Priority setting for research in healthcare: an application of value of information analysis to glycoprotein IIb/IIIa antagonists in non-ST elevation acute coronary syndrome. *Further information*

1. The disease area

Acute coronary syndrome (ACS) is a term that includes a range of patients with similar underlying pathology. At one end of the range are those patients with evidence of ST elevation on a resting electrocardiogram (ECG) who are eligible for treatment with thrombolysis and who may subsequently develop Q-wave on their ECG (i.e. full myocardial infarction (MI)). At the other are patients who are classified as having either unstable angina or non Q-wave MI. Non Q-wave MI is the term used when cardiac enzymes are elevated to a range that indicates that MI has occurred, but a Q-wave does not develop on ECG tracings. Unstable angina represents a spectrum of clinical states that fall between stable angina and acute MI and includes new onset and angina occurring >24 hours post MI.

Not only is unstable angina an unspecific diagnostic category, but patients also present with varying degrees of atherosclerosis, thrombus formation and vasospasm, each of which contributes to the morbidity and mortality associated with disease and therefore represents a potential target for intervention with medical therapy. Aspirin and heparin are typically used to reduce thrombus formation and nitrates are used to help reduce vasospasm. Interventional therapy typically involves percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). NHS Hospital Episode Statistics suggest that the incidence of unstable angina is around 1000 cases per million total population per year or around 10 per acute hospital per week. [9] Based on these estimates, this implies an annual incidence within the UK of around 59,756. [1]

2. The EVPI calculation

If there are j alternative interventions, each with uncertain parameters θ, the adoptions decision is to choose the intervention that generates the maximum expected net benefit:

$$Max_j E_\theta NB(j,\theta)$$

With perfect information, the decision maker would know how the uncertainties would resolve and would therefore select the intervention that maximises the net benefit for a particular value of θ:

$$Max_j NB(j,\theta)$$

However, given that the true values of θ are unknown, the expected value of a decision taken with perfect information is found by averaging the maximum net benefit over the joint distribution of θ:

$$E_\theta Max_j NB(j,\theta)$$

The EVPI is simply the difference between the expected value of the decision made with perfect information about the uncertain parameters θ and the decision made on the basis of existing evidence: [2]

$$EVPI = E_\theta Max_j NB(j,\theta) - Max_j E_\theta NB(j,\theta)$$

The value of perfect information about a parameter or a subset ϕ of all the uncertain parameters θ is the difference between the expected net benefit with perfect information about ϕ and the expected value with current information. With perfect information the value of ϕ is known and the expected net benefits are calculated over the remaining uncertainties (ψ):

$$Max_j E_{\psi/\phi} NB(j,\phi,\psi)$$

However, given that the true values of ϕ are unknown, the expected value of a decision taken with perfect information is found by averaging these maximum expected net benefits over the distribution of ϕ:

$$E_{\phi} Max_{j} E_{\psi/\phi} NB(j, \phi, \psi)$$

The expected value with current information is the same as before, so the EVPPI for the parameter or group of parameters ϕ is simply the difference between the expected value of a decision made with perfect information and the expected value with current information:

$$EVPPI_{\phi} = E_{\phi} Max_{j} E_{\psi/\phi} NB(j, \phi, \psi) - Max_{j} E_{\theta} NB(j, \theta)$$

3. Model structure

Figure 1 presents a schematic outline of the model structure. The model consisted of three components: baseline risk of non-fatal MI or death contingent on the interventional procedure undertaken (PCI or CABG or none) over a six month period; relative risks representing the treatment effects associated with the GPA strategies over the same six month period and a long term extrapolation. The first six months were modelled as a decision tree. Baseline risk data were taken from a UK source - PRAIS-UK - which is an observational cohort registry of 1046 patients with ACS who were admitted to 56 UK hospitals between 1998 and 1999. [6] The relative risks of death and non-fatal MI (compared to usual care) associated with each GPA-based strategy were derived from a random effects meta-analysis of all available trial data. [10-11]

The long-term extrapolation consisted of a four-state Markov model [4] which estimated long term costs and quality-adjusted survival duration contingent on patients' history during the first six-month period of the model. Transition probabilities

