



## Cost-effectiveness of PCSK9 inhibition in addition to standard lipid-lowering therapy in patients at high risk for vascular disease

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### ABSTRACT

**Background:** As proprotein convertase subtilisin-kexin type 9 (PCSK9) monoclonal antibodies are entering the market, we assessed the cost-effectiveness of PCSK9 inhibition added to standard lipid-lowering therapy in patient groups at high risk for major adverse cardiovascular events (MACE).

**Methods:** A lifetime Markov Model was designed to estimate healthcare costs, quality-adjusted life years (QALYs) and incremental cost-effectiveness ratios (ICERs) for PCSK9 inhibition added to standard therapy in patients with Familial Hypercholesterolemia (FH), patients with vascular disease at high MACE recurrence risk, and patients with vascular disease with diabetes mellitus. The balance between costs and health outcomes was established for a broad range of potential relative risk reductions and drug costs.

**Results:** The expected QALY gain per patient and ICER in the main scenario were 1.4 QALYs for €78,485/QALY gained in patients with FH, 0.22 QALYs for €176,735/QALY gained in those with vascular disease and a predicted risk of MACE  $\geq 30\%$  in 10 years, and 0.22 QALYs for €295,543/QALY gained in those with vascular disease and diabetes. Results were sensitive to assumptions on PCSK9 inhibitor treatment efficacy, and vascular event risks.

**Conclusion:** The costs and effects of PCSK9 inhibition added to standard lipid-lowering treatment in patient groups at high risk for MACE can be estimated and adapted to a specific clinical setting. PCSK9 inhibition could be cost-effective in patients with FH. In patients with vascular disease PCSK9 inhibition is less cost-effective, however, a price development may change clinical practice. This model may aid treatment and reimbursement decisions regarding PCSK9 inhibitors.

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### 1. Introduction

The burden of cardiovascular disease has decreased significantly in the past decades by the introduction of drugs that lower low-density lipoprotein cholesterol (LDL-c) [1]. Statins effectively lower LDL-c and risk of major adverse cardiovascular events (MACE), and addition of ezetimibe to a statin regimen may further reduce LDL-c and MACE risk [2]. However, some patients remain at high vascular risk because of uncontrolled LDL-c levels despite maximal lipid-lowering therapy [3]. Recently, monoclonal antibodies that bind to proprotein convertase subtilisin-kexin type 9 (PCSK9) have shown to lower LDL-c serum levels with 57% (95% confidence interval [CI] 54%–60%) compared to placebo

in patients with hypercholesterolemia when added to standard lipid-lowering treatment [4]. A recent large randomized trial revealed a 15% reduction with PCSK9 monoclonal antibodies on top of statin therapy on the incidence of MACE during a median follow-up duration of 2 years [5]. Combined secondary analyses on MACE of small clinical trials primarily evaluating the lipid-lowering effect of PCSK9 monoclonal antibodies revealed a relative risk reduction of 46% (95%CI 23%–62%) compared to standard lipid-lowering therapy [4,6,7]. PCSK9 monoclonal antibodies have been approved by the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) for treatment of hypercholesterolemia and are entering the market. Compared to other lipid-lowering drugs the price of PCSK9 monoclonal antibodies will be high which raises questions on cost-effectiveness [8]. In the present study we evaluated the cost-effectiveness of PCSK9 monoclonal antibodies for the treatment of hypercholesterolemia in addition to maximal lipid-lowering therapy in patients defined by the international guidelines being at (very) high risk for vascular disease, namely patients with Familial Hypercholesterolemia (FH) or clinically manifest vascular disease with or without diabetes [9,10]. In sensitivity analyses,

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effectiveness in terms of vascular risk reduction and drug costs are varied. The long-term effect of PCSK9 inhibitors on vascular events is still uncertain, and drug costs may differ between countries, between compounds and may change over time.

