Evidence-based guidelines, time-based health outcomes, and the Matthew effect

Marie-Louise Essink-Bot¹, Michelle E Kruijshaar¹, Jan J Barendregt¹,², Luc G A Bonneux³

Background: Cardiovascular risk management guidelines are ‘risk based’; health economists’ practice is ‘time based’. The ‘medical’ risk-based allocation model maximises numbers of deaths prevented by targeting subjects at high risk, for example, elderly and smokers. The time-based model maximises numbers of life years gained by treating the young and non-smokers, or ‘the one who has will be given more’ (Matthew 25:29). We explored practical consequences of risk- or time-based allocation. Methods: We used epidemiological modelling to generate semi-quantitative scenarios comparing the distributional effects of allocating a fixed number of prescriptions of a (hypothetical) preventive cardiovascular drug (‘CVStop’) either to avert the maximum number of deaths (risk-based) or to save the maximum number of life years (time based) in the male Dutch population. We subsequently asked 123 Dutch guideline developers which distribution they preferred. Results: Time- and risk-based allocations resulted in different distributions of the drug across the population. There were also differences in absolute numbers of life years gained and deaths averted, and in the distribution of these across the population. For example, risk-based allocation of ‘CVStop’ resulted in preferential treatment of elderly, leading to more deaths averted (mostly among 70 and above) but fewer life years gained, if compared with time-based allocation. The guideline developers experienced the choice dilemmas as difficult. No priority choice was dominant among the respondents. Conclusion: In evidence-based resource allocation the choice to save time or to avert deaths may introduce moral choices because of the various origins of increased disease risk. Evidence-based guideline development inevitably has moral implications.

Keywords: absolute risk, cardiovascular disease, ethics, evidence-based medicine, life years gained, practice guidelines, resource allocation

Resources in health care are limited, and many countries have adopted prescription guidelines for expensive preventive drugs that would benefit large populations. Guidelines for cardiovascular disease (CVD) prevention in most countries have been based on the reduction of absolute 10-year risks of coronary heart disease.¹⁻³ By targeting people at highest risk, health outcome benefit is intended to be maximised while keeping expenditure in check. Such a risk-based allocation model does not differentiate between prevention of a death at adult age or at old age; averting a death at age 35 is considered of the same importance as averting a death at age 80. The implicit value judgement is equivalence of deaths at any age.

Health economists have alternatively advocated maximisation of life years gained.⁴ This is in accordance with the principle of the British National Institute for Health and Clinical Excellence (NICE) to adopt the quality adjusted life year (QALY) as the principal measure of health outcome.⁵,⁶ Both life years gained and QALYS represent a time-based model for priority setting. A death prevented at a younger age yields more life years than a death prevented at old age, implying inequivalence of death at different ages. Time- and risk-based allocation models do not necessarily lead to the same results. Maximisation of life years gained may not be achieved by targeting people at highest risk of dying.⁷ Furthermore, the choice for either allocation model may cause ethical dilemmas because a high CVD risk can have different causes. Older people are at higher risk of CVD death, but they have a lower life expectancy. The same holds for smokers. A risk-based allocation model will prioritise treatment for elderly and smokers, whereas time-based allocation will earmark more budgets for younger persons and non-smokers. To explore how guideline developers deal with these dilemmas, we generated semi-quantitative scenarios comparing the different distributional effects of risk-based and time-based allocation, using epidemiological modelling. We then confronted a sample of Dutch guideline developers with these scenarios and asked them to express their choices. In this article, we present the scenarios because they illustrate the dilemmas associated with various causes of increased risk and reduced life expectancy: age, smoking, obesity and low-socio-economic status, and the results of the expert survey.

Design and methods

We used epidemiological modelling to generate semi-quantitative scenarios comparing the distributional effects of allocating 300,000 annual doses of a hypothetical preventive cardiovascular drug (‘CVStop’) in the male Dutch population, either to avert the maximum number of deaths (risk based) or to save the maximum number of life years (time based). CVStop was assumed to lower the risk of cardiovascular death by 30%, independent of the prior absolute risk. We estimated numbers of deaths averted and life years gained using life table analysis. The Dutch reference population was simulated by using the risk distributions from three Dutch population studies (ERGO, MORGEN, Globe) and predictive equations for...
cardiovascular death from the Framingham Heart study.\textsuperscript{9,10} The purpose of the modelling was to generate plausible choice scenarios for the internet survey (see below). Therefore, we did not estimate confidence intervals and used midpoint estimates only.

