

# A systematic review of economic evaluations of screening programmes for cardiometabolic diseases

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# A systematic review of economic evaluations of screening programmes for cardiometabolic diseases

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**Background:** The early detection and adequate management of cardiometabolic diseases (CMD) is becoming a priority to prevent future health problems and related healthcare costs. **Aim:** This study systematically reviewed the economic evaluations of screening programmes for the early detection of persons at risk for CMD. **Methods:** A systematic review was conducted using MEDLINE, Web of Science, NHSEED and the CEA registry to identify relevant articles published between 1 January 2005 and 1 May 2015. Two reviewers independently selected articles, systematically extracted data and critically appraised the study quality using the Extended Consensus on Health Economic Criteria (CHEC) List. **Results:** From the initial 2820 studies identified, 17 were included. Six studies assessed whether screening would be cost-effective, seven aimed to determine the most efficient screening programme and four assessed the cost-effectiveness of existing programmes. There were 11 cost-utility analyses using quality-adjusted life years (QALYs) or disability-adjusted life years. Decision-analytic modelling (e.g. Markov model) was most frequently used ( $n=10$ ), followed by simulation models ( $n=4$ ), observational ( $n=2$ ) and trial-based ( $n=1$ ) studies. All studies assessing the cost per QALY gained of screening for cardiovascular diseases and diabetes mellitus ( $n=8$ ) were below a threshold of £30 000, while those assessing chronic kidney diseases ( $n=2$ ) were above the threshold. **Conclusions:** In view of the heterogeneity in study objectives, country setting, screening programmes, comparators, methodology and outcomes, it is not possible to make clear recommendations about the economic value of screening programmes for CMD. Developing further screening programmes and conducting thorough economic analysis, including usual care, is needed.

## Introduction

Cardiometabolic diseases (CMD) and cardiometabolic risk factors are emerging concepts that include conditions and factors associated with increased risk of cardiovascular disease (CVD). International working groups have defined cardiometabolic risk as an umbrella term for a comprehensive list of existing and emerging factors that predict CVD and/or diabetes mellitus (DM) and other related syndromes.<sup>1,2</sup> CMD, defined here in line with Badenboerk et al.<sup>3</sup> as CVD, DM and chronic kidney disease (CKD), are becoming a major public health problem worldwide. CMD are an increasing major cause of disability and a leading cause of death among older people.<sup>4</sup> Between 1990 and 2010, the total number of deaths caused by CVD increased by more than 25% and those of DM and CKD nearly doubled.<sup>5</sup> About 60% of deaths from these diseases are attributable to the combined effect of four cardiometabolic risk factors, including high blood pressure, high body mass index, high blood glucose and high serum cholesterol—factors that could be reduced through dietary, behavioural and pharmacological interventions.<sup>4</sup> Early detection and adequate management of persons at risk for CMD have, therefore, become a priority in seeking to prevent future health problems and related healthcare costs. Accordingly, in recent years, several programmes for the early detection of persons at risk for CMD have been developed and assessed in different countries.

In a world with limited healthcare resources, economic considerations play an increasingly important role in decision-making.<sup>6</sup> In addition to being effective in detecting people at risk and/or in

preventing diseases or deaths, screening programmes for detecting persons at risk for CMD should also be cost-effective. Given the increasing prevalence and burden of CMD, there is an increasing need for economic evaluations, and some cost-effectiveness analyses have thus been performed to assess the (potential) cost-effectiveness of programmes that aim toward the early detection of persons at risk for CMD diseases.

To our knowledge, there is no overview of these studies assessing the cost-effectiveness of screening programmes for the early detection of patients with CMD. Synthesizing and reviewing the recent literature is important in order to inform decision makers about the (potential) economic value of such programmes, to identify gaps in the current evidence and to inform the development of future economic evaluations. We, therefore, undertook a systematic review of the literature to identify recent economic evaluations of screening programmes for the early detection of persons at risk for CMD in high-income countries.

## Methods

### Literature search

A literature search was conducted following the Centre for Reviews and Dissemination guidelines.<sup>7</sup> Pubmed (Ovid), Web of Science, the National Health Service Economic Evaluation Database (NHSEED) and the Cost-Effectiveness Analysis (CEA) Registry were searched to identify economic evaluations of programmes for the early detection of CMD in high-income countries. We restricted our search to

articles published between 1 January 2005 and 1 May 2015, since prevalence, cost and screening programmes are changing rapidly over time.

The economic search in PubMed (Ovid) used the filter NHS QIS brief that was shown to have the best sensitivity by the Canadian Agency for Drugs and Technologies in Health.<sup>8,9</sup> This filter was combined with the following additional search words: 'Mass screening (MeSH) or Primary prevention (MeSH) or Diagnostic services (MeSH) or Early diagnosis (MeSH) or Risk assessment (MeSH)' AND 'Metabolic Syndrome X (MeSH) or Cardiovascular diseases (MeSH) or Diabetes Mellitus Type 2 (MeSH) or Kidney failure, Chronic (MeSH) or Renal insufficiency' (MeSH). Human and original research filters were also applied. The same search words were used in the other databases. In addition, the references of eligible studies were searched to identify additional papers (snowball method) and citation searching was conducted for the eligible studies (forward citation tracking).