**2. Methods**

**2.1. Model structure**

A Markov model was designed to estimate costs, life years and quality-adjusted life years (QALYs) gained for PCSK9 inhibition in addition to standard lipid-lowering therapy for various patient groups at high risk for vascular disease (Fig. 1) [9,10]. These high risk groups were: 1) patients with familial hypercholesterolemia (FH) without a history of vascular disease, 2) patients with stable vascular disease and a 10-year recurrence MACE risk of  $\geq 20\%$  or  $\geq 30\%$ , and 3) stable vascular disease and type 2 diabetes. These groups partly overlap as patients with vascular disease and diabetes have a high recurrence MACE risk. Cost-effectiveness in patients with diabetes was assessed separately to account for diabetes treatment costs and the health impairment caused by diabetes. All patients started in the stable health phase at the left of the diagram. Each year a patient could transit to another state. After a vascular event the patient transitioned to the corresponding post-event state (myocardial infarction, stroke, revascularization or unstable angina). Multiple vascular events could occur during a lifetime. If patients died of any cause, they transitioned to the terminal 'death' health state.

**2.2. Model input**

**2.2.1. Event risks**

Model assumptions were made from a healthcare perspective in the Netherlands. Annual vascular event risks are presented in Supplementary Table 1. Event probabilities for patients with FH were based on observational Dutch multi-center studies [11–13]. Risk for recurrent events in FH patients was assumed to be 5 times higher than their primary event risk [12].

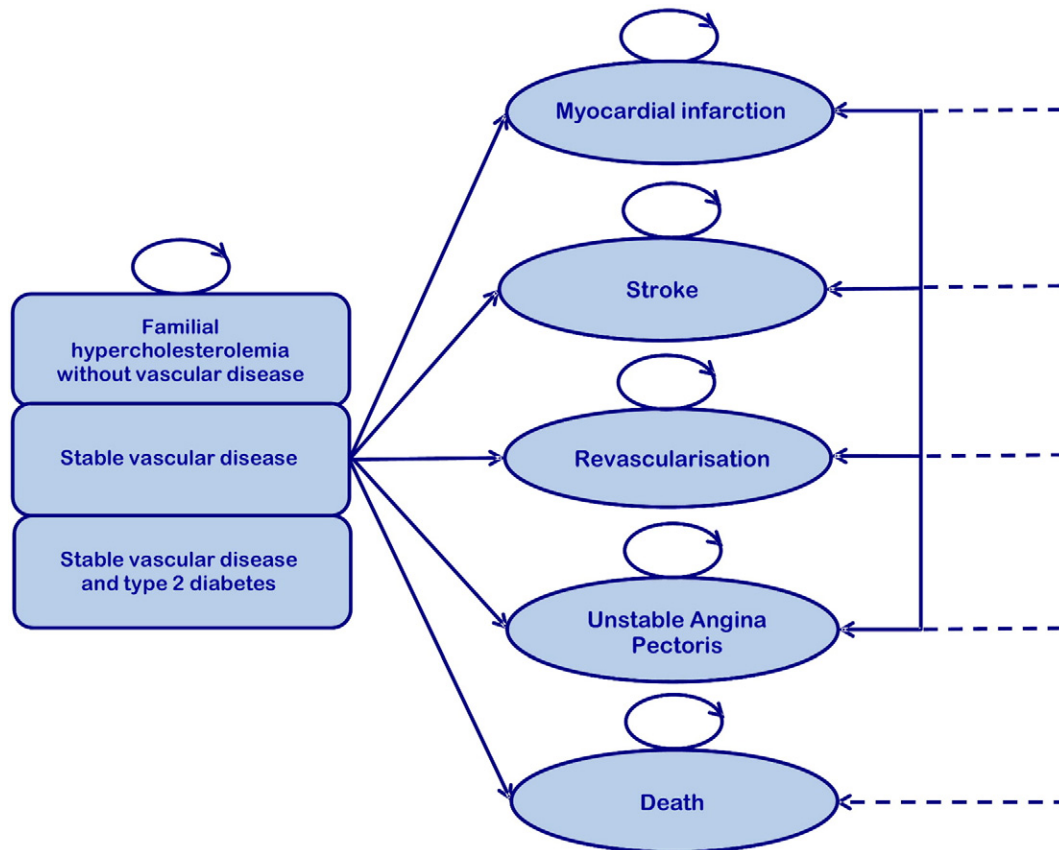
Event risks for a myocardial infarction, stroke or revascularization procedure in high risk patients with vascular disease and in patients with vascular disease and type 2 diabetes, were derived from the single-center prospective SMART (Secondary Manifestations of ARterial disease) cohort study (median follow-up duration 7 years).

