HCM SCD risk algorithm cost-effectiveness analysis

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0.1 Introduction

Sudden cardiac death (SCD) risk score algorithm details see (O'Mahony et al. 2014).

There have been previous cost-effectiveness analyses of ICD implants (Magnusson and Wimo 2020; Boriani et al. 2014; Bryant et al. 2007; Caro et al. 2007; Cowie et al. 2009; García-Pérez et al. 2015; Mealing et al. 2016; Sanders, Hlatky, and Owens 2005; Smith et al. 2013)

Cost-effectiveness of a cardiovascular risk prediction algorithm. (Zomer et al. 2017) for statins interventions and people with severe mental illness.

(Yao et al. 2007) use a Markov model and consider multiple implantations attempts if unsuccessful. (Colquitt et al. 2014) is a Health Technology Assessment which compares optimal pharmacological therapy (OPT) with or without ICD. (Tomini 2016) is a review of economic evaluation models for cardiac resynchronization therapy with implantable cardioverter defibrillators in patients with heart failure. (Ommen et al. 2020) 2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy.

0.2 Data

The main data set contains individual-level follow-up data of patients with HCM who may have been given an ICD due to some risk decision. Key cohort characteristics include the following. Patients were enrolled from the 6 health centres: Athens (474), Bologna (456), Coruna (590), London (1592), Murcia (404), Naples (156); The amount of censoring was 0 (3475), 1 (197); The mean age (sd) was 48 (16); The start of study data collection was in 1972 to 2011. Further plots are given in the Appendix. See (O'Mahony et al. 2014) for further details.

Health and cost data were obtained from literature and expert opinion. What values we wish to use will determine the form of the state model. For instance, if cost are only accrued on entry to a state then we may use a tunnel state. If cost depend on the patient history then we may need to duplicate a state.

Table 1 gives the unit cost and health values used in the model.

Table 1: Model parameter values. *either one-off/on state entry or recurring.

Description	Parameter	Value*	Range	Source
Health				
Manage with ICD	`u_icd`	0.637 QALY/year		Noyes et al. (2007)
Implantation procedure utility	`u_implant`	-0.016		Smith et al. (2013)
Shock utility	`u_shock`	-0.5		
HCM without ICD	`u_hcm`	1 QALY/year		
Death	`u_death`	0 QALY/year		
Cost				
ICD appointment	`c_appt`	£10		

Description	Parameter	Value*	Range	Source
Perform risk score	`c_rs`	£20?		
Implant ICD	`c_implant`	£4,666		EY02B Tariffs
Implant replacement	`c_repl`	£45,000		
Implant complication	`c_compl`	£28,839		Smith et al. (2013)
Non-fatal shock	`c_shock`	£22,880		UK Stroke Assoc.
HCM without ICD	`c_hcm`	0		
SCD	`c_scd`	0		
All-cause death	`c_death`	0		
Probabilities				
Initial implant complication	`p_compl`	0.047		Smith et al. (2013)
Replacement implant complication	`p_repl`	0.032		Smith et al. (2013)
Time horizon	`T`	12 years		
Implant replacement	`t_repl`	10 years		
Annual number of appointments	n_appt	2		

Table 2 gives the starting state populations for non-zero states.

Table 2: Starting state populations by decision rule.

Risk rule	State	Population
Observed	HCM ICD	559
-	HCM	3113
Score > 4%	HCM ICD	2561
-	HCM	1111
Score > 6%	HCM ICD	542
-	HCM	3130
Risk factor >0	HCM ICD	1785
-	HCM	1887
Risk factor >1	HCM ICD	481
-	HCM	3191
Risk factor >2	HCM ICD	78
-	HCM	3594

0.3 Methods

The individual-level patient data are first stratified in to two groups for each risk algorithm. These are

- Partition observed in data set
- ICD given if number of risk factors > 0, 1 or 2
- ICD given if risk score > 6%
- ICD given if risk score > 4%

We included the option of a fuzzy decision boundary such that near the threshold there is some random variation as to whether a patient received an ICD or not.

