Title: Prevention vs. Treatment in Cardiovascular Diseases: An updated Economic Systematic Review

Category: Prevention

Abstract

Background: Cardiovascular disease (CVD) represents a global burden with an estimated prevalence of 422.7 million cases in 2015. The financial burden of CVD in low to middle income countries was estimated to be an average of 5000 USD per episode. Regarding developed countries, in the USA the annual economic burden of CVD is estimated to be 403 billion USD, while in the European Union it was estimated to be 192 Billion Euros. This study aims to compare economic cost-effective analysis (CEA) of primary prevention programs for CVD as regards behavioral modifications (smoking cessation, Healthy Dietary intake and physical exercise) as well as screening and treatment of chronic medical conditions associated with increased risk of CVD including obesity, Hypertension, Hyperlipidemia and Diabetes.

Methods: We conducted a systematic literature review of journal articles published during the period 2017-2019 on Medline via PubMed with the relevant search term. Screening of studies and data extraction was done independently by three reviewers. Figure 1 shows the PRISMA flow diagram of the screening process. We enrolled the studies according to restricted inclusion criteria: studies with 1) full economic evaluation, 2) available full text, 4) only English studies, and 5) Primary or Model studies. Drummond's checklist was used in the quality appraisal for all studies used to inform this evidence synthesis.

Results: From a pool of 325 records, 59 full texts were read and 40 studies, which met our inclusion criteria, were retained for our qualitative synthesis. Most of the studies included both genders in the middle age. However, seven studies focused on the childhood stage. In terms of used model, 16 studies used Markov model, 12 used RCT, 5 used micro-simulations, and the others varied between retrospective study and linear regression model. Regarding the method of cost effectiveness, 75% of the studies used willingness-to-pay (WTP) method. The majority of studies was cost-effectiveness-analyses, were conducted in a US, UK, Ireland, Australia, and Spain setting, assessed clinical prevention (mainly drugs targeted blood pressure and cholesterol lowering), bariatric procedures, Sports and physical activities, and nutrition education programs. Concerning the financial and physical benefits, 85% of the studies reported that these programs are cost effective and two studies out of them considered these programs as a cost saving. Table 1 shows the summary of the included studies. Table 2 demonstrates that 60% of the studies were at low risk of bias, 32.5% at intermediate risk of bias, and only 7.5% at high risk of bias, according to Drummond's checklist.

Conclusion: This evidence synthesis provides an update of interventions that provide good value for money, health, and society in middle- and high-income countries. There is no significant difference between the individual or population-based interventions in terms of cost effectiveness. Targeting young (school) age groups was not very valuable compared to the middle age group. Moreover, this review has demonstrated the obvious lack of economic evaluations of broader health promotion interventions, when compared to clinical prevention. Finally, governments should engage more actively in the economic evaluation of prevention to fill the gap left by private industry in terms of the evaluation of broader public health interventions.

Study	Type of Model	Method of Cost effectiveness	Time horizon	Type of evaluation	Discounting %	Country	Intervention	ICER	Conclusion	Currency
Fitzgerald S 2018	Markov	Not stated	2016	CEA	NS	Ireland	Nutrition education and System-level dietary modification	€101.37/QALY	Cost-Effective	Euro
Chris Kypridemos 2018	Microsimulation	WTP	2016	CEA	3.50%	UK	1. Scenario (A): continuing current implementation of NHS Health Check; 2. Scenario (B): implementation 'targeted' toward areas in the most deprived quintile with increased coverage and uptake; 3. Scenario (C): 'optimal' implementation assuming optimal coverage, uptake, treatment, and lifestyle change; 4. Scenario (D): scenario A combined with structural population-wide interventions targeting unhealthy diet and smoking; 5. Scenario (E): scenario B combined with the structural interventions as above.	£11000/ QALY	Not Cost-effective	Sterling Pound
Adab P 2018	RCT	WTP	2014-2016	CEA	3.50%	UK	Active lifestyle and healthy Eating in School children	£42000/ QALY	Not Cost-effective	Sterling Pound