### Selection of studies

The search strategy was conducted following the PICO method: population (general population/people at risk for CMD from a high-income country), intervention (screening programme), comparator (another screening programme or no programme) and outcomes (full economic evaluation defined as a comparison of at least two interventions in terms of costs and health outcomes).<sup>10</sup> Studies were included if they concerned screening for at least one cardiometabolic condition including CVD, DM and/or kidney disease. Titles and abstract were screened by two researchers (M.H., S.M.). Exclusion criteria were the following: not original research, not an economic evaluation, not CMD and no primary prevention. A full text review was then performed independently by two researchers (M.H. and C.W.; or M.H. and S.M.). At this stage, we included only studies that assessed screening programmes of CMD and we excluded studies from low and middle-income countries to focus on high-income countries. Disagreements were resolved by discussion in the working group with all authors.

### Data extraction and quality appraisal

Data were extracted using a standardized extraction table that was piloted for two articles. Data extraction was performed by one reviewer (C.W. or M.H. or S.M.) and independently checked for accuracy by a second researcher (C.W. or M.H. or S.M.). Disagreements were resolved by discussion with the project team. Several study characteristics were included: year of publication, country, perspective of the economic evaluation, type of economic evaluation, methodology/model, sensitivity/uncertainty analyses, time horizon, discount rates, cost categories, disease, population, comparators and results. Incremental cost-effectiveness ratios (ICERs) were reported. To enable comparability across studies, all incremental ratios were converted to US\$,<sup>11</sup> using appropriate Purchasing Power Parity (PPP) conversion rates and rated up to 2014 US\$ using Consumer Price Indices (Index, 2010 = 100).

To interpret the cost-effectiveness of an intervention, we need to compare the ICER to a cost-effectiveness threshold that represents the decision maker's willingness to pay per effect unit. However, several limitations have been raised concerning the use of a single threshold.<sup>12,13</sup> Therefore, most European countries do not use a threshold for cost-effectiveness, with the exception of the United Kingdom, which uses an ICER threshold range of £20 000–30 000 per QALY gained.<sup>13</sup> The discussion about the use and level of ICER threshold values is ongoing in the UK. Despite potential limitations inherent in the use of a cost-effectiveness threshold, for this study, we used the threshold of £30 000 (US \$42 900) in line with the threshold used by the National Institute for Clinical Excellence (NICE) in the UK.

Studies were then appraised for quality using the Extended Consensus on Health Economic Criteria (CHEC) List.<sup>14</sup> Twenty items were scored using: Yes (1), Suboptimal (0.5), No (0) and Not Applicable. The maximum score was 19 for trial-based economic evaluations and 20 for model-based evaluations. Two reviewers (M.H. and C.W.) independently appraised the studies and disagreements were resolved in a consensus meeting.

## Results

### Study selection process

Figure 1 shows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>15</sup> flow chart for the selection of studies. The database search identified 2820 articles, of which, 145 were excluded as duplicates. After screening by title and abstract, 76 studies were identified. At the first stage, studies were excluded mainly because they were not original research ( $n=345$ ), not an economic evaluation ( $n=1891$ ) or they did not concern CMD ( $n=61$ ) or early detection ( $n=302$ ). After reading the full text of the remaining 76 articles, six articles were excluded because they were not original studies. Ten other studies were not economic evaluations, 32 did not concern early detection of CMD and 11 were performed in developing countries. Therefore, 17 studies were included for the analysis.<sup>16–32</sup>

### Overview of included studies

The characteristics of included studies are reported in table 1. Three of the 17 studies<sup>19,21,24</sup> were conducted in the period 2005–9 and 14 between 2010 and May 2015. Most studies were conducted in Europe ( $n=10$ ). Four studies were conducted in North America (US or Canada)<sup>22,25,26,30</sup> and three in Australia.<sup>18,19,23</sup> Eleven studies performed a cost-utility analysis (CUA), and six studies conducted a cost-effectiveness analysis. Quality-adjusted life-years (QALY) were used in ten studies and disability-adjusted life years (DALY) were used in one study for the CUA.<sup>19</sup> Life years gained were used as an outcome in one study. Other outcomes included event-free time,<sup>16</sup> the number of diabetes cases,<sup>18</sup> the number of diabetes cases prevented,<sup>24</sup> the number of screenings needed to detect one case of DM<sup>20</sup> and the number of high risk persons identified.<sup>32</sup>

Model-based economic evaluations were used in 10 studies,<sup>17,19,21,23,24,26–30</sup> of which eight applied a Markov model. Four studies used simulation models such as life tables modelling,<sup>31,32</sup> microsimulation<sup>22</sup> or the Archimedes model.<sup>25</sup> Two studies used observational data<sup>16,18</sup> and a trial-based economic evaluation was conducted in one study.<sup>20</sup> Most studies used a healthcare (payer) perspective ( $n=13$ ). Only one study reported using a societal perspective<sup>27</sup> and one study used a combination of healthcare and societal perspectives.<sup>24</sup> All studies included direct medical costs; two studies additionally analysed direct non-medical costs.<sup>24,27</sup> Of the two studies with stated societal perspectives, only one also incorporated indirect costs.<sup>24</sup> Twelve studies considered a lifetime (or long) time horizon. Two studies used a time horizon shorter than 5 years<sup>16,24</sup> and two studies<sup>18,20</sup> did not use a time horizon (since they focused on number of cases detected). All but one study<sup>20</sup> reported details on conducted sensitivity and uncertainty analyses. Fifteen studies carried out deterministic sensitivity analyses, six studies probabilistic sensitivity analyses and two studies used bootstrapping to determine the uncertainty of their results.

