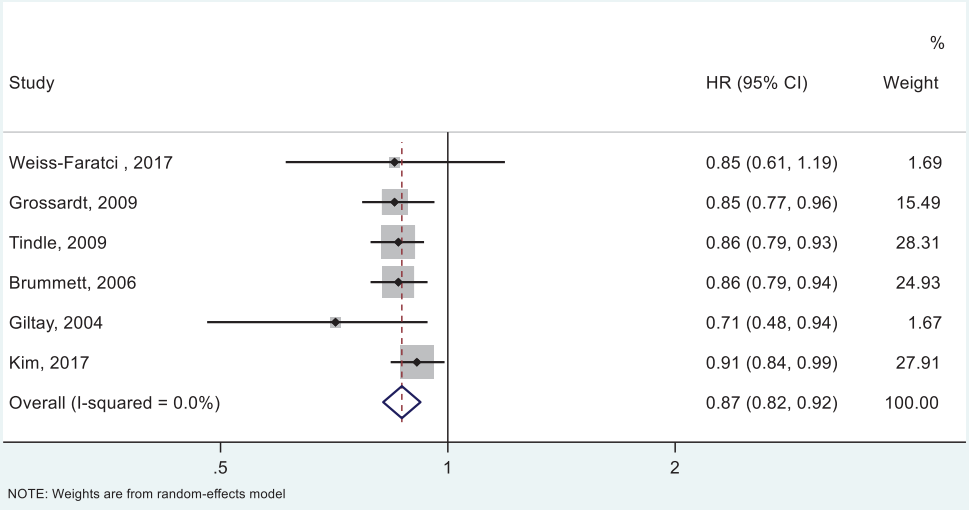

Figure 2 Optimism and all-cause mortality. The forest plot of point estimates and confidence intervals also includes variance, which was used in the inverse variance correction.

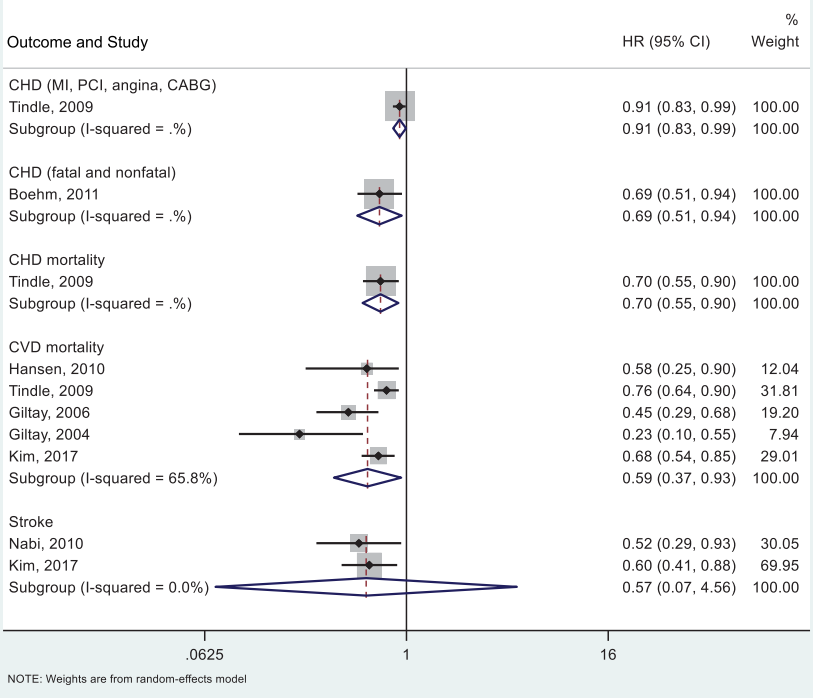

Figure 3 Optimism and cardiovascular events. The forest plot of point estimates and confidence intervals also includes variance, which was used in the inverse variance correction.

consistent with the prior meta-analysis reviewing studies completed prior to July 2, 2019 by Rozanski and colleagues[2] In the present study, the overall pooled hazard ratio for cardiovascular mortality among individuals with high optimism levels was 0.59, while the overall pooled hazard ratio for all-cause mortality among individuals with high optimism levels was 0.87. In addition, there was a non-significant trend toward a reduction in stroke risk with a pooled hazard ratio of 0.57.

The evidence suggests that optimism could influence cardiovascular health and ultimately improve survival. There are several possible mechanisms through which optimism could lead to a lower risk of cardiovascular events and all-cause mortality.

