Chapter 2  Cost-effectiveness research on preventive interventions: a survey of the publications in 2008

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ABSTRACT

Background
In recent years the literature regarding the cost-effectiveness of disease prevention and health promotion has grown exponentially. Aim of this study is to investigate: (i) how many and what type of economic evaluations have been published in 2008 (ii) the diseases or health problems (WHO-ICD-10 chapters) the economic evaluations of preventive interventions focus on, in relation to the global burden of disease (iii) the cost-effectiveness of these interventions.

Methods
Literature study of economic evaluations on preventive interventions in PubMed and Scopus.

Results
In 2008, 232 economic evaluations of preventive interventions have been published. 75% (n=175) of these studies used costs per (Quality Adjusted) Life Year gained as outcome measure. Most economic evaluations focus on the prevention of infectious diseases (31,5%, n=73) and cancers (21%,n=49) Infectious diseases are responsible for the highest global burden of disease (19,8%), followed by mental and behaviour disorders (11,7%). Of the included economic evaluations, 80% remained below a threshold of €50.000 and 60% below €20.000 per (QA)LY.

Conclusion
This study shows that many economic evaluations of preventive interventions use a generic outcome measure. This adds to the comparability of different studies on the cost-effectiveness of prevention. Although the focus of published economic evaluations in general corresponds well with those diseases that cause a large share of
the world’s burden of disease, mental and behavioural diseases and diseases of the respiratory system remain underrepresented. Finally, it appears that the vast majority of published economic evaluations of preventive measures show favourable cost-effectiveness levels.
Introduction
Prevention is a comprehensive concept that can be distinguished into three forms of preventive actions: health protection, health promotion and disease prevention. Health protection interventions reduce health risks by changing the physical or social environment. Health promotion interventions, including health education, frequently take the form of public information and lifestyle campaigns focused on the general population or certain population groups. Disease prevention concern actions to prevent the occurrence of a specific disease (e.g. by vaccination) or to detect (a predisposition towards) a disease in an early stage (screening)(Hollander et al., 2007). Scientific research and technological advance continuously generate new possibilities for prevention. This includes new preventive interventions as well as new developments in existing prevention. Before an intervention may be implemented, a firm evidence base for its effectiveness is needed. The effects of an intervention should be scientifically proven and clinically relevant. However, in light of increasing health care costs and limited resources, an intervention should not only be effective, but efficient (cost-effective) too. Nowadays, decision makers and policy makers require information about the effectiveness of an intervention in relation to its costs. The question to answer is: does the intervention provide good value for money? Economic evaluations provide the information to answer this question by comparing analysis of costs and effects of two or more interventions(Drummond et al., 2005).

In recent years the literature regarding the cost-effectiveness of disease prevention, health promotion and health protection has grown exponentially. The aim of the present study is to investigate: (i) how many and what type of economic evaluations have been published in 2008 (ii) the diseases or health problems (WHO-ICD-10 chapters) the economic evaluations of preventive interventions focus on, in relation to the global burden of disease (iii) the cost-effectiveness of these interventions.

Methods
Economic evaluations were identified by searching PubMed and Scopus. The search includes the keywords: ‘cost-effectiveness’, ‘cost-utility’, ‘prevention’, ‘health
promotion’, ‘health protection’ etc. (complete search in appendix 1). After reading the abstracts, the full cost-effectiveness analyses were selected, and classified according to the chapters of the WHO-ICD 10 of the diseases they focus on (WHO, 2007). Preventive interventions on smoking and alcohol abuse also have effects on COPD (smoking) and morbidity caused by accidents (alcohol). These interventions were not registered for example as prevention of COPD or travel accidents but as prevention of smoking or alcohol abuse and thus registered as prevention of mental and behavioral disorders, according to the International Statistical Classification of Diseases and Related Health Problems (WHO, 2007). Accordingly, obesity interventions were classified as prevention of endocrine, nutritional and metabolic diseases. In a next step, the proportion of economic evaluations focused on the prevention of diseases in the ICD-10 chapters was qualitatively compared with the proportion of global burden of disease in these chapters. We included only original full economic evaluations, which mean a comparison of two or more interventions with each other or with usual care. We did not perform a full quality check according to the guidelines of Drummond (Drummond & Jefferson, 1996). The following study characteristics were extracted: the type of intervention, the target group, the type of economic evaluation, and the base case incremental cost-effectiveness ratio (ICER). If economic evaluations present more than one base case scenario (e.g. for different target groups or age categories), all base case ICERs were included. The median value of selected ICERs was calculated. To include all studies in this calculation, a value of €0 was used for ‘dominant’ interventions, and a value of €200,000 was used for ‘dominated’ interventions. To be able to compare the outcomes (cost-effectiveness levels) of the economic evaluations with different base years and different currency units, all local currencies were first transferred to the Euro currency values of that time, following the advice of the Organization for Economic Co-operation and Development. Next, they were recalculated to 2008 values, using the price index of Statistics Netherlands (OECD, 2009; CBS, 2009).
Short explanation on economic evaluations