### Results of included studies

Table 2 presents characteristics of the studied population, the interventions and comparator, and the main results of the articles. Most studies compared a screening programme to no screening/usual

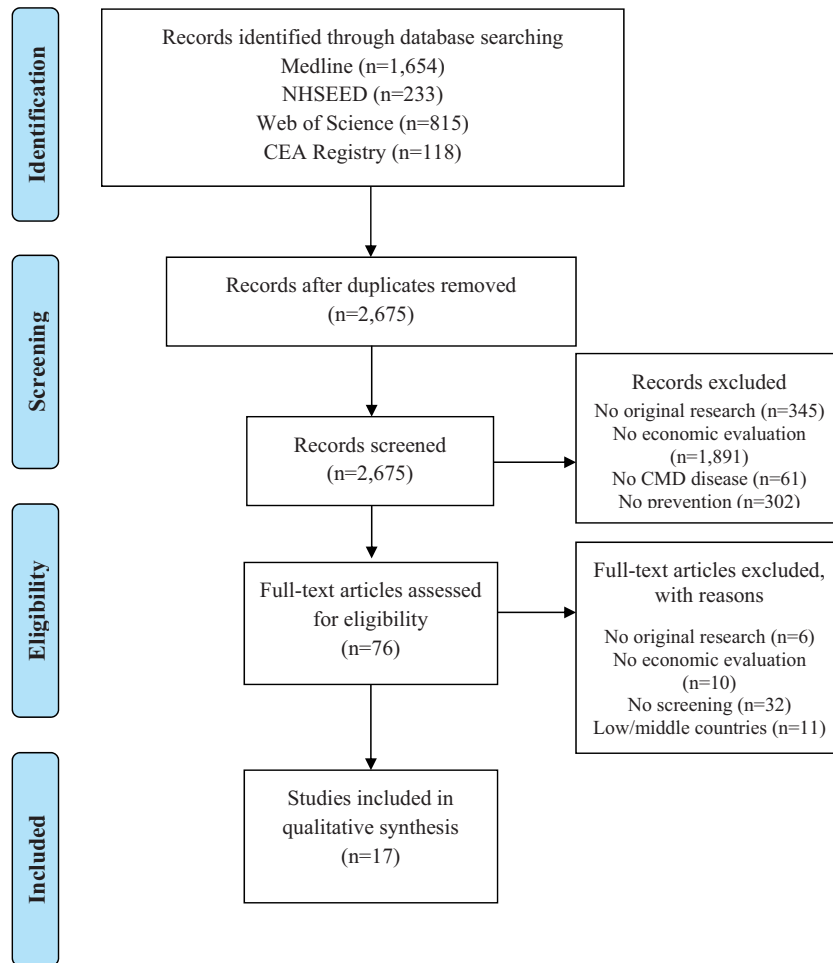


Figure 1 Literature search PRISMA flow chart

care. Different study aims were investigated. First, six studies aimed at assessing whether early detection (followed by management) of CMD can be cost-effective.<sup>17,19,22,26–28</sup> Second, seven studies aimed to determine the most efficient screening programme<sup>18,20,21,23,25,31,32</sup>; of these, three studies assessed only the screening procedure without any management intervention.<sup>18,20,32</sup> Some of these studies specifically aimed to determine the optimal screening age<sup>25</sup> or the cost-effectiveness of mass versus targeted screening.<sup>20,32</sup> Ten studies were concerned with universal screening, five studies with targeted screening (of the high-risk population), one with opportunistic screening and one combined universal and targeted screening. Third, four studies estimated the cost-effectiveness of existing programmes for detecting CMD.<sup>16,24,29,30</sup> Different study populations were also investigated. Nine studies assessed the cost-effectiveness of the early detection of DM,<sup>18–21,24,25,27,28,30</sup> while four concerned CVD or chronic heart disease (CHD),<sup>16,29,31,32</sup> two CKD<sup>22,26</sup> and two combined screening for several diseases.<sup>17,23</sup> Two studies included usual care while 15 compared the intervention with no screening.

All ICERs of the interventions (expressed in costs [2014 US\$] per outcome) are presented in table 2. The early detection of CMD provided generally better economic results in the population at high risk<sup>16,20,32</sup> or with opportunistic screening,<sup>20,31</sup> although results can differ between gender and age groups.<sup>25,27</sup> In addition, figure 2 presents the ICERs for all studies ( $n=10$ ) that used QALYs as the outcome measure for estimating the cost-effectiveness of the early detection of CMD. All ICERs of early detection programmes for CVD and DM were below a threshold of US \$42 900 (equivalent to £30 000) per QALY gained.<sup>21,23,25,27,28,31</sup> The two studies<sup>22,26</sup>

assessing the cost-effectiveness of the early detection of CKD were above a threshold of US \$42 900 per QALY gained. Among the ten studies assessing the cost per QALY gained, only two studies compared universal screening with usual care.<sup>17,23</sup>