0.3.1 Markov model

Th patient data give us starting state populations for HCM with ICD and HCM without ICD which will be different for each risk decision rule. Further, the transition probabilities from these states will differ because of the case mixes.

A diagram of the current cohort model is given in Figure 1.

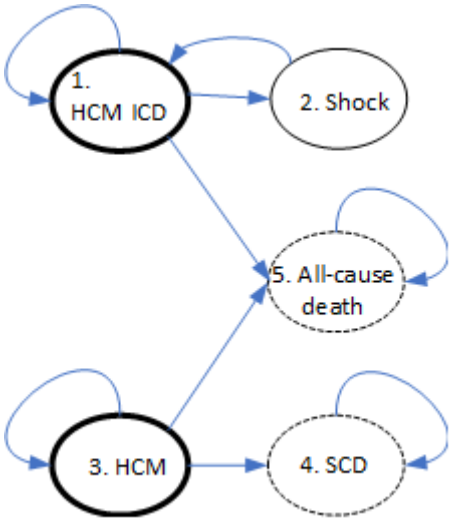

Figure 1: Markov model diagram. Bold circles represent starting states and dashed circles represent sink states.

Assuming that shocked patients return to the HCM ICD state then the transition matrix looks like the following.

$$\begin{pmatrix} p_{11} & p_{12} & 0 & 0 & p_{15} \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & p_{33} & p_{34} & p_{35} \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

We have used a year step size but if e.g. cost are accrued at different intervals then this can be adapted. The time horizon is set at 12 years from time of implant.

0.3.2 State health and cost equations

We assume that an ICD patient has 2 annual appointments. All shocks are treated the same in terms of costs and health impact. Implantation can have complications. The cost of an implant complication is taken as a weighted sum of infection and dislodgement cost with values from (Smith et al. 2013). Subscript s denotes the state number and superscript denotes the intervention either ICD or not.

- Annual health:

$$e^0_{s=1}(t) = e^1_{s=1}(t) = \text{u\_hcm} + \text{u\_icd}$$
$$e^0_{s=3}(t) = e^1_{s=3}(t) = \text{u\_hcm}$$
$$e^0_{s=2}(t) = e^1_{s=2}(t) = \text{u\_shock}$$

$$e^0_s(t) = e^1_s(t) = 0, \quad s = 4, 5, 6$$

- Initial costs:

$$c^0_{s=1}(t=0) = \text{c\_icd} + \text{p\_compl} \times \text{c\_compl}$$

$$c^1_{s=1}(t=0) = \text{c\_icd} + \text{c\_rscore} + \text{p\_compl} \times \text{c\_compl}$$

- Annual cost:

$$c^0_{s=1}(t) = c^1_{s=1}(t) = \text{2c\_appt}, \quad t \neq \text{t\_repl}$$

$$c^0_{s=2}(t) = c^1_{s=2}(t) = \text{c\_shock}$$

- Implant replacement cost

$$c^0_{s=1}(t) = c^1_{s=1}(t) = \text{2c\_appt} + \text{c\_repl} + \text{p\_compl} \times \text{c\_compl}, \quad t = \text{t\_repl}$$

0.3.2.1 Transition probability inference Using WinBUGS (Zhang 2014) called from R, each new data set is used to generate posterior samples of transition probabilities. Denote x as the observed number of transitions, p the probability of a transition and n as the total number of transitions from a given state. The hyperparameters α characterise the prior knowledge on p. Superscripts indicate the decision rule used.

$$x^{(1)}_{i.} \sim \text{Multinomial}(p^{(1)}_{i.}, n^{(1)}_i), \quad i = 1, 3$$

$$x^{(2)}_{i.} \sim \text{Multinomial}(p^{(2)}_{i.}, n^{(2)}_i), \quad i = 1, 3$$

$$p^{(1)}_{i.} \sim \text{Dirichlet}(\boldsymbol{\alpha}^{(1)}), \quad i = 1, 3$$

$$p^{(2)}_{i.} \sim \text{Dirichlet}(\boldsymbol{\alpha}^{(2)}), \quad i = 1, 3$$

For all sink states,

$$p^{(s)}_{ij} = \begin{cases} 1 & \text{if } i = j; \\ 0 & \text{if } i \neq j. \end{cases}$$

0.4 Results

We give results of the model fitting and cost-effectiveness analysis.