We presented the resulting scenarios in an interactive internet-based survey. Generally, the survey asked participants to choose explicitly between different scenarios for the distribution of 300 000 annual doses of the hypothetical drug ‘CVStop’ in the male Dutch population. After a general introduction, the survey described four choice dilemmas, relating to age, smoking, obesity, and socio-economic status, respectively. In the choice dilemma relating to age, a respondent was confronted with two different age distributions of treatment with CVStop. In the first, all men aged 35–80 years with an annual risk of cardiovascular death of \(\geq 1.4\%\) received treatment. In the second, only men aged 35–70 years, but with a lower annual risk of cardiovascular death of \(\geq 1.0\%\), received treatment. Numbers of averted deaths, the proportion of these among persons older than 70, and life years gained were specified for both scenarios. After expressing their preference for one of these scenarios, respondents were asked to specify the upper age limit for treatment they deemed acceptable. The internet survey then continued with similarly formatted choice dilemmas relating to smoking (respondents were asked to choose between four distributions by subsequent choices between two options at a time, and including an option ‘no choice’), obesity (three distributions), and socio-economic status (two distributions).

The internet programme provided standardised textual on line help on request.

A total of 123 medical experts involved in development of Dutch CVD practice guidelines were asked to complete the internet questionnaire. We chose for an internet-based questionnaire to facilitate the respondents, who could complete the survey at the time and place of their own choice, and because of the opportunities to provide direct feedback to each individual respondent: ‘Your choice will have the following consequences, is that what you want? If yes, please confirm; if not, please reconsider your choice.’

We received 32 completed and 6 partly completed surveys (total response: 38/123 = 31\%). Mean age of the respondents was 52 years (range 36–68 years), 80\% were male and 67\% were medical professionals. We asked an aselective sample of non-respondents for the main reasons for non-participation.

Ethics approval was not required for this study in the Dutch legal system because patients were not involved.

**Results**

**Age**

The risk of CVD increases with age. The explorative modelling illustrated that, given a fixed budget, we can choose to gain more life years by treating a younger population at a relatively low threshold for the risk of cardiovascular death. This requires an upper age limit for treatment. On the other hand, we can avert more deaths by extending the treatment to the elderly population. In the latter case we need to increase the risk threshold: for every elderly subject treated, a younger one cannot be treated. If the upper age limit for a preventive treatment is extended from, for example, age 70 to age 80, a concomitant raise of the risk threshold is needed to avoid running out of the budget.

We asked the participants to the internet survey to choose between two extreme scenarios for distribution of CVStop. In the first, 300 000 year doses were allocated to the male Dutch population between 35 and 70 years of age who had an absolute annual risk of cardiovascular death of \(\geq 1.0\%\). The 300 000 doses were estimated to prevent 1200 deaths and save 18 500 life years (about 15 life years gained per death averted).

In the second age scenario, the doses were allocated to Dutch men between ages 35 and 80 with a higher annual risk of CVD death of \(\geq 1.4\%\). In comparison with the first age scenario, the target population was increased with men between 70 and 80, and they were at higher risk. To stay within the budget, the number of eligible persons under 70 had to be reduced: the risk threshold for treatment had to be raised. The 300 000 doses of CVStop were estimated to prevent more deaths (1630) but save less life years (17 000; 11 years per death prevented).

In total, 24 (63\%) respondents in the internet survey favoured age scenario 1 and 14 respondents (37\%) chose age scenario 2. Though generally in favour of a time-based approach (age scenario 1), respondents were prepared to compromise: on average, an upper age limit of 74 was deemed acceptable. The large standard deviation of 5.5 years reflected the serious discordance of opinions in this matter.

**Smoking**

Smoking not only increases the risk of CVD death, but also of death from other causes. The epidemiological modelling showed, for example, that if 300 000 year doses of CVStop were allocated to Dutch males (smoking prevalence 35\%) between ages 35 and 70 with an annual CVD mortality risk \(\geq 1.0\%, 80\%\) of the subjects to get treatment would be smokers. Lowering the CVD mortality risk of smokers by treating them with CVStop was estimated to result in lower numbers of life years gained than treating non-smokers with the same CVD mortality risk, because smokers have a lower life expectancy.

Table 1 shows part of the smoking dilemma as it was presented to the guideline developers in the internet survey. Smoking-scenario 1 was in accordance with the cholesterol practice guideline in place in the Netherlands at the time of the survey (2003), in which smoking was regarded as an independent contributing factor to CVD risk. In smoking-scenario 2, the risk of smoking was excluded from the treatment indication, resulting in equal smoking prevalences in the treated group and in the general population. Smokers only received treatment in smoking-scenario 2 if their annual risk of CVD death exceeded the risk threshold because of other risk factors than smoking.