### Quality appraisal of included studies

In table 2, the total score per study can be found. The average score was 15.76 (maximum of 20), ranging from 10.50 to 18.50. In addition, Supplementary File 1 shows, for each item of the CHEC checklist, the proportion of studies with score of 1, 0.5 or 0. The economic study design was appropriate in most studies, with the exception of one study that did not include an appropriate comparison and outcome. However, only eight studies correctly reported the structural assumption and validation of the model. In five studies, competing alternatives are not clearly described and a well-defined research question is not posed in an answerable form. Furthermore, the description of the study population was not optimal in six studies, while only nine studies used an appropriate time horizon (i.e. lifetime horizon). The identification, measurement and valuation of costs as well as measurement of outcomes are generally appropriate, although some studies (between three and four per item) did not provide sufficient explanation regarding these components. Overall, an appropriate incremental analysis of costs and outcomes of alternatives was performed in the studies (12 out of 16 potential studies), and sensitivity analyses were conducted in most studies ( $n=16$ ). The conclusions follow from the data reported in all studies. However, generalizability was addressed satisfactorily in only three studies.

**Table 1** Characteristics of economic evaluations for screening programmes for cardiometabolic diseases

| Author, year                    | Disease      | Analysis | Perspective                | Country     | Time horizon | Discount rates (cost, outcome) | Outcome  | Method/Model            | Sensitivity analysis/uncertainty assessment |
|---------------------------------|--------------|----------|----------------------------|-------------|--------------|--------------------------------|--|-------------------------|---|
| <i>Diabetes mellitus Type 2</i> |              |          |                            |             |              |                                |  |                         |   |
| Icks (2007) <sup>24</sup>       | DM           | CEA      | Health insurance, societal | Germany     | 3 yr         | 0%, 0%                         | Diabetes cases prevented                         | Decision analytic model | U, P  |
| Colaguri (2008) <sup>19</sup>   | DM           | CUA      | NR                         | Australia   | 10 yr        | 3%, 3%                         | DALY   | Decision analytic model | U   |
| Gillies (2008) <sup>21</sup>    | DM           | CUA      | NR                         | UK          | Lifetime     | 3.5%, 3.5%                     | QALY   | Markov                  | U   |
| Dalsgaard (2010) <sup>20</sup>  | DM           | CEA      | Healthcare                 | Denmark     | No           | NR                             | Number needed to screen to detect one case of DM | Trial-based             | NR  |
| Kahn (2010) <sup>25</sup>       | DM           | CUA      | Healthcare                 | US          | Lifetime     | 3%, 3%                         | QALY   | Archimedes model        | U   |
| Schaufier (2010) <sup>28</sup>  | DM           | CUA      | Health insurance           | Germany     | Lifetime     | 5%, 0%                         | QALY   | Markov                  | U   |
| Chen (2011) <sup>18</sup>       | DM           | CEA      | Healthcare                 | Australia   | No           | NA                             | Case of prevalent or incident diabetes           | Epidemiological         | U, B  |
| Neumann (2011) <sup>27</sup>    | DM           | CUA      | Societal                   | Germany     | Lifetime     | 3%, 3%                         | QALY   | Markov                  | U   |
| Sullivan (2011) <sup>30</sup>   | DM           | CUA      | Payer                      | US          | 10y          | 3%, 3%                         | QALY   | Markov                  | U, P  |
| <i>Cardiovascular disease</i>   |              |          |                            |             |              |                                |  |                         |   |
| Lawson (2010) <sup>32</sup>     | CVD          | CEA      | NR                         | Scotland    | Lifetime     | NR                             | High-risk person identified                      | Simulation model        | E, T  |
| van Gils (2011) <sup>31</sup>   | CVD          | CUA      | Healthcare                 | Netherlands | Lifetime     | 4%, 1.5%                       | QALY   | Simulation model        | P   |
| Sovic (2013) <sup>29</sup>      | CVD          | CUA      | Health insurance           | Poland      | 10 y         | 5%, 3.5%                       | QALY   | Markov                  | U   |
| <i>Chronic kidney disease</i>   |              |          |                            |             |              |                                |  |                         |   |
| Hoerger (2010) <sup>22</sup>    | CKD          | CUA      | Healthcare                 | US          | lifetime     | 3%, 3%                         | QALY   | Microsimulation         | U   |
| Manns (2010) <sup>26</sup>      | CKD          | CUA      | Healthcare                 | Canada      | Lifetime     | 5%, 5%                         | QALY   | Markov                  | P   |
| <i>Chronic heart disease</i>    |              |          |                            |             |              |                                |  |                         |   |
| Aljutaili (2014) <sup>16</sup>  | CHD          | CEA      | Healthcare                 | Germany     | Maximum 4y   | 5%, 5%                         | Event-free time                                  | Observational           | U, B  |
| <i>Multiple disease areas</i>   |              |          |                            |             |              |                                |  |                         |   |
| Howard (2010) <sup>23</sup>     | DM, HT & CKD | CUA      | Healthcare                 | Australia   | lifetime     | 5%, 5%                         | QALY   | Markov                  | U, P  |
| Boersma (2010) <sup>17</sup>    | CVD, CKD     | CEA      | Healthcare                 | Netherlands | 8y           | 4%, 1.5%                       | LY   | Markov                  | U, M, P                                     |

B, bootstrapping; CHD, chronic heart disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DALY, disability-adjusted life-years; DM, diabetes mellitus Type 2; E, analysis of extremes; GP, general practitioner; HT, hypertension; LY, life-years; M, multivariate sensitivity analysis; P, probabilistic sensitivity analysis; QALY, quality-adjusted life-years; T, threshold analysis; U, univariate sensitivity analysis; y, years. NA, not applicable; NR, not reported.