Mark Nuijten 2018	RCT	WTP	2013	CEA	5%	USA	Optifast in class 1 and 2 obesity and bariatric surgery in class 3 to 4	$6,475/ QALY	Cost-Effective	USD
Borisenko O 2018	Markov	WTP	2011	CEA	3%	Belgium	Bariatric surgery	€2809/ QALY	Cost-Effective	Euro
Stam-Slob M 2018	Markov	WTP	2014	CEA	3%	Netherlands	PCSK9 inhibition added to standard therapy in patients with Familial Hypercholesterolemia, patients with vascular disease at high MACE recurrence risk, and patients with vascular disease with DM	€78,485/QALY	Cost-Effective	Euro
Gc V, 2017	Retrospective study	WTP	2011-2019	CEA	3.50%	UK	Pedometer interventions, advice/counseling in primary care, and action planning interventions.	£687.50/QALY	Cost-Effective	Sterling pound
Panca M 2018	Markov	WTP	2013-2014	CUA	3.50%	UK	Bariatric surgery of 18 adolescents with severe obesity	£1978/ QALY	Cost-Effective	Sterling pound
Gray et al 2018	RCT	Not stated	3.5 years	CEA	3.50%	UK	Football Fans in Training (FFIT) program, incremental physical activity and dietary changes into daily.	£1790–£2200/ QALY	Cost-effective	English pound
Popp J 2018	Microsimulation	WTP	2010-2013	CEA	3%	USA	A Quit and Win Smoking Cessation Program for College Students	$1,759/ QALY	Cost-Effective	USD
Sanchez-Santos R 2018	Markov	WTP	2008-2013	CEA	3%	Spain	Bariatric surgery versus conservative management for morbidly obese patients	€5,966/ QALY	Cost-Effective	Euro

Mozaffarian D. 2018	Microsimulation	WTP	2009–2014	CEA	3%	USA	Financial incentives and disincentives through the SNAP	$5,216/ QALY	Cost-Effective	USD
Lan Gao, 2019	Markov	WTP	2014-2015	CEA	3%	Australia	Reducing sitting time of office-based workers	$43,825/QALY	Cost-Effective	Australian dollars, 2016
Ralph Chapman, 2018	ITHIM	Not stated	2011 and 2012	CBA	3.5%	New Zealand	Active travel (walking and cycling)	NS	Positive return on investment	NS
Timothy McKnight, 2018	Linear regression model	Not stated	2009 and 2017	CBA	NS	USA	Lecture topics included stress management, nutrition, healthy eating, reading food labels, fitness, disease prevention, and healthy aging.	NS	$34 per kg lost	USD
Monica Panca, 2018	RCT	WTP	2013-2014	CUA	NS	UK	12 one-to-one sessions across 6 months, addressing lifestyle behaviors and focusing on motivation to change and self-esteem rather than weight change, delivered by trained graduate health workers in community settings.	£120,630/ QALY	Cost-Effective	GBP
Michael J Sweeting, 2018	Markov	WTP	2012-2014	CEA	3.50%	UK	Screening women for abdominal aortic aneurysm	30 000 /QALY	Cost-Effective	Sterling pound
Cindy M. Gray, 2018	RCT	WTP	2011-2012	CEA	3.50%	UK	Weight management program for men delivered through professional football clubs FFIT	£1790–£2200 /QALY	Cost-Effective	GBP

Hayden McRobbie 2019	RCT	WTP	2012 - 2015	CEA	No	UK	Weight action Program and Practice nurse intervention	£7742/QALY	Cost-Effective	GBP
Dominika Högberg 2018	Markov	WTP	NS	CEA	3.50%	Sweden	ultrasound screening for ACAS with subsequent initiation of preventive therapy versus not screening	€5744/ QALY	Cost-effective	Euro
Sanjay Basu 2018	Microsimulation	Not stated	2017	CEA	3%	Palestine	A transition from traditional food aid to either (i) a debit card restricted to food purchases, (ii) cash, or (iii) an alternative food parcel with less grain and more fruits and vegetables, each valued at $30/person/month.	$414/ QALY	Unclear	USD
Mauri´lio de Souza Cazarim 2018	Quasi-experimental study	WTP	March to November 2014	CEA	not specified	Brazil	Compare SAH treatment with PC management and conventional treatment for hypertensive patients offered by the PHS.	$42.95/QALY	Cost-Effective	USD
Max Korman 2018	Markov	WTP	One Year	CEA	4%	Norway	PCSK9 inhibitors for prevention of coronary heart disease, ischemic strokes, and death among high-risk patient subpopulations.	€94,000–213,000/ QALY	Cost-effective	Euro
Wei Yang 2017	Markov	NS	10-year	CEA	3.5%	UK	Plant sterol or stanol-enriched functional foods as a primary prevention strategy for people with cardiovascular disease risk	<£20,000/ QALY	cost-effective	GBP