Optimism may influence overall cardiovascular health indirectly through changes in behavior. For example, it is possible that individuals who are happier or more optimistic tend to sleep better, exercise more, eat more healthily, be more physically active, have a larger support network as they are more sociable, and be less likely to use tobacco products, leading to overall improved health outcomes.[20]

In addition, optimism may influence cardiovascular health biologically via neurohormonal regulatory processes. Several neural studies have shown that happiness is associated with activation of the striatum, amygdala, hippocampus, anterior cingulate cortex, and other regions of the limbic system, while psychological distress (eg, anger, anxiety, depression, post-traumatic stress disorder) is associated with activation of the hypothalamic-pituitary-adrenal axis, leading to the risk of developing cardiovascular disease.[21-24] One study showed that prolonged neuroinflammation could impair brain function, resulting in changes in mood and behavior.[25] The emotion of happiness is associated with increased levels of several hormones, including dopamine,[26] serotonin,[27] norepinephrine, melatonin,[28] and endorphins.

Optimism has been associated with lesser stress responses and a reduced cortisol level at awakening, particularly under situations of high stress.[29,30] By extension, optimistic individuals may be less susceptible to the stress-induced reductions in goal orientation[31] and be better able to regulate emotions.[32] In this context, it is noteworthy that humans show stronger ventrolateral prefrontal (inferior frontal gyrus) activity when they overestimate the likelihood of positive events hypothetically happening to them and that more optimistic individuals show reduced ventrolateral coding of potential negative events.[22] Ventrolateral prefrontal activity (and connectivity with the amygdala) has consistently been associated with emotion regulation and may underpin the increased capacity of optimistic individuals to maintain a positive outlook.[33,34]

Another mechanism through which optimism may influence metabolic and inflammatory pathways is through changes in diet. Several studies have demonstrated that positive psychological health has been linked exclusively to elevated high-density lipoprotein cholesterol levels.[35-37] Other studies have found associations between optimism with both higher high-density lipoprotein cholesterol and lower triglycerides,[38] or lower levels of inflammation[39,40] and endothelial dysfunction.[40] Some studies have found negative effects associated with clinically elevated (≥3 mg/L) C-reactive protein,[39,41] and reducing effects of Mediterranean dietary patterns on markers of inflammation in humans.[42]

Finally, recent research has demonstrated bidirectional communication between the central nervous system and gut microbiota (aka the gut-brain axis). Optimism may have an influence on variations in the microbiome, leading to potential changes in concentrations of hormones, neurotransmitters, and immunological factors.[43-46] Lactobacilli and inflammation are also recognized for their impact on neural pathways, and when an imbalance occurs, mood disorders can develop.[47]

Altogether, optimism is associated with improved health outcomes via a multifactorial array of mechanisms including immune-mediated, inflammatory, metabolic, genetic, and behavioral processes. It has been shown that genetics play an important role in both mood and emotional characteristics,[48] and heritability of optimism is estimated to be around 30%.[49,50] Example genes that have been associated with happiness include 5-*HTTLPR* and *MAOA*. However, genetic factors were not evaluated in this study. Prospective studies and randomized controlled trials are needed to further evaluate whether pessimism is a contributor to pathophysiologic dysfunction.

CLINICAL SIGNIFICANCE

Optimism has proven to have a beneficial effect on clinical health outcomes. The recent American Heart Association statement from 2021 also suggested consideration of psychological health in the evaluation and management of patients with, or at risk for, cardiovascular disease.[1] In fact, lack of optimism could relate to higher rates of clinical depression—which is ultimately related to poorer cardiovascular health.

At present, there is a need for the development of optimism promotion/training for patients with cardiovascular disease risk factors. For example, those with diabetes may be more depressed compared with healthy individuals due to their lifestyle limitations. Optimism intervention/training could include psychotherapy, stress management programs, physical activity programs, wellness programs, and meditation training. These interventions have been shown to be beneficial based on meta-analyses of randomized clinical trials.[51] Cognitive behavioral therapy is an effective treatment for depression and raises levels of optimism. Antidepressant drug treatment relieves depression and can mitigate effects on cardiovascular health.

In addition, it is clear that certain types of diet and the associated improvements in mental health significantly affect other organ systems, such as the endocrine, immune, and gastrointestinal systems. One example is the Mediterranean diet, which promotes healthy eating, and is associated

with a host of benefits, including anti-inflammatory properties. Consuming a well-balanced diet (low in sugar, fatty foods) could help promote more comprehensive, healthy lifestyles.