Table 2 Results of economic evaluations for screening programmes for cardiometabolic diseases

| Author, year  | Disease | Population  | Screening type | Screening/intervention  | Control                    | Cost categories   | Currency price, year | Results (base case)  | CHEC score |
|---|---------|---|----------------|---|----------------------------|---|----------------------|--|------------|
| <i>Diabetes mellitus Type 2</i><br>Licks (2007) <sup>24</sup> | DM      | 60–74yr (BMI > 24 and pre-diabetes status)  | Targeted       | Education, screening and prevention by either lifestyle intervention or metformin   | No screening               | Direct medical (intervention; practitioner, oral glucose tolerance test, visits with GP, diabetologist and diabetes educator), direct non-medical (education of healthcare staff; patient time), indirect (patient time, time of healthcare professional) | €2004                | US \$37 810 per case prevented for lifestyle vs. no intervention (societal) Metformin dominated  | 14         |
| Colagiuri (2008) <sup>19</sup>                                | DM      | 55–74 year and high risk 45–54 year (obesity, hypertension, family history of DM) | Targeted       | Screening and prevention by lifestyle activity  | No screening               | Direct medical (intervention; GP, specialist and visits to other healthcare professionals, in-hospital costs, prescription medication, diabetes-related supplies)   | AUS \$2000           | US \$52 469/DALY   | 13.5       |
| Gillies (2008) <sup>21</sup>                                  | DM      | Hypothetical population aged 45 year  | Universal      | Screening for DM to enable early detection and treatment<br>Screening for DM and IGT and lifestyle intervention in IGT<br>Screening for DM and IGT and pharmacological treatment in IGT | No screening               | Direct medical (intervention; test, nurse cost, GP, dietician, group exercise session; pharmaceuticals, various treatment costs)  | UK £2006             | US \$29 085/QALY (screening for DM)<br>US \$12 830/QALY (for screening for DM and IGT followed by lifestyle intervention)<br>US \$14 436/QALY (for screening for DM and IGT followed by pharmacological treatment) | 16.5       |
| Dalsgaard (2010) <sup>20</sup>                                | DM      | High-risk aged 40–69 year   | Opportunistic  | Opportunistic screening direct<br>Opportunistic screening subsequent  | Mail-distributed screening | Direct medical (intervention; invitation letter, consultations including blood glucose, blood test, laboratory cost)  | €NR                  | Mail distributed: US \$1449/case<br>Direct: US \$968/case<br>Subsequent: US \$996/case subsequent  | 10.5       |

(continued)

Table 2 Continued

| Author, year                   | Disease | Population                             | Screening type | Screening/intervention   | Control                    | Cost categories  | Currency price, year | Results (base case)  | CHEC score |
|--------------------------------|---------|--|----------------|--|----------------------------|--|----------------------|--|------------|
| Kahn (2010) <sup>25</sup>      | DM      | Simulation of individuals aged 30 year | Universal      | 8 screening strategies differing in age at initiation and frequency  | No screening               | Direct medical (intervention; screening, diagnosis treatment, monitoring costs of Type 2 diabetes and complications/coronary artery disease, stroke/hypertension/hyperlipidaemia/congestive heart failure, emergency visits, office visits/admissions, and procedures) | US \$2006            | US \$12 355/QALY starting at 30 year repeated every 3 year.<br>US \$18 228/QALY starting at 45 year repeated every 1 year.<br>US \$11 437/QALY starting at 45 year repeated every 3 year<br>US \$11 502/QALY starting at 45 year repeated every 5 year<br>US \$30 251/QALY starting at 60 year repeated every 3 year | 16         |
| Schaufier (2010) <sup>28</sup> | DM      | 35–75 year                             | Universal      | Screening followed by lifestyle intervention<br>Screening followed by metformin treatment  | Usual care                 | Direct medical (intervention; oral glucose test, diagnosis verification, type 2 DM costs without complications, DM standard therapy, various treatment costs)  | €2006                | US \$789/QALY lifestyle intervention vs. usual care<br>US\$456/QALY metformin vs. usual care   | 18         |
| Chen (2011) <sup>18</sup>      | DM      | > 25 year                              | Universal      | 4 screening strategies   | NA                         | Direct medical (intervention; GP consultation, fasting plasma glucose test, diabetes prevention-lifestyle modification programme)  | AUS \$2009           | Australian Type 2 Diabetes Risk Assessment Tool (AUSDRISK1) lower costs per cases of diabetes prevented  | 14         |
| Neumann (2011) <sup>27</sup>   | DM      | Aged 30 year or 50 year                | Universal      | Screening followed by inclusion in a structured programme aimed at lifestyle change (motivational analysis, exercise programmes and dietary counselling) and follow-up mentoring | No screening, no treatment | Direct medical (intervention folders, course and follow-up monitoring, healthcare costs of various states), direct non-medical (transportation)  | €2007                | US \$34 580/QALY in men aged 30 year<br>US \$20 761/QALY in men aged 50 year<br>US \$37 854/QALY in men aged 70 year<br>US \$43 159/QALY in women aged 30 year<br>US \$29 154/QALY in women aged 50 year<br>US \$26 705/QALY in women aged 70 year   | 18         |
| Sullivan (2011) <sup>30</sup>  | DM      | NR                                     | Universal      | Screening with impaired fasted glucose (IFG) & PreDx Diabetes Risk Score (DRS)<br>Screening with IFG only  | No screening               | Direct medical (intervention; DRS test, annual screening for diabetes, annual direct medical costs for diabetic/non-diabetic population)   | US \$2007            | US \$19 527/QALY for IFG + DRS vs. no screening  | 16         |