Risk for unstable angina was 2.8 times higher than for a myocardial infarction [14]. A detailed description of the design of the SMART study conducted at the tertiary care hospital University Medical Center (UMC) Utrecht in the Netherlands has been published previously [15]. Study approval was obtained from the medical ethical committee and patients gave informed consent for participation in the SMART study. High risk was defined according to the World Health Organization as a predicted 10-year risk for MACE (myocardial infarction, stroke and cardiovascular mortality) recurrence  $\geq 20\%$  or  $\geq 30\%$  [16]. MACE recurrence risk was estimated using the SMART risk score, recently validated in multiple cohorts of patients with vascular disease at different locations [17,18]. Patients with vascular disease and diabetes had a median predicted 10-year MACE risk of 25% (interquartile range [IQR] 17–39%). In patients with vascular disease, the risk of a second event and third event was assumed to be equal.

Characteristics from the study populations on which model event risks were based are shown in Supplementary Table 2. Event risks increased with age, according to the Systemic Coronary Risk Evaluation (SCORE) chart for primary events and the SMART risk score for recurrent events [17,19]. The probability of death from any cause and the 1-year probability of death after a myocardial infarction or stroke were age-dependent and obtained from Dutch nationwide registries [14,20]. Mortality rates in Dutch males are comparable to other West-European countries, rates in Dutch females are slightly higher than in females from Mediterranean countries [21]. Moreover, the probability of death for a patient with vascular disease or diabetes was estimated by multiplying the probability of death for a person with the same age in the general population by a disease-specific mortality multiplier (Supplementary Table 1) [22,23].

**2.2.2. PCSK9 treatment effect**

The expected PCSK9 inhibitor relative treatment effect was based on the mean decrease in absolute LDL-c levels in trial populations [4,10,24]. Mean baseline LDL-c was 3.15 mmol/l, which was lowered with 48% (1.5 mmol/l) when PCSK9 inhibition was added to the combination of a statin and ezetimibe [4]. Assuming a hazard ratio (HR) for MACE of 0.79 per mmol/l absolute LDL-c reduction, the relative MACE risk reduction with PCSK9 inhibition added to statin and ezetimibe would be 30% ( $HR = 0.79^{1.5} = 0.70$ ) [1]. In additional scenario analyses, we modelled the PCSK9 inhibitor treatment effect for a lower or higher baseline LDL-c. For patients with vascular disease (and diabetes) we derived event risks from SMART patients in the lowest and the highest quartile of baseline LDL-c. The PCSK9 treatment effect for these patients was estimated as shown in the example above. Moreover, we estimated cost-effectiveness ratios based on the results from a recent clinical trial on the effect of PCSK9 inhibition on cardiovascular



**Fig. 1.** Markov model with health states (boxes) and possible transitions (arrows). Each year patients can transit to another health state or stay in their original health state. Patients could have multiple events during a lifetime as the model had matching post-event states.

outcomes [5]. Thereafter, the balance between costs and health outcomes was established for a broad range of potential PCSK9 inhibitor relative treatment effects.

### 2.2.3. Costs

The annual cost of standard lipid-lowering therapy was the mean cost in euros of the generic usual-dose statins plus ezetimibe once daily (Supplementary Table 3) [25]. Annual cost of PCSK9 inhibition was €6000 in the base case analysis based on estimated drug costs in different European countries [25,26]. These drug costs vary between countries and therefore the balance between costs and health outcomes was studied for a wide range of potential drug costs from €500 to €11,000 euro/year. Vascular event costs and post-event costs were obtained from observational studies and nationwide registries [27–31]. The cost of a revascularization procedure was a weighted mean for a percutaneous coronary intervention and a coronary artery bypass graft [32]. Annual costs for diabetes care were based on a recently performed cluster randomized trial in the Netherlands [33]. Annual pharmacy costs, laboratory costs for a lipid profile and one doctor's visit per year were included [34,35]. Costs were updated to 2014 with Dutch consumer price indices [36].

### 2.2.4. Health outcomes

Health outcomes were measured in mean life years and quality-adjusted life years (QALYs) per patient with and without PCSK9 inhibition. QALYs are the multiplication of the amount of life years a patient is in a certain health state and the utility belonging to that health condition. A utility is a value that scales the quality of life between 1 (perfect health) and 0 (death). A patient that lives for 10 years with a disease that has a utility of 0.8 attributes  $10 \times 0.8 = 8$  QALYs. Utilities for stable vascular disease, diabetes and post-event states were derived from the literature and adjusted for age (Supplementary Table 3) [37–39].