0.4.1 Model fitting

Figures 2 and 3 give histograms of posterior distributions for state transition probabilities for no groups without and with ICD implants.

Figure 4 gives an example of state occupancy over time plot. This shows that for the new algorithm there are fewer SCD and more shocks.

0.4.2 Cost-effectiveness

Table 3: Cost-effectiveness statistics

Strategy	Cost, c	Δc	QALYs, e	Δe	ICER
Baseline					
$> 4\%$					
$> 6\%$					
> 1 risk factor					
> 2 risk factors					

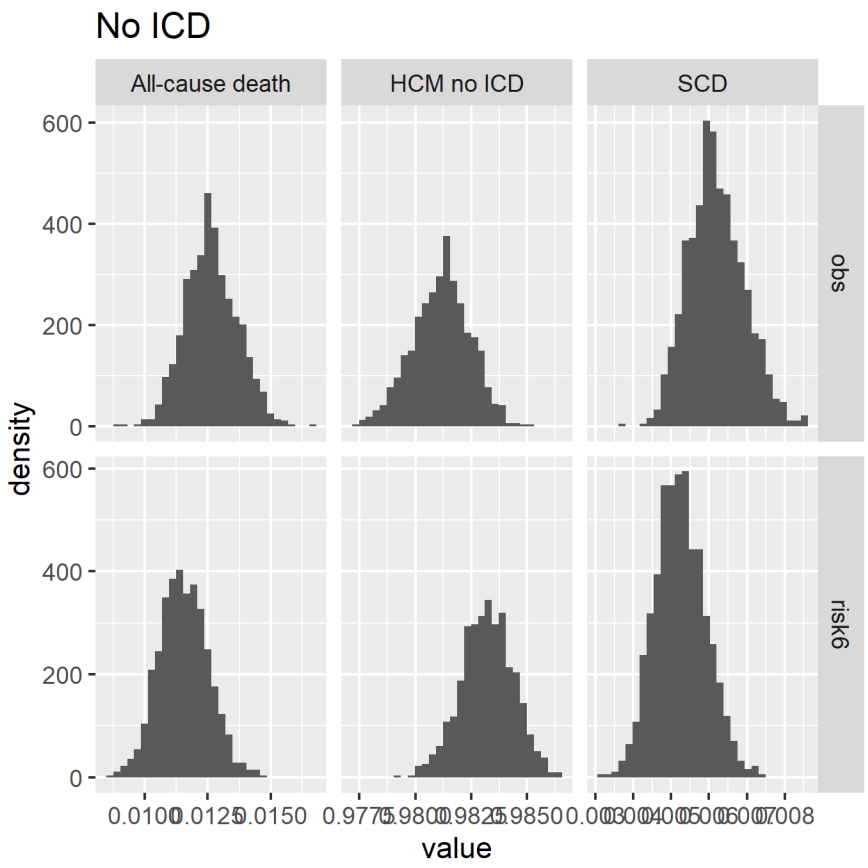

Figure 2: Histogram of posterior distributions for state transition probabilities.