(continued)

Table 2 Continued

| Author, year  | Disease | Population  | Screening type     | Screening/intervention   | Control                            | Cost categories  | Currency price, year | Results (base case)   | CHEC score |
|---|---------|---|--------------------|--|------------------------------------|--|----------------------|---|------------|
| <i>Cardiovascular disease</i><br>Lawson (2010) <sup>32</sup>  | CVD     | 40–74 year  | Universal/targeted | Mass-screening of individuals in deprived communities<br>Targeted screening of individuals with a family history<br>Targeted screening of individuals in deprived communities or with a family history<br>Targeted screening of individuals with a family history and living in deprived communities | No screening                       | Direct medical (intervention); costs of contacting people and arranging appointments, costs of screening appointment, laboratory costs of testing, cost of follow-up appointment                                   | £2008                | US \$336/case identified by mass screening<br>US \$150/case identified in living in deprived communities<br>US \$137/case identified in individuals with family history<br>US \$90/case identified in individuals with family history and living in deprived communities<br>US \$137/case identified in individuals with family history or living in deprived communities<br>Between US \$10 016 and US \$15 595/QALY | 15         |
| van Gils (2011) <sup>31</sup>                                 | CVD     | Simulated individuals from Dutch population aged 45–75 year | Opportunistic      | Opportunistic screening followed by polypill   | Usual care                         | Direct medical (intervention); GP visit, laboratory testing, medication, drug delivery; adverse event  | €NR                  | US \$11 650/QALY for men<br>US \$49 086 for women   | 17         |
| Sovic (2013) <sup>29</sup>                                    | CVD     | High risk patients age 57 year                              | Targeted           | Risk assessment and nurse-led CVD primary prevention programme   | No risk assessment (control group) | Direct medical (intervention); training for nurses/GP time, phone calls, questionnaires, blood glucose/blood lipid tests, printed material programme, medication, cost of usual care, various disease states/death | PLN 2010             | US \$85 799/QALY vs. no screening<br>US \$170 422/QALY vs. usual care   | 17.5       |
| <i>Chronic kidney disease</i><br>Hoerger (2010) <sup>22</sup> | CKD     | Hypothetical population aged 50–90 year                     | Universal          | Microalbuminuria screening followed by pharmacological treatment   | Usual care                         | Direct medical (intervention); screening, diagnosis cost, specialist follow-up, GP, drug therapy, general medical costs, stage 5/end-stage renal disease costs)  | US \$2006            | US \$85 799/QALY vs. no screening<br>US \$170 422/QALY vs. usual care   | 17.5       |

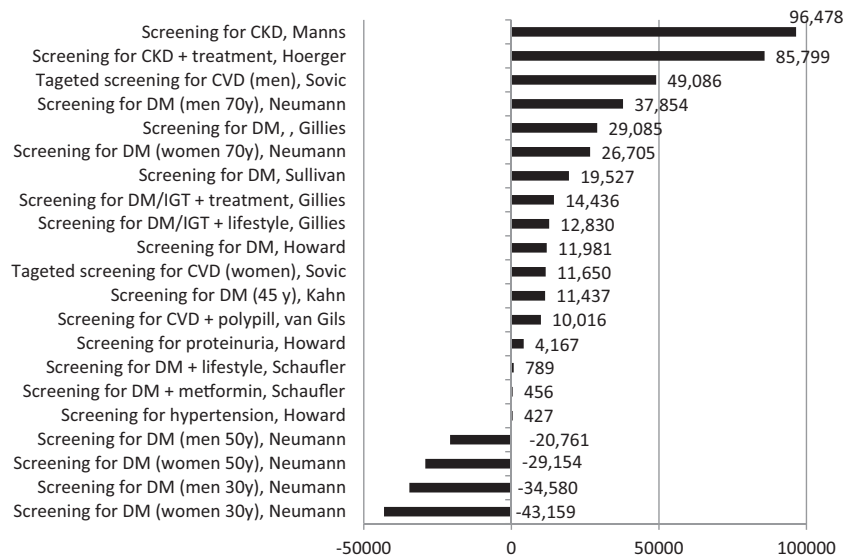
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Table 2 Continued