Finally, mental health within the workplace is a key factor for the promotion of optimism and happiness. On average, full-time American workers spend more than one-third of their day, 5 days per week at their workplace; therefore, this is an important setting for health promotion and disease prevention programs. Examples of health promotion within the workplace include health education classes, partnerships with local fitness facilities, promotion of company policies that facilitate healthy behaviors (such as a tobacco-free campus policy), providing employee health insurance coverage for appropriate preventive screening, and through actions such as making healthy foods available and accessible through vending machines or cafeterias. Further prospective trials will be needed to prove the effectiveness of these measures in the prevention of cardiovascular disease, including stroke.

Limitations

The present study has significant limitations, and the results should be interpreted with caution. First, the relationship between optimism and cardiovascular health is likely due to multifactorial factors including inflammatory process, genetic risks, pathogens, and environmental stressors. Thus, the included studies did not correct for all potential confounders or investigate potential mechanisms. Second, the variables adjusted for by each study are inconsistent, leading to substantial heterogeneity. Third, at the psychological levels, optimism is associated with biased belief updating, higher confidence, and higher willingness to exert effort and take risks, leading to unmeasured behavioral confounders.[22,52] Finally, the measurements of optimism for each study are different.

CONCLUSIONS

The present study showed that optimism seems to be associated with a lower risk of cardiovascular events and all-cause mortality. Future studies should seek to better define the biobehavioral mechanisms underlying this association and evaluate the potential benefit of interventions designed to promote optimism.

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SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjmed.2021.12.023.

APPENDIX

eMethods: Search Strategies

For literature prior to June 2019, see Rozanski and colleagues[2] for the search terms. Web of Science was substituted for Scopus for this search update because of availability.

Database: PubMed <June 2019 to Present> Search Strategy:

("Cardiovascular Diseases"[Mesh] OR "Stroke"[Mesh] OR cardiovascular events OR stroke OR coronary artery disease OR coronary heart disease OR ischemic heart disease OR cardiovascular disease) AND ("Optimism"[Mesh] OR "Pessimism"[Mesh] OR optimism[tw] OR pessimism[tw])

Database: PsycINFO <June 2019 to Present. Search Strategy: ((optimism or pessimism or optimistic explanatory style).mp.) and ((exp Cardiovascular Disorders/ or cardiovascular events.mp.) or coronary artery disease.mp. or coronary heart disease.mp. or exp Heart Disorders/ or ischemic heart disease.mp. or cardiovascular disease.mp.)

Database: Web of Science <June 2019 through Present> Search Strategy: TS=((optimism OR pessimism) AND (cardiovascular events OR stroke OR coronary artery disease OR coronary heart disease OR ischemic heart disease OR cardiovascular disease))

Supplementary Table Characteristics of Included Studies Using the Modified Newcastle-Ottawa Scale for Assessing the Quality of the Non-Randomized Studies

Study, Year (Reference)	Selection				Comparability	Outcome		
	Representativeness of the exposed cohort for the general population in the community	Selection of the non-exposed cohort from the same community as the exposed cohort (drawn from the same community as the exposed cohort)	Ascertainment of exposure (validated questionnaire or measurement tool)	Demonstration that outcome of interest was not present at start of study (no heart failure signs or symptoms at start of study)	Comparability of cohorts on the basis of the design or analysis (study controls for sex and cardiovascular risk factors)	Assessment of outcome (physician's diagnosis OR objective measurements)	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts (completed or loss follow up <20%) or (the statistical test used to analyze the data is clearly described and appropriate)
Weiss-Faratci, 2017		✓	✓	✓	✓	✓	✓	✓
Kim, 2017		✓	✓	✓	✓	✓	✓	✓
Boehm, 2011	✓	✓	✓	✓	✓	✓	✓	✓
Hansen, 2010	✓	✓	✓	✓	✓	✓	✓	✓
Nabi, 2010	✓	✓	✓	✓	✓	✓	✓	✓
Grossardt, 2009	✓	✓	✓	✓		✓	✓	✓
Tindle, 2009		✓	✓	✓	✓	✓	✓	✓
Brummett, 2006		✓	✓	✓		✓	✓	✓
Giltay, 2006		✓	✓	✓	✓	✓	✓	✓
Giltay, 2004		✓	✓	✓	✓	✓	✓	✓