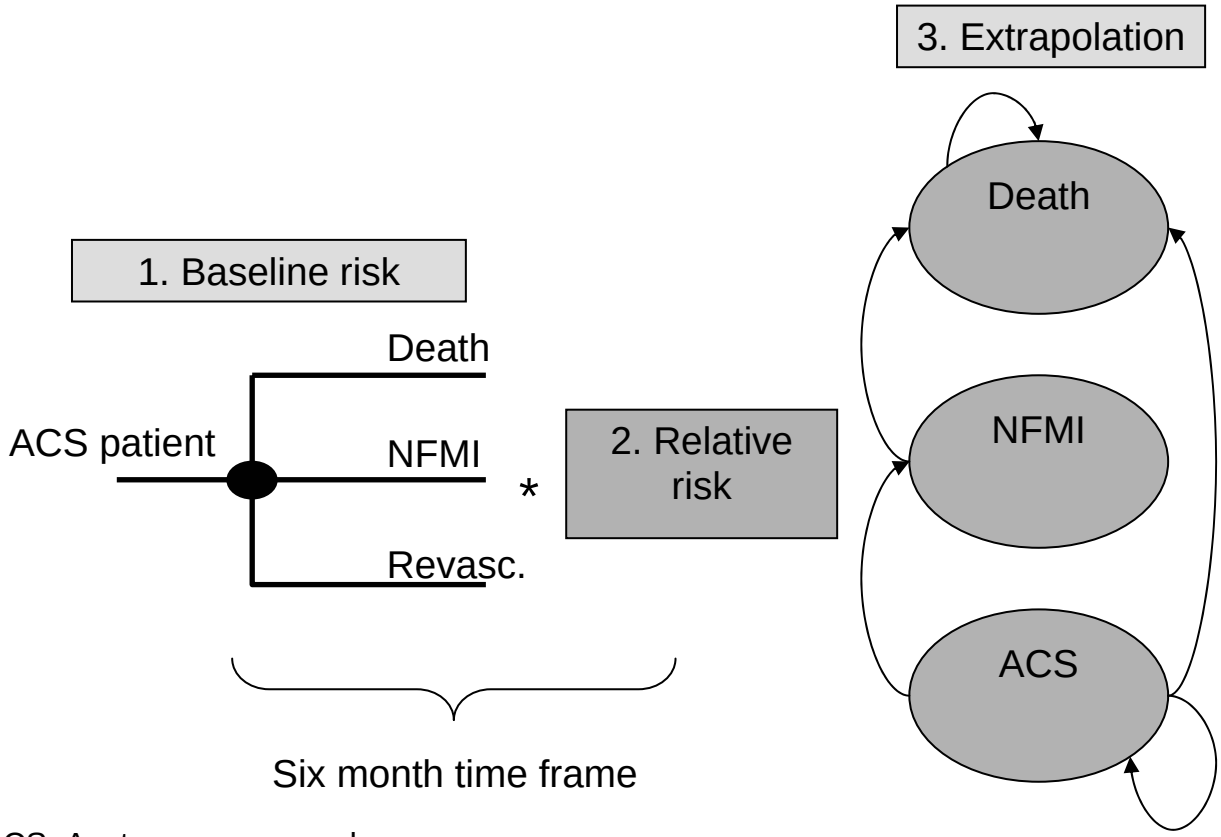
and health-state costs were estimated from data from two cohorts of the Nottingham Heart Attack Register (NHAR).[5] [8] The quality adjustment to life years was undertaken by assuming a single utility value for all living patients based on published data. [7] Table 1 details the principal parameter values used in the base case model. The model was fully probabilistic and incorporated distributions to reflect the uncertainty in the mean values of the input data which was propagated through the model using Monte Carlo simulation. [3] Baseline probabilities, utility estimates and the probability of any particular resource use were modelled as beta-distributions; hospital length of stay, relative risks, transition probabilities and utility estimates were incorporated as lognormal distributions.

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Figure 1 Schematic outline of the model structure



ACS: Acute coronary syndromes
NFMI: Non fatal MI
Revasc.: revascularisation

Table 1 A summary of the parameters used in the model together with sources

Parameter and source			NFMI	Death
Baseline risk (probabilities) [6]				
PCI			0.036	0.033
CABG			0.064	0.106
No revasc.			0.047	0.071
Relative risk [10]				
Strategy 1			0.94 (0.87 – 1.02)	0.81 (0.70 – 0.93)
Strategy 2			0.70 (0.48 – 1.03)	1.22 (0.61 – 2.46)
Strategy 3			0.67 (0.57 – 0.79)	0.77 (0.57 – 1.05)
Utility weight [7]			0.8 (SD 0.09)	0.8 (SD 0.09)
Transition probabilities [5] [8]				
			To	
		ACS	NFMI	Post NFMI	Death
From	ACS	0.90 (0.89 – 0.92)	0.02 (0.01 – 0.03)	-	0.08 (0.06 – 0.09)
	NFMI	-	-	0.79 (0.72 – 0.85)	0.21 (0.15 – 0.28)
	Post NFMI	-	-	0.93 (0.90 – 0.95)	0.07 (0.05 – 0.10)
	Death	-	-	-	1

NFMI: Non fatal myocardial infarction. PCI: Percutaneous coronary intervention. CABG: Coronary artery bypass grafting. ACS: Acute coronary syndromes. SD: standard deviation. Unless otherwise indicated ( ) = 95% confidence interval.