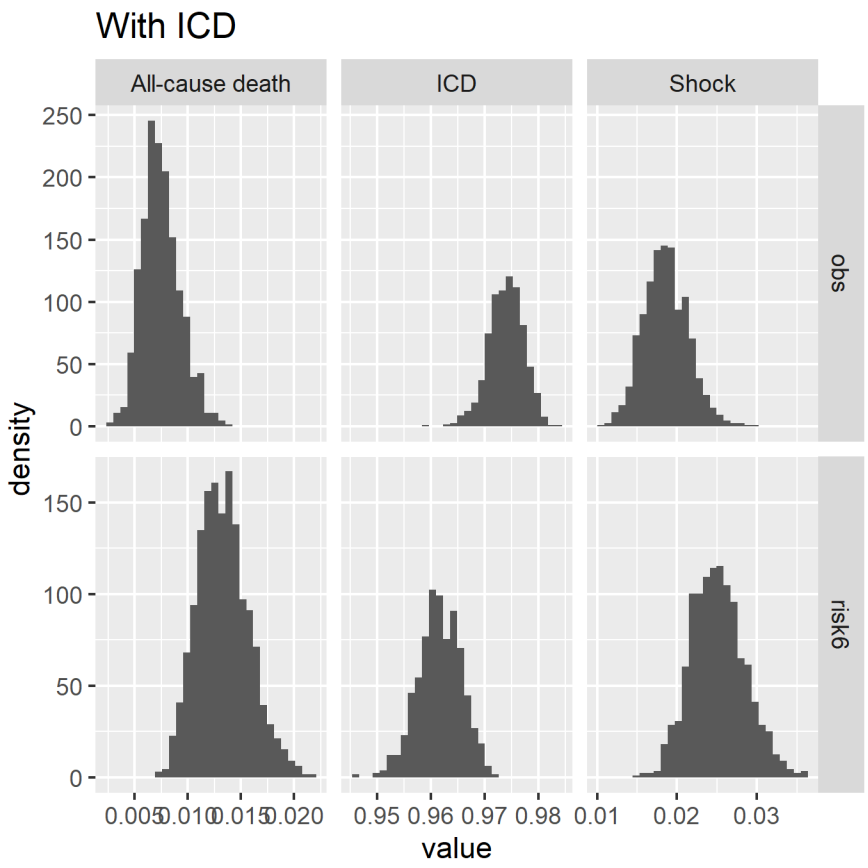

Figure 3: Histogram of posterior distributions for state transition probabilities.

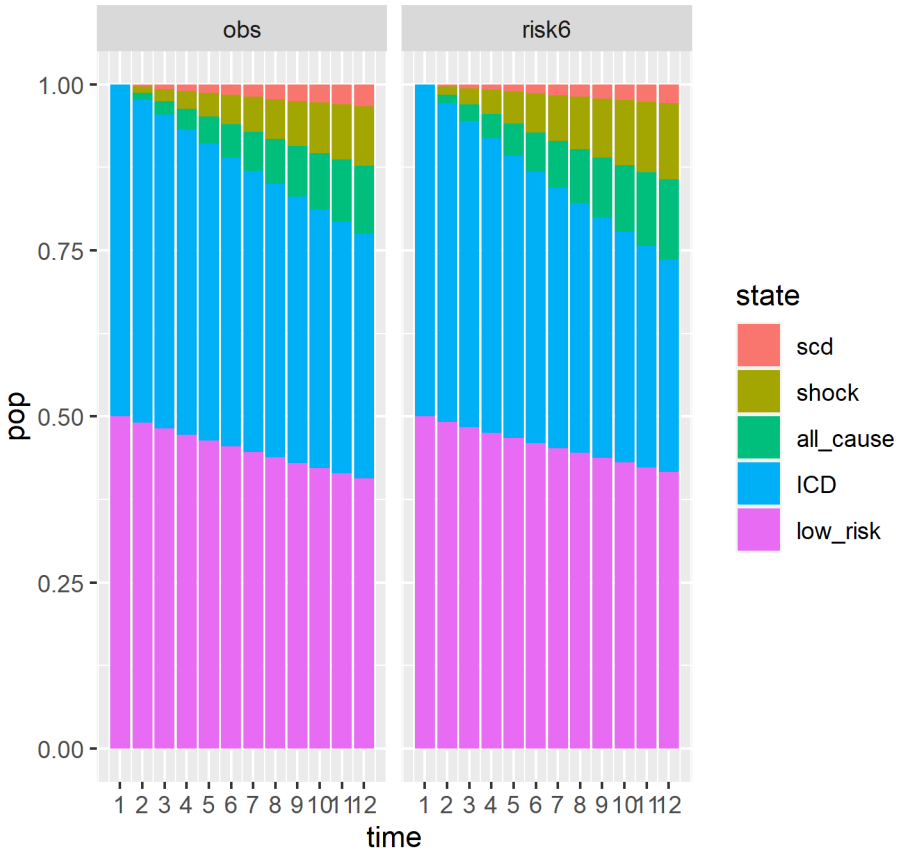

Figure 4: State occupancy over time.