### 2.3. Analyses

A hypothetical cohort of 10,000 patients for each high risk group entered the Markov model. The model was run for the standard lipid-lowering treatment strategy and the strategy in which PCSK9 inhibition was added to the standard regimen. When starting in the stable health phase FH patients were on average 45 years of age, patients with stable vascular disease and  $\geq 20\%$  10-year MACE risk 67 years of age, those with stable vascular disease and  $\geq 30\%$  10-year MACE risk 70 years of age, and those with diabetes and stable vascular disease were on average 63 years of age [11,12,15,23]. Furthermore, we performed a sensitivity analysis in patients with vascular disease aged  $\leq 65$  years. The model was run for a lifetime horizon, i.e. until all patients had died. Event and drug costs, life years and QALYs were calculated for the different groups and treatment strategies. Incremental cost-effectiveness ratios (ICERs) were estimated by dividing the difference in costs by the difference in QALYs with and without PCSK9 inhibition. A discount rate of 3.0% was applied for both costs and health outcomes [40]. The analysis was repeated for different event probabilities, drug costs, event costs, PCSK9 inhibitor treatment efficacies, discount rates and mortality multipliers, adjusting one model assumption at a time (lower and upper bound from Supplementary Tables 1 and 3). In a probabilistic sensitivity analysis with Monte Carlo simulations (1000 times), all model assumptions were varied at the same time choosing random values from the beta distribution for event probabilities and utilities, the gamma distribution for costs and mortality multipliers and the lognormal distribution for the hazard ratio of PCSK9 inhibition versus standard lipid-lowering therapy. The chance that PCSK9 inhibition would be a cost-effective therapy was presented in a graph for different thresholds in euros willing to pay for an additional QALY.

All model assumptions and calculations can be found in the supplementary Excel file for transparency and to enable the reader to adapt them to another clinical setting.

## 3. Results

### 3.1. Incremental costs and effects for PCSK9 inhibitors in FH patients

PCSK9 inhibition yields 2.3 life years and 1.4 QALYs per patient with FH without vascular disease at baseline (mean age of 45 years) when added to standard lipid-lowering therapy (Table 1). Expected lifetime costs for PCSK9 inhibition in addition to standard lipid-lowering treatment are €108,414 per FH patient, resulting in an ICER of €78,485 euros per QALY gained.

The expected costs for one QALY gained are below €80,000 if the relative risk reduction with PCSK9 inhibition is  $\geq 30\%$ ,  $\geq 23\%$  or  $\geq 15\%$  for annual PCSK9 inhibitor treatment costs of €6000, €4500 or €3000 respectively (Fig. 2A–C). Assuming a relative risk reduction of 30%, the estimated costs for one QALY gained in patients with FH are below €80,000 for annual PCSK9 inhibitor drug costs  $\leq$ €6000, and below €20,000 for drug costs  $\leq$ €1500 (Fig. 3).

### 3.2. Incremental costs and effects for PCSK9 inhibitors in patients with vascular disease

For patients with vascular disease, 0.25 QALY may be saved with PCSK9 inhibition for those with  $\geq 20\%$  risk (mean age 67 years), and 0.22 QALY for those with  $\geq 30\%$  risk of MACE in 10 years (mean age 70 years). Expected incremental costs during a patient's lifetime are €47,799 for those with  $\geq 20\%$  risk, and €39,411 for those with  $\geq 30\%$  risk of MACE in 10 years. ICERs in patients with vascular disease are €193,726 euros per QALY gained for those with  $\geq 20\%$  risk, and €176,736 euros per QALY gained for those with  $\geq 30\%$  risk of MACE in 10 years.

For patients with vascular disease and  $\geq 30\%$  risk of MACE in 10 years, the ICER falls below €100,000/QALY if the relative risk reduction with PCSK9 inhibition is  $\geq 52\%$ ,  $\geq 40\%$  or  $\geq 27\%$  for annual PCSK9 inhibitor treatment costs of €6000, €4500 or €3000 respectively. Assuming a relative risk reduction of 30%, expected costs per QALY are below €100,000 if annual PCSK9 inhibitor treatment costs are  $\leq$ €3000, and  $\leq$ €3250 for patients with vascular disease and a 10-year MACE risk of  $\geq 20\%$ , and  $\geq 30\%$  respectively.