There are different forms of economic evaluations: cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA). These three approaches differ in the way in which effects of an intervention are measured. In a CEA, the effects are measured in the most appropriate natural or physical unit (e.g. cases prevented, or life years gained (LYG)). In a CUA, the effects of an intervention are measured in a generalized unit: the number of quality adjusted life years (QALY) gained or disability adjusted life years (DALY) avoided. In a CBA, all costs and effects of an intervention are measured in monetary units, including effects as life years gained and quality of life. The outcome of economic evaluations is expressed as a ratio of costs (C) and effects (E):

$$\frac{C_{\text{new}} - C_{\text{usual care}}}{E_{\text{new}} - E_{\text{usual care}}}$$

This ratio is called incremental cost-effectiveness ratio (ICER): the difference in costs between the new intervention and the comparator (i.e. usual care) is divided by the difference in effects between the new and comparator intervention. If a new intervention is more effective and less costly than the comparator, than the intervention is ‘dominant’ over the comparator. If a new intervention is less effective and more costly, than it is ‘dominated’ by the comparator (Drummond, 2005). In a situation where better effectiveness goes along with higher costs, or vice versa, where less effects comes with less costs, it is possible to calculate the ICER, the ratio of costs to effects. Once the ICER of a new intervention is calculated, the next question to answer is: when is an intervention considered to be cost-effective? In other words: when does an intervention present good value for money? The answer on this question depends on the cost-effectiveness threshold that is used. In the UK, for instance, the National Institute for Health and Clinical Excellence (NICE) uses a threshold value of £20,000-£30,000 (€27,000-€40,500) per QALY (Buxton, 2006). In the Netherlands a frequently cited threshold value is €20,000 per QALY (Pomp et al., 2007; van den
Berg et al., 2008). In the US $50,000 (€44,000) per QALY has been cited as an acceptable cut off value (Hirth et al., 2000).

*The global burden of disease*

One DALY can be thought of as one lost year of “healthy” life, and the burden of disease can be thought of as a measurement of the gap between current health status and an ideal situation where everyone lives into old age, free of disease and disability (WHO, 2008). The top ten of diseases with the greatest burden of disease, expressed in DALYs, in 2004 shows that infectious and parasitic diseases cause the largest burden of disease globally (figure 1). Mental- and behavioural disorders were second with 11.7 % of the total disease burden being caused by these diseases. External causes of morbidity and mortality, such as accidents and diseases of the respiratory system were situated on the third (10.4%) and the fourth place (10.3%), followed by diseases of the circulatory system (9.9%) (WHO, 2004).

**Results**

In the calendar year 2008 we identified 501 studies. After we read the abstracts we included 232 published original economic evaluations on preventive interventions. We excluded systematic reviews, meta-analyses, editorials and comments. Of the 232 economic evaluations, 116 studies were CUAs, and 44 were CEAs with outcome measure LYG. In 15 studies both QALY and LYG as outcome measure were presented. So, 75% ( n=175) of the included economic evaluations calculated the ICER in costs per (QA)LY gained. In 38 CEAs the outcome measure was ‘cases prevented’. Only 19 economic evaluations are CBAs (Table 1).

Figure 1 shows both the distribution of economic evaluations and of the global burden of disease among the ICD-10 chapters. Most economic evaluations focus on the prevention of infectious diseases (73), cancers (49), cardiovascular diseases (23) and mental- and behaviour disorders (16) and on diseases of the musculoskeletal system and connective tissue (15). Less evaluations are focused on endocrine, nutritional and metabolic diseases (11), pregnancy, childbirth and the puerperium (11), diseases of the
digestive system (6), diseases of the respiratory system (4) and congenital malformations, deformations and chromosomal abnormalities (3). Exploratory comparison with the distribution of the world’s burden of disease indicates that economic evaluations of interventions that prevent infectious diseases and cancers are overrepresented compared with the burden of disease in these chapters, and that economic evaluations on the prevention of mental- and behavioral disorders, diseases of the respiratory system, pregnancy, childbirth and the puerperium and external causes of morbidity and mortality are underrepresented in comparison with the burden of disease.