Figure 5 gives the CEAC and Figure 6 gives the CE-plane.

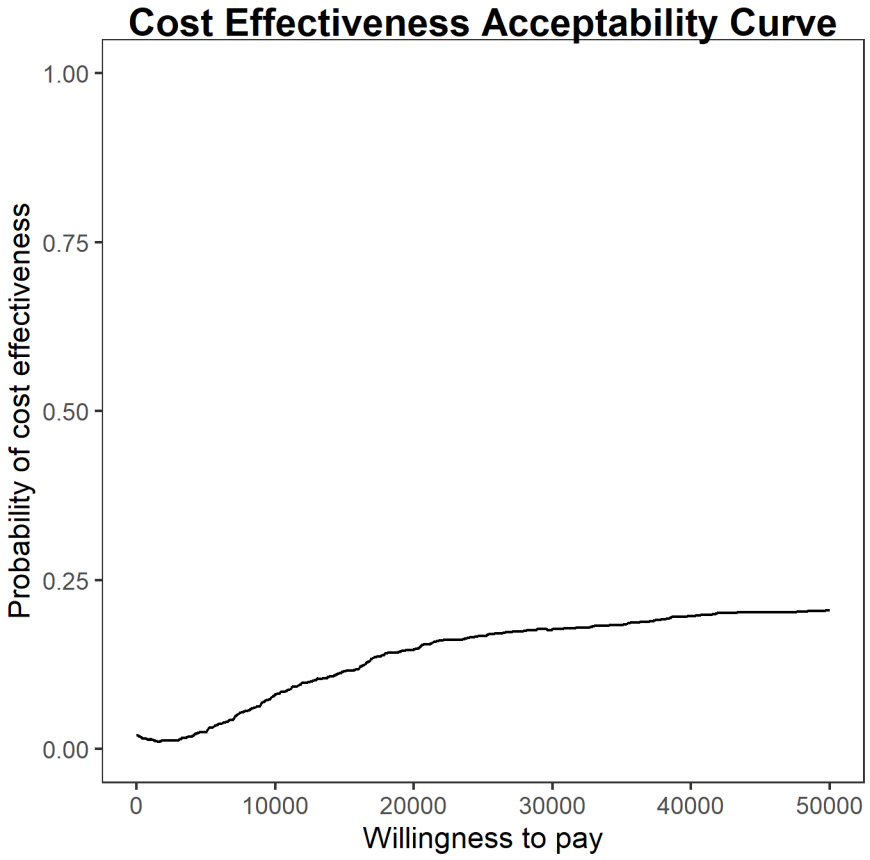

Figure 5: Cost-effectiveness acceptability curve (CEAC).

0.5 Discussion

Decision making as to whether have the implant is shared between patient and medical professional. The SCD risk score is a support tool which contributes to the final decision. An SCD risk score of 6% is treatment recommendation for one patient versus another. There could be individual preferences that out-weighs the risk score and mean a patient chooses the alternative.

Having more robust quality of life data will help to make such decisions. more embedded PROMs research

Informatics Consult (Lai et al. 2021) automation to scale evidence generation and to accelerate the return of results within clinical time-scales.

We did not include CRT-D or s-ICD but that can be overcome by sensitivity analyses that show e.g. the main message is that conclusions about the ICER etc will be robust to most departures from base assumptions other than tweaks in utility (which are the part of the model based on the weakest data!)

(Olivotto et al. 2020) The role of new DMARDs and their ability to influence quality of life. So if both ICD and non-ICD patients experience significant increases in QoL, are these equally distributed?