### 3.3. Incremental costs and effects for PCSK9 inhibitors in patients with diabetes

An estimated 0.22 QALY is saved with PCSK9 inhibitor treatment per patient with vascular disease and diabetes (mean age of 63 years). Predicted lifetime costs for PCSK9 inhibitor therapy are €63,489 per patient, resulting in an ICER of €295,543 per QALY gained.

For patients with vascular disease and diabetes, an ICER below €100,000/QALY would be achieved with a relative risk reduction  $\geq 85\%$ ,  $\geq 66\%$  or 47% for annual PCSK9 inhibitor treatment costs of €6000, €4500 or €3000 respectively. Assuming a relative risk reduction of 30%, annual PCSK9 inhibition treatment costs  $\leq$ €1750 result in an ICER below €100,000/QALY.

### 3.4. Incremental costs and effects for PCSK9 inhibitors in patients with vascular disease aged $\leq 65$ years

For patients aged  $\leq 65$  years, PCSK9 inhibition yields 0.53 QALY in those at  $\geq 20\%$  risk for MACE in 10 years (mean age 58 years), and 0.61 QALY per patient for those at  $\geq 30\%$  risk for MACE in 10 years (mean age 59 years). Estimated incremental costs during a patient's lifetime are €74,022 for those with  $\geq 20\%$  risk, and €71,859 for those with  $\geq 30\%$  risk of MACE in 10 years. ICERs in patients with vascular disease are €139,020 euros per QALY gained for those with  $\geq 20\%$  risk, and €117,288 euros per QALY gained for those with  $\geq 30\%$  risk of MACE in 10 years.

### 3.5. Scenario analyses

ICERs are most sensitive to assumptions on PCSK9 inhibitor treatment efficacy (Supplementary Fig. 1), which closely relates to the absolute LDL-c reduction. Assuming a 15% relative risk reduction in the incidence of MACE [5], 0.66 QALY is gained per patient with FH for €161,676/QALY, 0.11 QALY is gained per patient with vascular disease at  $\geq 30\%$  MACE recurrence risk for €359,778/QALY, and 0.11 QALY is gained per patient with vascular disease and diabetes for €600,038/QALY. Event probabilities and the annual costs of PCSK9 inhibitor treatment affect the results as well. In a scenario analysis with 50% lower vascular event probabilities, PCSK9 inhibition gains 1.6 life years and 0.9 QALY per FH patient, resulting in an ICER of €135,012 euros per QALY gained. If the mean age of patients with FH is increased to 60 years, approaching the mean age of patients with vascular disease, a mean of 1.0 QALY is gained per patient with PCSK9 inhibition for €80,782.

**Table 1**  
Main results for the different treatment strategies.

	Familial hypercholesterolemia		Vascular disease and 10-year MACE risk $\geq 20\%$		Vascular disease and 10-year MACE risk $\geq 30\%$		Vascular disease and diabetes	
	Standard therapy	PCSK9 inhibition	Standard therapy	PCSK9 inhibition	Standard therapy	PCSK9 inhibition	Standard therapy	PCSK9 inhibition
Costs per patient (€)								
Treatment	11,606	123,112	5087	52,684	4247	44,149	6155	63,489
Event and post-event care	13,858	10,766	22,030	22,232	21,085	20,593	46,404	54,155
Total	25,464	133,878	27,116	74,916	25,331	64,742	52,559	117,644
Expected age at death	73		76		78		76	
Life-years gained		2.3		0.36		0.32		0.40
QALYs gained		1.4		0.25		0.22		0.22
ICER (€/QALY)		78,485		193,726		176,735		295,543

Results of the probabilistic sensitivity analyses are presented in Supplementary Fig. 2. The probability that PCSK9 inhibition in addition to standard lipid-lowering therapy is cost-effective compared to standard lipid-lowering treatment alone is shown for various thresholds of willingness to pay in euros per QALY gained. For example, if one is willing to pay €100,000 per additional QALY, the chance that PCSK9 inhibition is a cost-effective strategy is 70% for patients with FH, 9% for patients with vascular disease and a 10-year MACE recurrence risk of  $\geq 30\%$  and 1% for patients with vascular disease and diabetes. Estimated mean QALY gain in the Monte Carlo simulations was 1.3 (95%CI 0.45–2.2) for patients with FH, 0.22 (95%CI 0.03–0.50) for patients with vascular disease at  $\geq 30\%$  10-year MACE risk and 0.22 (95%CI 0.02–0.50) for patients with vascular disease and diabetes.