Figure 2. shows the distribution of incremental cost per (QA)LY gained. The 175 economic evaluations that calculated costs per (QA)LY gained, presented 267 base case ICERs. Of these 80% was below €50.000, 60% was even below €20.000, and 15% was dominant compared to usual care or no intervention. Only 4% interventions were evaluated as being dominated by the reference scenario. The calculated median value of these base case ICERs was €12.500.

Discussion

We identified a relatively large number of economic evaluations of preventive interventions that were published in 2008. The vast majority of these economic evaluations used a generalized outcome measure, like a QALY or LYG. In principle, this implies that different preventive interventions can be compared easily. The outcomes of these economic evaluations may help policy-makers to prioritize between different possibilities to spend their, usually restricted, budget.

With regard to our second question, comparison of economic evaluations of preventive interventions with global disease burden shows several interesting observations. First, of all WHO-ICD chapters, chapter 1 (certain infectious and parasitic diseases) was addressed relatively often in published economic evaluations, and these diseases also contribute the most to the global burden of disease. However, economic evaluations of the prevention of infectious diseases frequently focus on vaccination of certain diseases in the western world that does not cause much of the
global infectious disease burden. Infectious diseases that cause much burden in developing countries, such as malaria, were less frequently addressed in economic evaluations. In conclusion, vaccination against relatively infrequent infectious diseases in the developed world gets disproportional much attention in cost-effectiveness analyses. Furthermore, mental- and behavioral diseases rank second with regard to global burden of disease. Nevertheless, these diseases were the subject of only 7% of included economic evaluations. This might be related to the limited availability of effective preventive interventions in this area. In general, economic evaluations are being built on sound effectiveness data derived from intervention trials and hence, without such data, economic evaluation research is useless. Besides, the ICD chapter on mental and behavioral diseases also includes mental diseases caused by Parkinson disease, multiple sclerosis, Alzheimer and other dementias. For this particular field of neurological diseases, even fewer effective preventive interventions are available than for other mental illnesses.

The same applies to for external causes of morbidity and mortality, diseases of the respiratory system including asthma and COPD, for endocrine, nutritional and metabolic diseases: although the global disease burden is relatively high, few economic evaluations on effective preventive interventions are available. It is useful to invest in more research on cost-effective interventions to prevent the diseases in these chapters, not only because of their current burden but also because the prevalence of many of these diseases is expected to increase in the future. For instance, the prevalence of diabetes, a main disease in the chapter of endocrine, nutritional and metabolic diseases, is expected to increase sharply in the near future. In the Netherlands, an absolute increase from 740,000 patients in 2007 to 1,3 million patients in 2025 was recently predicted (Baan et al., 2009).

Most of the economic evaluations show the interventions to be cost-effective. Preventive interventions have a median cost-effectiveness ratio of €12,500 per (QA)LY. This rather favorable ratio raises the following question: does prevention, assuming favorable effectiveness, by definition provide good value for money?

However, here are some factors which should be considered and which could have
resulted in an unrealistically favorable cost-effectiveness ratio. First, publication bias is expected to play a role here, as studies reporting favorable cost-effectiveness ratios may be more easily published than studies demonstrating interventions not to be cost-effective at all. Second, it is also thinkable that most of the economic evaluations were conducted in the knowledge there will be a favorable outcome. Also assumptions of costs and effects made in economic evaluation can bias the outcome in a favorable direction (van Gils et al., 2009).

This study shows that many economic evaluations target on diseases which are not responsible for a great burden of disease. For policy makers it is important, taking into account the demographic developments, that more research is done on the (cost)-effectiveness of diseases with an (expected) great burden of disease.

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**References**


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Appendix

Figure 1. Percentage of economic evaluations and global burden of disease as classified in ICD-10 chapters
ICERs (QA)LYG

Figure 2. Frequency distribution of 267 ICERs: cost (10,000 Euro’s) / (QA)LY