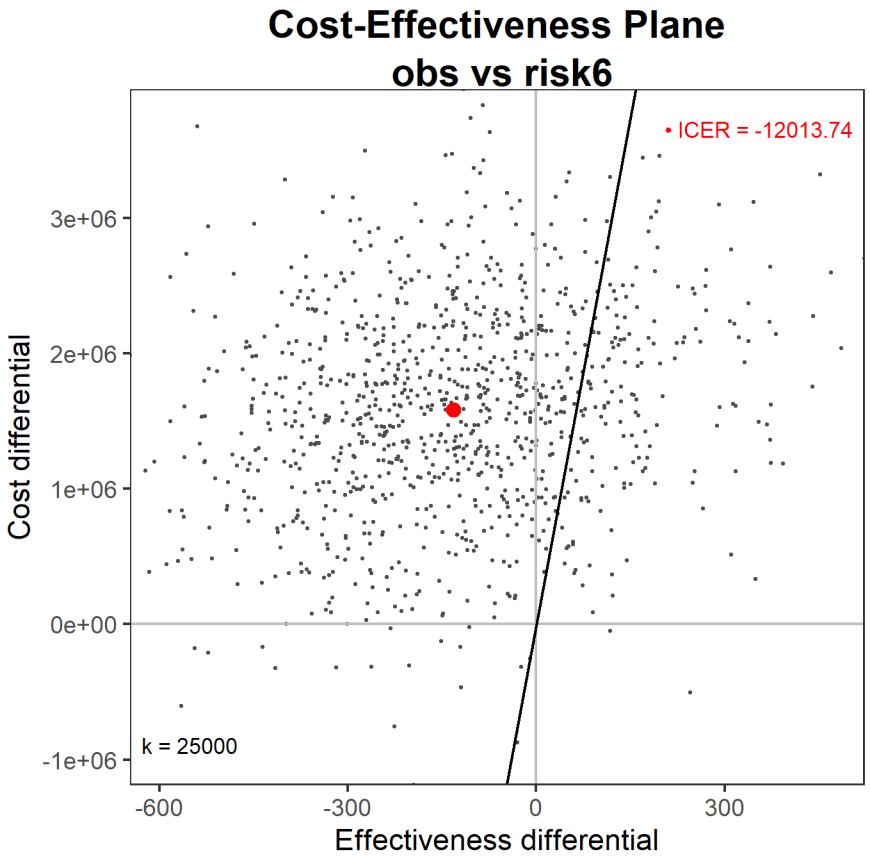

Figure 6: Cost-effectiveness plane.

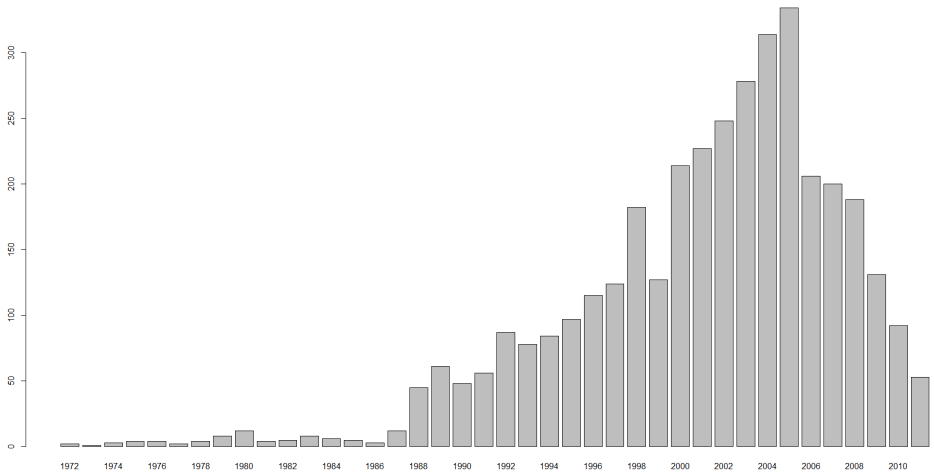

Figure 7: Year of study entry bar plot.

1 Appendix

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