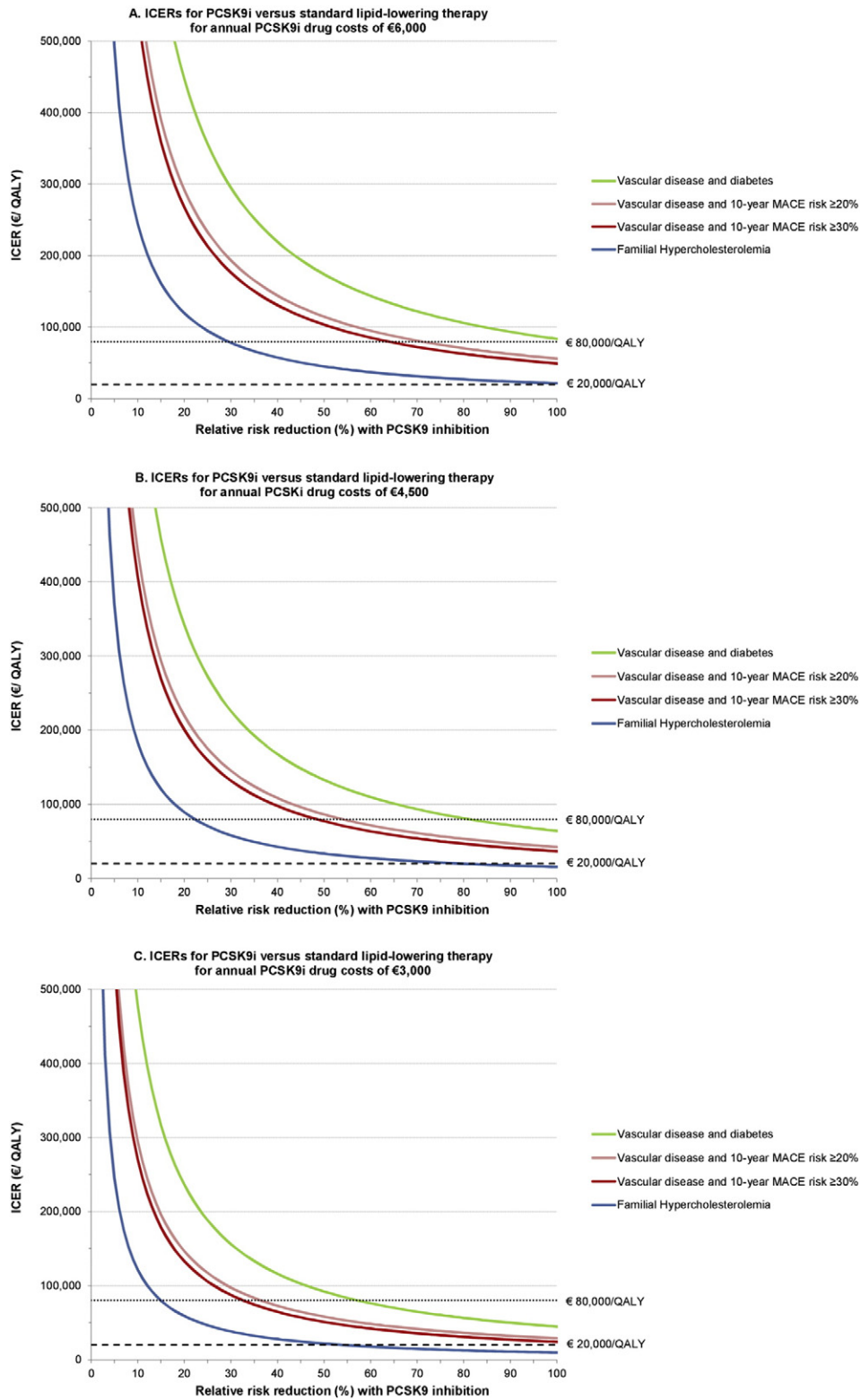
#### 4. Discussion

A lifetime model was developed to estimate expected costs and health outcomes for PCSK9 inhibition in addition to standard lipid-lowering treatment compared to standard lipid-lowering treatment alone in heterozygous FH patients, patients with vascular disease at high recurrence risk, and patients with vascular disease and diabetes. More health gain is expected with PCSK9 inhibition in patients with FH than in patients with vascular disease with and without diabetes. The balance between costs and health outcomes is most favorable for those with FH with an expected ICER of €78,485 (\$88,091) per QALY gained, compared to an ICER of €176,735 (\$198,411) per QALY gained for patients with vascular disease and a  $\geq 30\%$  risk of recurrent MACE in 10 years, and €295,543 (\$331,717) per QALY gained for patients with vascular disease and diabetes. ICERs were estimated for a wide range of possible relative risk reductions with PCSK9 inhibition and costs of these drugs, which shows that the ICER is likely to be  $\leq$ €100,000 per QALY in patients with FH compared to  $\geq$ €100,000 per QALY in high risk patients with vascular disease or vascular disease and diabetes. The supplementary material holds a file in which model assumptions can be adapted to a specific clinical setting and to change costs and effectiveness of PCSK9 inhibitor treatment.

Previous studies show a substantial reduction in LDL-c levels and MACE after 2 years by PCSK9 monoclonal antibodies in patients at high risk for vascular disease in addition to standard lipid-lowering treatment, strongly suggesting a beneficial effect of these drugs on vascular outcomes [5–7]. Two reports have been published recently for cost-effectiveness estimations of PCSK9 inhibition in the United States of America (USA) for patients with FH or vascular disease [41–43]. The Comparative Effectiveness Public Advisory Council-Institute for Clinical and Economic Review (CEPAC-ICER) concludes that while PCSK9 inhibitors are highly efficacious in lowering LDL-c and are likely to reduce MACE risk, cost-effectiveness ratios are above the current standards of dollars willing to pay per extra QALY in the USA [42,43]. They conclude that for the USA health care setting, a substantial price reduction to \$4536 would be necessary to meet a willingness to pay threshold of \$100,000/QALY [42]. We found a more