The majority of respondents to the internet survey favoured exclusion of smoking as a priority setting variable, in accordance with their preference for gaining life years in the age dilemma (table 1).

**Obesity**

The Dutch cardiovascular disease guideline in place in 2003 excluded obesity as a separate risk factor. However, because obesity is related to other risk factors (hypertension, diabetes) Dutch obese subjects in 2003 still had a higher chance of being treated than subjects of normal weight. In agreement with these practice guidelines, 17 respondents to the internet survey preferred exclusion of the additional risk imposed by obesity from prescription of CVStop. Six respondents would prefer to add obesity as a separate risk factor, implying maximisation of the numbers of averted deaths. On the other hand, 10 respondents preferred to go beyond exclusion of obesity as a risk factor from prescription guidelines for CVStop, by opting for correction of the classical risk factors for obesity (i.e., hypertension only contributes to the risk for the part that is not attributable to obesity). The majority of the respondents favouring exclusion of the additional risk imposed by obesity is consistent with a preference for saving life years and thus with
the response patterns in the choice dilemmas relating to age and smoking.

Socio-economic status

Lower socio-economic status (SES) is associated with a higher CVD risk and a lower life expectancy, partly due to a higher prevalence of life style determinants (e.g., smoking). Participants in the internet survey were provided with a fictitious example in which the population consisted of a high socio-economic class (20% of the population) and a low one. Maximising life years gained by distributing 300,000 doses of CVStop was estimated to result in 1200 life years gained, of which 1000 in the high socio-economic class and 200 in the low one (SES-scenario 1). Out of 33 respondents, 19 preferred this option. SES-scenario 2, representing maximal investment in health of the low socio-economic class (300 life years gained in this group and 0 in the high socio-economic class), was preferred by 7 respondents. The remaining 7 did not want to make a choice. In response to a separate question, respondents were prepared to give up 2.7 days of the 12 days’ total gain in life expectancy of the population to invest in reducing the health gap between the two socio-economic classes.

Discussion

We illustrated by explorative epidemiological modelling that the choice of the measure of health benefit (averted deaths or life years gained) in evidence-based resource allocation has practical consequences. Maximising the number of averted deaths (risk-based) leads to allocation of a CVD preventive drug to subjects with the highest risk, that is, elderly, smokers, obese persons, and subjects of low SES. Maximising life years gained by distributing 300,000 doses of CVStop was estimated to result in 1200 life years gained, of which 1000 in the high socio-economic class and 200 in the low one (SES-scenario 1). Out of 33 respondents, 19 preferred this option. SES-scenario 2, representing maximal investment in health of the low socio-economic class (300 life years gained in this group and 0 in the high socio-economic class), was preferred by 7 respondents. The remaining 7 did not want to make a choice. In response to a separate question, respondents were prepared to give up 2.7 days of the 12 days’ total gain in life expectancy of the population to invest in reducing the health gap between the two socio-economic classes.

Conclusion

Even evidence-based allocation of expensive therapies can lead to differential distributions, depending on the choice between events prevented or time gained as health outcome. The choice for either one introduces difficult moral choices because of the variety of origins of increased disease risk. It is important to be aware of the nature and size of the ethical distributional dilemmas that are inevitable in evidence-based guideline development.

Acknowledgements

The Netherlands Organization for Health Research and Development (Zorg Onderzoek Nederland) financially supported the study, grant number 14900.0003. The authors were granted the right of independent publishing of the results. The work presented in this paper was presented by Dr Kruijshaar at the second Annual Meeting of the Health Technology Assessment International Society, Rome, Italy, 20–22 June 2005, and by Dr Essink at the Annual Conference of the European Society for Medical Decision Making at Birmingham, UK, 12 and 13 June 2006. We thank the anonymous reviewer for most helpful comments on a previous version.
**Key points**

- Maximisation of life years gained (time based) does not lead to the maximum number of deaths prevented (risk based) in cardiovascular disease prevention.
- These (different) health outcomes are reached through directing preventive treatment at different target groups in the population.
- Risk-based allocation favours subjects with the highest risk, that is, elderly; smokers; obese persons; and the lower socio-economic class.
- Time-based resource allocation widens health gaps between population groups determined by age, smoking behaviour, body weight, and socio-economic class.
- Guideline developers need to be aware of the nature and size of the inevitable ethical distributive dilemmas in evidence-based resource allocation.

**References**


Received 25 May 2006, accepted 29 August 2006