International Journal of Cardiology 176 (2014) 980–987

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Is it cost-effective to use a test to decide which individuals with an intermediate cardiovascular disease risk would benefit from statin treatment?

L.T. Burgers [a,b,*,1], S.T. Nauta [c,1], J.W. Deckers [c,1], J.L. Severens [a,b,1], W.K. Redekop [a,b,1]

[a] Institute for Medical Technology Assessment, Erasmus University Rotterdam, Rotterdam, Netherlands
[b] Institute of Health Policy & Management, Erasmus University Rotterdam, Rotterdam, Netherlands
[c] Department of Cardiology, Thorax Center, Erasmus Medical Center, Rotterdam, Netherlands

ARTICLE INFO

Article history:
Received 7 February 2014
Received in revised form 21 August 2014
Accepted 25 August 2014
Available online 2 September 2014

Keywords:
cost-effectiveness
test
prevention
cardiovascular disease
statins
decision modelling

ABSTRACT

Background: The 2012 European guidelines recommend statins for intermediate-risk individuals with elevated cholesterol levels. Improved discrimination of intermediate-risk individuals is needed to prevent both cardiovascular disease (CVD) and statin side-effects (e.g. myopathy) efficiently since only 3-15 in every 100 individuals actually experience a cardiovascular event in the next 10 years. We estimated the potential cost-effectiveness of a hypothetical test which helps to determine which individuals will benefit from statins.

Methods and results: Prognosis of different age- and gender-specific cohorts with an intermediate risk was simulated with a Markov model to estimate the potential costs and quality-adjusted life-years for four strategies: treat all with statins, treat none with statins, treat according to the European guidelines, or use a test to select individuals for statin treatment. The test-first strategy dominated the other strategies if the hypothetical test was 100% accurate and cost no more than €237. This strategy and the treat-all strategy were equally effective but the test generated lower costs by reducing statin usage and side-effects. The treat-none strategy was the least effective strategy. Threshold analyses show that the test must be highly accurate (especially sensitive) and inexpensive to be the most cost-effective strategy, since myopathy has a negligible impact on cost-effectiveness and statin costs are low.

Conclusion: Use of a highly accurate prognostic test could reduce overall CVD risk, frequency of drug side-effects and lifetime costs. However, no additional test would add usefully to risk prediction over SCORE when it does not satisfy the costs and accuracy requirements.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death across Europe and one of the major causes of disability [1]. Due to its high prevalence and morbidity rate, the economic burden of CVD is also substantial. Means to prevent CVD include lifestyle modification and medicines such as statins[2,3]. Although the annual costs of generic statins per individual are low, the budgetary impact of wide-scale statin usage is substantial due to the high prevalence and lifetime utilization. Since preventive statin treatment is associated with some risk, e.g. myopathy, the use of statins is not cost-effective in individuals at low risk[4]. In subjects at higher risk, however, the issue may be quite different.

Risk scores such as the Framingham risk score (FRS) [5] and the Systematic coronary risk evaluation (SCORE) method [6] are well-accepted tools to estimate the 10-year risk of (non-) fatal CVD and decide which individuals qualify for statin treatment. The most recent 2012 European guidelines[7] make use of the SCORE, which categorises individuals into three risk categories (low, intermediate, high). Individuals at intermediate risk with an elevated cholesterol level are recommended to receive statin therapy. However, only 3-15% of them actually develop a cardiovascular event. In theory, tests could potentially be used to reclassify some of these intermediate-risk individuals into a lower or higher risk category[8], with subsequent implications for their medical treatment. This would lead to better discrimination and thus a reduction in costs and an increase in effectiveness since cardiovascular events and unnecessary usage of statins would be prevented. However, the discriminative ability of biomarkers such as C-reactive protein beyond traditional markers (SCORE) is only modest[9]. The limited prognostic value of the risk scores and traditional markers as well as the rapid increase in the prevalence of CVD risk factors necessitates the development of other strategies to predict and prevent the development of CVD.

* Corresponding author at: Institute for Medical Technology Assessment, Erasmus University Rotterdam, Rotterdam, Netherlands. Tel.: +31 104088948; fax: +31 104089094.
E-mail address: burgers@bmg.eur.nl (L.T. Burgers).

[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

http://dx.doi.org/10.1016/j.ijcard.2014.08.134
0167-5273/

Therefore, the aim of our study was to use the 10 year SCORE risk to estimate the potential 10-year cost-effectiveness of a (theoretical) test compared with a treat-none strategy, treat-all strategy, and a strategy based on European guidelines. In addition, we examined the conditions (accuracy estimates and costs) under which the use of a novel test (e.g. biomarker) would be cost-effective.

2. Methods

The cost-effectiveness of a test was estimated for eight age- and gender-specific cohorts of individuals with an intermediate risk (3-15%) of developing a first-time CVD event in the next 10 years [7]. The SCORE risk equation was used to identify individuals with an intermediate risk based on age, gender, systolic blood pressure, total cholesterol and smoking status. SCORE risk estimates were multiplied by a factor of three to obtain the risks of non-fatal and fatal events, as proposed by the European Society of Cardiology (ESC) guidelines[7]. We subsequently modelled the prognosis of eight cohorts, defined by the SCORE, of men and women with an age of 50, 55, 60, and 65 years.