favorable cost-effectiveness ratio for European FH patients, which is to a great extent explained by lower mean drug costs in Europe (a scenario analysis with USA drug costs increased the ICER to  $\pm$ €200,000/QALY). Furthermore, event risks in the present study were higher as we also took revascularization procedures and angina pectoris into account. Another report written from a USA payer perspective concludes that PCSK9 inhibition in patients with FH or vascular disease may be cost-effective, with lower costs per QALY gained in patients with FH than in patients with vascular disease [41]. Recently, a cost-effectiveness analysis for the Norwegian situation found that PCSK9 inhibition would only be cost-effective for patients aged  $\geq 65$  years at very high risk and a history of myocardial infarction [44]. The Markov Model included pre- and post-health states for myocardial infarction and stroke. Revascularization procedures and heart failure were not modelled. The cost-effectiveness of secondary prevention was only modelled for patients with a history of myocardial infarction. The differing conclusion from the Norwegian study and the present study may be due to the differences in the Markov Model as revascularization, heart failure and stroke are costly events which incur a higher risk of both vascular death and death due to other causes. The authors from the Norwegian study note that with lower drug prices, PCSK9 inhibition may be more attractive for younger patients at high risk. This is in line with the present study which focuses on the European health care setting with many scenario analyses on possible treatment effects and costs of PCSK9 inhibitor treatment. There is quite some difference in cost-effectiveness between patient groups. Patients with FH have the highest QALY gain and the lowest costs per QALY gained. This could be partly, but not entirely due to the lower mean age of patients with FH compared to patients with clinically manifest vascular disease, with more potential life years to be saved in patients with FH. Their high overall QALY gain may further be explained by high LDL-c serum levels, even when treated with statins in combination with ezetimibe. Therefore, a larger LDL-c reduction can be achieved in FH patients. In patients with clinically manifest vascular disease with or without diabetes, the recurrent vascular risk is caused by various risk factors including LDL-c. Consequently, patients with clinically manifest vascular disease have a higher risk of death due to other causes than MACE which limits the health gain with PCSK9 inhibition. Vascular event probabilities were higher for patients with vascular disease and high LDL-c levels which resulted in a more beneficial cost-effectiveness ratio. However, the ICER in these patients was still  $\geq$ €100,000 per extra QALY.