| Author, year   | Disease      | Population                | Screening type | Screening/intervention  | Control                        | Cost categories  | Currency price, year | Results (base case)  | CHEC score |
|--|--------------|---------------------------|----------------|---|--------------------------------|--|----------------------|--|------------|
| Manns (2010) <sup>26</sup>                                     | CKD          | Individual cohort         | Universal      | Population-based screening  | No screening                   | Direct medical (intervention; screening, specialist visit, testing, radiological studies, biopsy/pathology, medication/agents, multidisciplinary clinic)                                       | CA \$2009            | US \$96 478/QALY   | 18.5       |
| <i>Chronic heart disease</i><br>Aljutaili (2014) <sup>16</sup> | CHD          | Subjects age over 45 year | Targeted       | Individualised prevention programme: screening for CHD, risk factor assessment, early detection and secondary prevention of CHD                 | No screening (matching groups) | Direct medical (intervention; hospital costs, pharmaceutical costs, physician costs, other costs, e.g. physiotherapy)  | €2010                | US \$28 516 per event-free year (high risk)<br>US \$71 385 (medium-risk group)<br>US \$253 865 (low-risk group)<br>US \$36 904 in the group with CHD | 13         |
| <i>Multiple disease areas</i><br>Howard (2010) <sup>23</sup>   | DM, HT & CKD | 50–69 year                | Universal      | Screening for and intensive treatment of diabetes, hypertension and proteinuria   | Usual care                     | Direct medical (intervention; screening tests; treatment interventions, e.g. including drug costs, consultation visits various specialists, diagnostic test, dialysis costs, transplant costs) | AUS \$2008           | US \$11 981/QALY for DM<br>US \$427/QALY for hypertension<br>US \$4167/QALY for proteinuria in diabetics   | 17         |
| Boersma (2010) <sup>17</sup>                                   | CVD, CKD     | 28–75 year                | Universal      | Pre-screening of urinary albumin concentration for further urinary albumin excretion and treatment with angiotensin-converting enzyme inhibitor | No screening<br>No treatment   | Direct medical (intervention; costs of screening/pre-screening, treatment costs including drug costs and primary care costs, hospitalisation costs, dialysis costs)                            | €2008                | €22 000/LYG  | 16.5       |

CHD, chronic heart disease; CKD, chronic kidney disease; CVD, cardiovascular disease; HT, hypertension; NA, not applicable; NR, not report.



**Figure 2** Incremental cost per QALY gained (expressed in 2014 US\$) of economic evaluations for screening programmes of cardiometabolic diseases

## Discussion

This review identified 17 economic evaluations of screening programmes for CMD. Most studies compared a screening programme to no screening or usual care, with only one study comparing different screening programmes. The studies differed substantially in terms of study objectives, country setting, screening type and programmes, management components, methodology and study outcomes. In view of this heterogeneity, it is not yet possible to make clear recommendations about the economic value of early detection for CMD.

In this study, we focused on studies that included early detection of CMD. Studies that assessed only the economic value of interventions for managing persons at risk for CMD without early detection were, therefore, excluded from this review. Other studies have already reviewed the cost-effectiveness of management programmes for CMD, discussing the most efficient way to manage patients with some CMD.<sup>33–35</sup>

Based on our review and reported CUAs, it seems at first glance that the early detection of CMD, especially for DM and CVD, seems to represent good value for money using the NICE threshold for cost-effectiveness, while early detection for CKD does not seem to be cost-effective. However, the economic value could depend on the screening type and programme (an opportunistic programme appears to be more cost-effective), the management of the intervention, target population and comparator. Most CUA studies compared the programme with no screening/treatment and not to usual care as would be optimal for policy decisions. Using no screening/treatment as comparator could lead to overrating the economic value, as usual care is associated with better outcomes than no treatment. Furthermore, the number of undetected patients has diminished over time because physicians have become more alert to detecting undiagnosed patients and persons at risk for DM and CMD in their daily practice.<sup>36</sup> This may imply that the economic value of screening for new cases will decline. Designing and assessing further programmes for early detection and adequate management are, therefore, needed and would require a thorough economic analysis including a fair comparison with usual care. Some programmes are already in development such as the INTEGRATE study that aims to assess the (cost-)effectiveness of a CMD prevention programme coupled with an individualized lifestyle intervention.<sup>3</sup> Looking at the methodological quality of economic evaluations, additional points for improvement can be suggested.

Future economic evaluations should include a societal perspective, a long-term follow up and use QALY as outcome as long as no other and better measurements exists, and usual care should be included as comparator. Further studies should also better describe the structural assumptions and validation methods of the model, the population and comparator, while the generalizability of the findings should be discussed in the discussion. We also observed very few trials data, and studies were mainly model-based economic evaluation or simulation models. More well-designed trials on the effect of screening programmes would be required to adequately assess the health benefits of such programmes. Further, we did not identify any study that assessed the economic and outcomes implications of an intervention on all CMD conditions at one time.