Ruth F. Hunter 2018	RCT	NS	2014 - 2015	CEA	No	Northern Ireland	The Physical Activity Loyalty Scheme (PAL) intervention	£290,178 /QALY	Not Cost-effective	GBP
Marta Conesa 2018	RCT	NS	2007-2010	CEA	not specified	Spain	Health promoter agents (HPAs) and EdAl intervention	€968.66/QALY to avoid one case of obesity	Cost-Effective	Euro
O.Borisenk 2017	Markov	WTP	10-year and lifetime	CUA	3.5%	England	Bariatric surgery, including gastric bypass, sleeve gastrostomy and adjustable gastric banding; and non-surgical usual care.	€12,449/ QALY	Cost-Effective	BGP and Euro
Monica Panca, 2018	Linear regression model \ CUA alongside RCT	WTP	2013 till 2014	CUA	No	UK	12 one-to-one sessions across 6 months, addressing lifestyle behaviors and focusing on motivation to change and self-esteem rather than weight change, delivered by trained graduate health workers in community settings	£120,630/ QALY	Not Cost-effective	GBP
Kavita Singh, 2018	Markov	WTP	2010 - 2013	CEA	NS	India	Use of Multidrug Pill In Reducing cardiovascular Events (UMPIRE)	$34–$36/ QALY	Cost-Effective	Indian Rupees

Adnan Alsumali, 2018	Many Models	WTP	NR	CEA	NS	US	Bariatric surgery among patients with morbid obesity	$12900/QALY	Cost-Effective	USD
Lars Lindholm, 2018	Retrospective cohort	NS	1990-2006	CEA	NS	Sweden	Västerbotten Intervention Program; individual disease prevention efforts among the middle-aged population with community-oriented health promotion activities.	NS	Cost-Effective	SEK
Smith, A. J, 2018	Decision-model	NS	2016-2017	CEA	NS	US	Targeted screening of hyperlipidemia	$1980/QALY	Cost-Effective	USD
Jonathan Pearson-Stuttard 2018	Micro-simulation	WTP	2017-2036	CEA	3%	Synthetic population based on US IMPACT Food Policy Model	Lowering Sodium consumption	< $100,000/QALY	Cost-Effective	USD
Ben Ewald 2017	RCT	Not stated	12 months	CEA	No	Australia	Face-to-face coaching and telephone coaching over 12 weeks were compared with a control group using the outcome of step count for one week at baseline, three months and twelve months.	Not calculated	Cost effective	AUD
Michael W. Beets 2017	RCT	WTP	2014-2015	CEA	NS	USA	Comprehensive intervention in afterschool programs to achieve healthy eating and physical activity policies. The intervention was based-upon the STEPs (Strategies To Enhance Practice)	Not calculated	Un clear	USD

David D. Kim 2018	Markov	WTP	Lifetime and 5 years post-surgery	CEA	3%	US	Bariatric procedures	Kim 2018 jpeg	Cost-Effective	USD
Mundt 2018	RCT	Not stated	2013-2015	CEA	not measured	USA	Incentive-based stop-smoking intervention that paid Medicaid recipients who smoke to take calls from a tobacco quit line.	$2600/ QALY	Cost-Effective	USD
Xiaolei Xie 2018	Markov	WTP	2015 to 2025	CEA	3%	China	Intensive hypertension control	7876 CNY/ QALY	Cost-Effective	CNY
Ana Maria Mantilla Herrera 2018	Markov	WTP	lifetime horizon	CEA	3%	Australia	The Health Star Rating (HSR) system is a voluntary front-of-pack labeling (FoPL) initiative endorsed by the Australian government in 2014	4752 AUD/ QALY	Cost-Effective	AUD