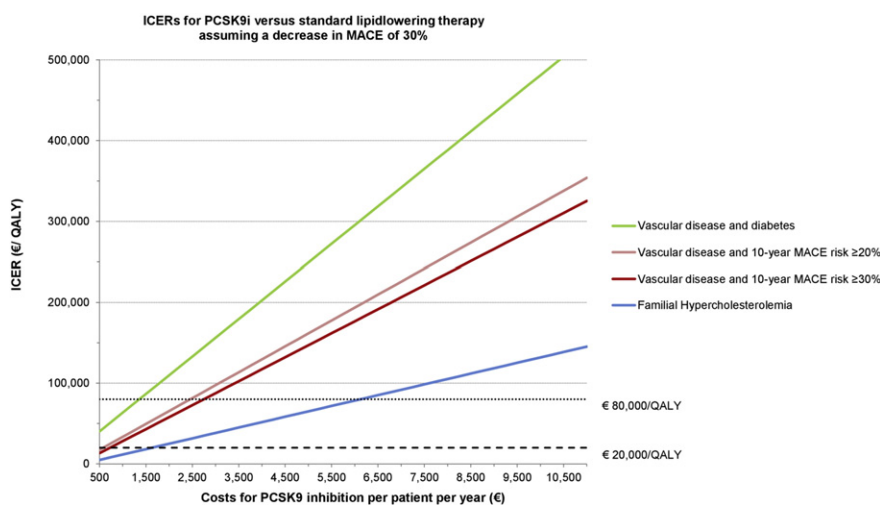
The Markov Model in this study was robust and representative for clinical practice. This is the first study to assess costs and health outcomes for patients in a European health care setting, and to select patients according to their predicted MACE risk. Moreover, extensive scenario analyses were performed, in particular for costs and effects of PCSK9 inhibitor treatment. There are several considerations that need to be addressed when interpreting the model results. The long-term relative effect of PCSK9 inhibition on MACE is unknown. Event probabilities in FH patients were mainly derived from older studies and might be



**Fig. 2.** Incremental cost-effectiveness ratios (ICERs) for PCSK9 inhibition versus standard lipid-lowering therapy for varying relative treatment effects of PCSK9 inhibitors. Annual costs of PCSK9 inhibition were assumed to be a) €6000 per patient, b) €4500 per patient or c) €3000 per patient. *PCSK9i* = *PCSK9 inhibition*.

lower in current times because of improved cardiovascular preventive strategies. Therefore, we performed a scenario analysis with 50% lower event probabilities, based on a recent study that assessed the effect of increased statin use on coronary artery disease and mortality in FH patients [45]. PCSK9 inhibitor treatment costs may decrease over time and are likely to drop after patent expiration. As we model lifelong

treatment with PCSK9 inhibition, lower treatment costs in the future would decrease the costs per QALY gained. Also, costs may differ between countries. We have not included possible costs or health impairment by any side effects of PCSK9 inhibitor treatment as there are no results of blinded long term follow-up trials yet. Quality of life was not lowered for subcutaneous injections with PCSK9 inhibitors,



**Fig. 3.** Incremental cost-effectiveness ratios (ICERs) for PCSK9 inhibition versus standard lipid-lowering therapy for varying annual costs of PCSK9 inhibition. The relative risk reduction with PCSK9 inhibition was assumed to be 30%.  $PCSK9i = PCSK9$  inhibition.

currently administered every 2 to 4 weeks. We assumed that standard lipid-lowering treatment consisted of a usual-dose statin and ezetimibe, as optimal therapy in those with refractory hypercholesterolemia should be a combination of the maximally tolerated statin dose and another lipid-lowering therapy [46]. Although some patients are not treated as such in the PCSK9 inhibitor trials and in clinical practice, this will not greatly impact the results as statins and ezetimibe are less costly than PCSK9 inhibitors.

## 5. Conclusions

We derived a model to estimate the costs and health outcomes of PCSK9 inhibition in addition to standard lipid-lowering treatment in different patient groups at high risk of vascular disease. The balance between costs and health outcomes was best for patients with FH. Depending on the drug price, and the willingness to pay per additional QALY, PCSK9 inhibition may be cost-effective for patients with FH. The cost-effectiveness ratio of PCSK9 inhibition is less favorable in patients with vascular disease at high risk for MACE or patients with vascular disease and diabetes. With current drug prices, the cost-effectiveness ratio is above an acceptable willingness to pay threshold in these patients. This model may be helpful in making decisions as to which patient groups are treated with PCSK9 inhibition to reduce the risk of (recurrent) vascular events, and to negotiate on pricing and reimbursement of these drugs.

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## Disclosures

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2017.10.080>.

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