It should also be noted that despite QALYs being the preferred outcome for economic evaluation, there is some controversy on the use of QALY, and several agencies, such as the Institute for Quality and Efficiency in Health Care (IQWiG) in Germany, do not consider QALYs in their assessment methods.<sup>37,38</sup> Recently, a European study even suggested that the QALY multiplicative model is an invalid measure, which could explain why costs per QALY gained estimates may vary greatly, leading to inconsistent recommendations relevant to providing access to innovative medicines and health technologies.<sup>39</sup>

There are some potential limitations to our study. First, we included research published in English and did not look at grey literature. In addition, since prevalence, cost and screening programmes are changing rapidly, we restricted our search to the last decade and to articles published after 2005. It could, therefore, be possible that we missed some studies, although that should not alter our conclusion. Finally, we also excluded studies from low and middle-income countries. Given different prevalence and healthcare costs, our findings may, therefore, not be generalizable to developing countries. In addition, the transferability of some countries is very uncertain, since usual care could differ widely between countries and, therefore, impact the cost-effectiveness of programmes.

In conclusion, this review identified different studies that assessed the cost-effectiveness of screening programmes for CMD and aimed to determine the most efficient screening programmes. CUAs suggest that screening programmes for DM and CVD could represent especially good value for money, while early detection for CKD seems not to be cost-effective. Unfortunately, CUAs mainly compared the screening programme to no screening/

treatment and not to usual care. In addition, opportunistic screening is associated with better economic outcomes.

There is, however, a huge heterogeneity in study objectives, country setting, screening type and programmes, comparators, methodology and study outcomes. Although methodological alignment is necessary, and pivots on the use of published guidelines in order to increase comparability, it is nevertheless challenging to formulate clear and uniform policy recommendations about the economic value of the early detection of CMD across countries, given the heterogeneity of health systems among countries.

## Supplementary data

Supplementary data are available at *EURPUB* online.

*Conflicts of interest:* None declared.

### Key points

- In view of the heterogeneity in study objectives, country setting, screening types and programmes, comparators, methodology and outcomes, it is not possible to make clear recommendations about the economic value of early detection for cardiometabolic diseases.
- All studies ( $n=8$ ) assessing the cost per QALY gained of early detection for cardiovascular diseases and diabetes mellitus were below a threshold of £30 000, while those assessing chronic kidney diseases ( $n=2$ ) were above £30 000.
- Developing further screening programmes for the early detection of cardiometabolic diseases and conducting thorough economic analysis which includes usual care is needed in the future.

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## Association between unmet healthcare needs and health-related quality of life: a longitudinal study

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**Background:** As life expectancy has increased overall, health-related quality of life is now more important than ever. This is especially relevant in countries such as South Korea that are concerned about unmet healthcare needs and health-related quality of life (HRQoL). Thus, we investigated the relationship between unmet healthcare needs and HRQoL in the general population. **Methods:** We used data from the 2011 to 2013 Korea Health Panel Survey, which included data from 8150 baseline participants of 19 years of age or older. We measured HRQoL using the EQ-5D and EQ-VAS indices. In addition, we used generalized estimating equations to perform a longitudinal regression analysis. **Results:** Approximately 13.1% of the participants ( $n=1068$ ) experienced unmet healthcare needs. Individuals with unmet healthcare needs due to economic hardship tended to have lower values than those without unmet healthcare needs for EQ-5D and EQ-VAS indices (EQ-5D:  $-2.688$ ,  $P < 0.0001$ ; EQ-VAS:  $-5.256$ ,  $P < 0.0001$ ). Additionally, when stratified by gender, both male and female subjects who had unmet healthcare needs and low economic status had a drastic decrease in HRQoL regardless of the reasons for their unmet healthcare needs. **Conclusions:** Unmet healthcare needs influences HRQoL, which was more pronounced in economically vulnerable groups. Thus, interventions to address HRQoL problems should focus on implementing a guarantee of healthcare services for economically vulnerable groups.

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## Introduction

The importance of life satisfaction in the public health field has become more prominent; we are living in a ‘homo hundred’ era, meaning that humans are now living up to 100 years of age. As life expectancy increases, health-related quality of life (HRQoL) has become an important focus for researchers and policy-makers.<sup>1</sup> Notably, this concept is especially relevant in countries such as South Korea that have concerns about health-related satisfaction. In Korea, subjective health satisfaction was lowest among the Organization for Economic Cooperation and Development (OECD) countries. According to the OECD report, the proportion of Korean adults who deemed their health condition as good or better than good dropped from 44.8% in 2009 to 35.1% in 2013, which was about half of the OECD average of 69.2%.<sup>2</sup> It is indicated that Korean population faces a lower HRQoL. Hence, it is necessary to approach health-related life satisfaction issues in terms of

promotion and identification of the factors that influence HRQoL in Korea.

HRQoL has been studied as an outcome in a variety of populations and settings.<sup>3</sup> Previous studies performed to clarify the factors affecting HRQoL have generally considered relevant physical function (overall physical health, physical functioning, pain, and fatigue) and disease-specific conditions (e.g., cancer, chronic disease).<sup>4–8</sup> Furthermore, socio-economic status has been identified as a significant factor affecting HRQoL.<sup>9</sup> Meanwhile, it is necessary to view HRQoL in terms of diverse perspective because HRQoL is a multi-dimensional concept that includes complex domains related to physical, mental, emotional and social functioning.<sup>10,11</sup> In particular, considering that few studies reported that unmet health care needs impacts HRQoL<sup>12–14</sup> and that unmet healthcare needs issues had become a growing concern to public health in Korea,<sup>15,16</sup> we focused on HRQoL related to unmet healthcare needs.