Table 1: Summary of Included Studies

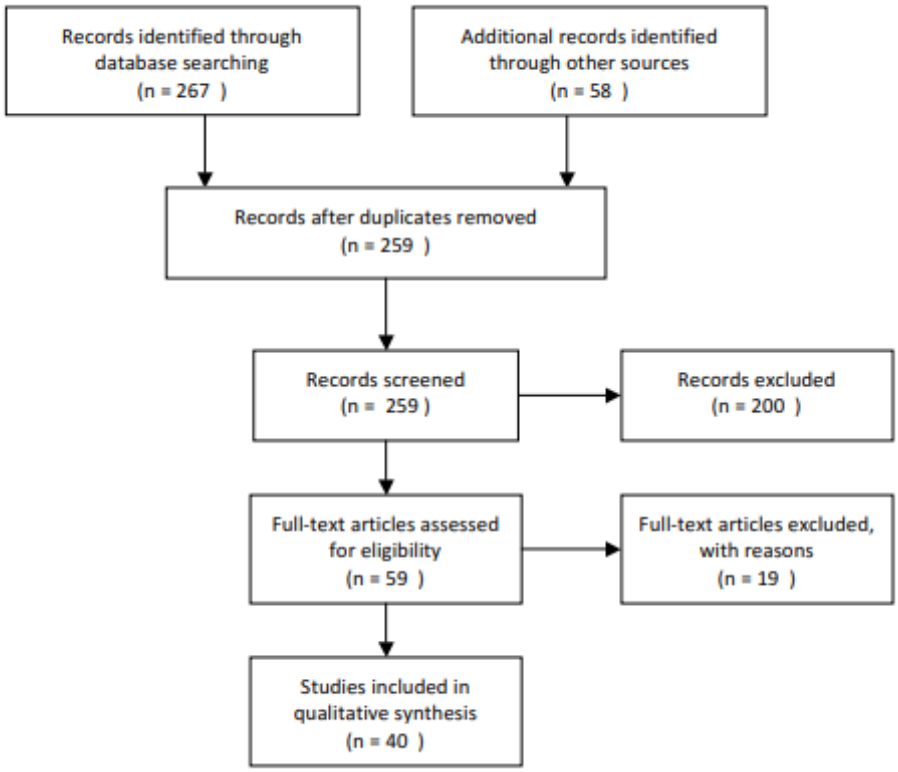
NS; Not stated, NR: Not reported, USD: United State Dollar, RCT: Randomized Control Trial, CEA: Cost-effectiveness analysis

Study	Score	Interpretation
Fitzgerald, 2018	8	Low Bias
Kypridemos, 2018	10	Low Bias
Adab, 2018	9	Low Bias
Nuijten, 2018	7	Intermediate Bias
Borisenko, 2018	8	Low Bias
Stam-Slob, 2018	7	Intermediate Bias
Gc V 2017	10	Low Bias
Panca, 2018	10	Low Bias
Gray et al, 2018	7	Intermediate Bias
Popp, 2018	8	Low Bias
Sanchez-Santos R, 2018	10	Low Bias
Mozaffarian, 2018	9	Low Bias
Gao, 2019	8	Low Bias
Chapman, 2018	10	Low Bias
McKnight, 2018	6	Intermediate Bias
Panca, 2018	5	Intermediate Bias
Sweeting, 2018	8	Low Bias
Gray, 2018	9	Low Bias
McRobbie, 2019	8	Low Bias
Högberg, 2018	6	Intermediate Bias
Basu, 2018	8	Low Bias
Cazarim, 2018	9	Low Bias
Korman, 2018	5	Intermediate Bias
Yang, 2017	10	Low Bias
Hunter, 2018	8	Low Bias
Conesa, 2018	7	Intermediate Bias
O.Borisenk, 2017	6	Intermediate Bias
Panca, 2018	10	Low Bias
Singh, 2018	7	Intermediate Bias
Alsumali, 2018	8	Low Bias

Lindholm, 2018	8	Low Bias
Smith, 2018	5	Intermediate Bias
Stuttard, 2018	9	Low Bias
Ewald, 2017	10	Low Bias
Beets, 2017	4	High Bias
Kim, 2018	3	High Bias
Mundt, 2018	7	Intermediate Bias
Xie, 2018	6	Intermediate Bias
Herrera, 2018	10	Low Bias

Table 2: Drummond's Quality assessment scoring.

Figure 1: PRISMA Flow Diagram



Graphical Abstract shows the role of Preventive measures