2.1. Strategies

We compared the costs and effectiveness of four strategies: 1) "treat-all" strategy, where all individuals receive statin treatment; 2) a "treat-none" strategy, where none of the individuals receive statin treatment, 3) a "guidelines" strategy, where individuals receive statin treatment according to the ESC guidelines on CVD prevention[7] (which recommend that statins should only be given to those with total cholesterol level ≥5 mmol/L and/or low-density lipoprotein cholesterol level ≥3 mmol/L) and 4) a "test-first" strategy, where statin treatment is recommended for individuals having a positive test result. A positive test result suggests that a first-time CVD event in the next 10 years will occur if statin treatment is not provided.

2.2. Model structure

For each strategy, the prognosis of a cohort of individuals for the next 10 years was modelled in a Markov model (Microsoft Excel™ 2010) with eight health states (Fig. 1). A time horizon of 10 years was chosen since the SCORE only provides an accurate estimate of 10-year risks. All individuals started in the "intermediate risk" state and annual transition probabilities determined the likelihood of moving to other health states (Table 1). Individuals experiencing a non-fatal CVD event (myocardial infarction (MI), stroke or revascularization) or a statin-induced non-fatal adverse event (myopathy) moved to the post-event states afterwards the event. Individuals experiencing cardiovascular or non-cardiovascular fatal events moved to the absorbing health states "cardiovascular death" and "non-cardiovascular death", respectively. In all strategies, individuals experiencing a cardiovascular event received statin treatment afterwards. Statin treatment was discontinued permanently if individuals developed myopathy and its discontinuation also meant loss of the protective effects of the statins.

2.3. Input parameters

A literature search using PubMed was performed to obtain input values. Table 1 shows the input parameters for the subgroup of men aged 65 years, illustrative for the eight cohorts that were modelled.

2.3.1. Risks

The risk of developing (non-) fatal CVD events (MI, stroke, angina-induced revascularization and cardiovascular death) was obtained from the SCORE chart by taking the average of all possible combinations with an intermediate risk in each gender- and age-specific cohort. Based on the randomized controlled trials (RCTs) included in the meta-analysis of Brugts et al. [3] we divided the individuals treated according to the guidelines into two groups: 1) individuals with elevated cholesterol levels, indicated for statin treatment and 2) individuals with normal cholesterol levels. We assumed that individuals with normal cholesterol levels had the lowest possible intermediate risk of CVD in their respective gender- and age-specific cohort (Appendix A). In our analyses, individuals with elevated cholesterol levels were assigned inherently higher risk than the average intermediate risk in the same gender- and age-specific cohort to ensure that the average risk remained unchanged when the two groups were combined. A meta-analysis [3], UK audit data [10], the FRS [5] and three RCTs [11–13] were used to estimate age- and gender-specific relative proportions of the CVD events. The annual probabilities of developing myopathy and (non-) fatal rhabdomyolysis caused by statins were based on Law et al. [14]. Mortality was based on national and international mortality statistics[10, 15–20].

The sensitivity and specificity of the hypothetical test were both assumed to be 100% in the base-case scenario and the impact of their values was explored through sensitivity analyses. Therefore, in the base-case scenario it is assumed that the test will discriminate absolutely and perfectly all individuals who will experience a cardiovascular event over the specified time period and those who will not.

2.3.2. Cost, treatment effectiveness and quality of life

The impact of changes in 10-year risks of CVD events was translated into costs and quality-adjusted life-years (QALY). Costs (2012 €) and QALYs were estimated from a health care sector perspective and discounted at 4% and 1.5%, respectively, in accordance

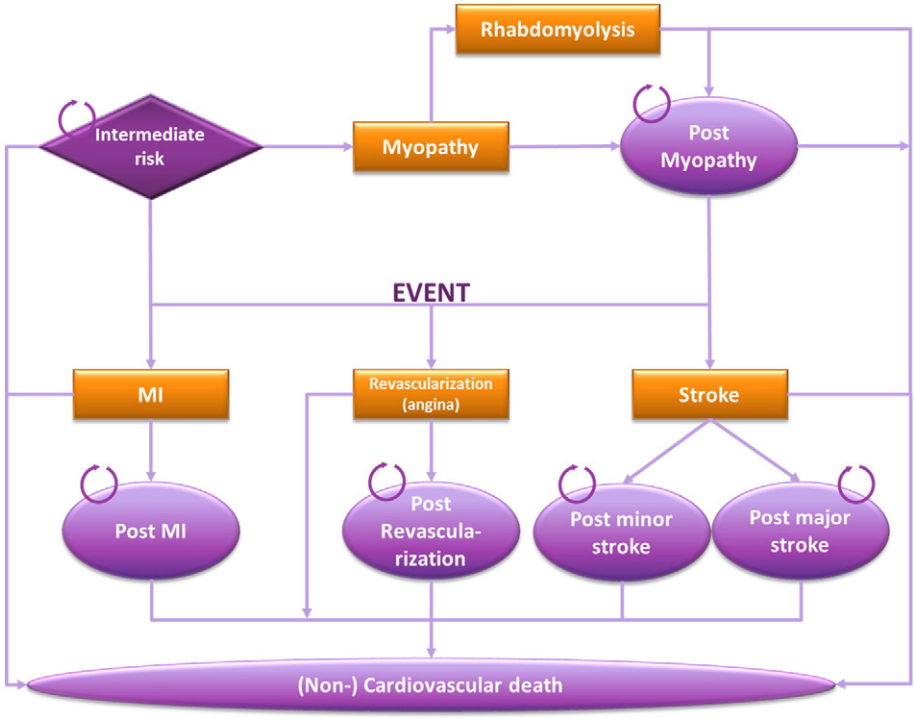

Fig. 1. Model structure*. *Cardiovascular death and non-cardiovascular death are presented as one state in this Figure. Rectangles are (non) cardiovascular events and ovals are disease states. MI, myocardial infarction.