

## Appendix – online supplementary information

### A1 Permitted transitions in simulation model

#### Event free state to primary states

Event free to Primary Stable Angina (SA)

Event free to Primary Unstable Angina (USA)

Event free to Primary AMI

Event free to Primary TIA

Event free to Primary Stroke

Event free to Fatal CVD event (FCVD)

Event free to Death other causes (DOC)

#### Primary states to subsequent states

PRIMARY\_SA to SECONDARY\_(USA or 1st AMI or 1st Stroke or FCVD or DOC) else post SA

PRIMARY\_USA to SECONDARY\_(1st AMI or 1st Stroke or FCVD or DOC) else post USA

PRIMARY\_AMI to SECONDARY\_(1st AMI or 1st Stroke or FCVD or DOC) else post AMI

PRIMARY\_TIA to SECONDARY\_(1st AMI or 1st Stroke or FCVD or DOC) else post TIA

PRIMARY\_Stroke to SECONDARY\_(1st Stroke or FCVD or DOC) else post Stroke

#### Post-primary states to subsequent states

Post PRIMARY\_SA to SECONDARY\_(USA or 1st AMI or 1st Stroke or FCVD or DOC) else post SA

Post PRIMARY\_USA to SECONDARY\_(1st AMI or 1st Stroke or FCVD or DOC) else post USA

Post PRIMARY\_AMI to SECONDARY\_(1st AMI or 1st Stroke or FCVD or DOC) else post AMI

Post PRIMARY\_TIA to SECONDARY\_(1st AMI or 1st Stroke or FCVD or DOC) else post TIA

Post PRIMARY\_Stroke to SECONDARY\_(1st Stroke or FCVD or DOC) else post Stroke

#### Secondary state transitions

SECONDARY\_SA to SECONDARY\_( (USA or 2nd AMI or 2nd Stroke or FCVD or DOC) else post SA

SECONDARY\_USA to SECONDARY\_( (2nd AMI or 2nd Stroke or FCVD or DOC) else post USA

SECONDARY\_AMI to SECONDARY\_( (2nd AMI or 2nd Stroke or FCVD or DOC) else post AMI

SECONDARY\_TIA to SECONDARY\_( (2nd AMI or 2nd Stroke or FCVD or DOC) else post TIA

SECONDARY\_Stroke to SECONDARY\_( (2nd Stroke or FCVD or DOC) else post Stroke

Post SECONDARY\_SA to SECONDARY\_(USA or 2nd AMI or 2nd Stroke or FCVD or DOC) else post SA

Post SECONDARY\_USA to SECONDARY\_(2nd AMI or 2nd Stroke or FCVD or DOC) else post USA

Post SECONDARY\_AMI to SECONDARY\_(2nd AMI or 2nd Stroke or FCVD or DOC) else post AMI

Post SECONDARY\_TIA to SECONDARY\_(2nd AMI or 2nd Stroke or FCVD or DOC) else post TIA

Post SECONDARY\_Stroke to SECONDARY\_(2nd Stroke or FCVD or DOC) else post Stroke

Notes to A1: SA = Stable angina; USA = Unstable angina; AMI = Acute myocardial infarction; TIA = Transient ischaemic attack; FCVD = Fatal cardiovascular disease event; DOC = Death other causes

This is the same list of permitted transitions described as in Ara et al <sup>1</sup> and Ara et al <sup>2</sup>. A1 contains the same information as Table 82 in Ara et al <sup>1</sup>.

## INPUT VALUES, REFERENCES AND PROBABILITY DISTRIBUTIONS FOR MODEL PARAMETERS

Table A2 provides a map to the various model parameters, input values, and associated probability distributions from which input values for specific model runs were drawn, and which are presented in more detail where applicable.

### A2 Key input parameters and associated probability distributions

Parameter	Input values	Probability distribution	Comments
<b>Health state utility values</b>	Various; listed in Table A3	Normal	Ara and Wailoo <sup>3</sup> recommend the use of normal distributions to characterise the uncertainty in mean utilities
<b>Health state costs</b>	Various, listed in Table A4	Gamma	A number of sources, eg Gray et al <sup>4</sup> , recommend using gamma distributions in characterising uncertainty in cost variables
<b>Incidence rates for primary CVD events</b>	Various, listed in Table A5 and Table A6	N/A	We follow Ward et al <sup>5</sup> and Ara et al <sup>2</sup> in using the mean values of published incidence rates in each model run
<b>CVD Risk</b>	Based on age and sex adjusted QRISK2 scores from baseline and 12m follow-up that are	N/A	The variance structures underlying the QRISK2 algorithm are not published and hence we

presented in Table 1 in the main text, and then adjusted subsequently using the QRISK2 algorithm

could not characterise uncertainty in this measure. See Discussion in main paper.

**Risk of death from non-CVD causes**

Based on standardised mortality ratios published by the ONS

Normal distribution

We follow Ara et al<sup>2</sup> in using a normal distribution for model draws

## UTILITIES

Ara and Brazier<sup>6</sup> was used as the source of state-specific utilities other than TIA, which are based on Luengo-Fernandez et al<sup>7</sup>. It was assumed that the utility estimates for angina in Ara and Brazier related to stable angina, and that unstable angina health utilities would be 90% of the stable angina values, as in Ara et al.<sup>2</sup>

As further noted in the main text, any 'third' events, i.e. those occurring after a secondary event, have the same utility as the 'second' event.

### A3 Health state utility values

Health state	Mean utility value
Primary stable angina	0.615
Primary unstable angina	0.556
Primary AMI	0.721
Primary TIA	0.760
Primary stroke	0.626
Post-primary angina	0.775
Post-primary unstable angina	0.701
Post-primary AMI	0.742
Post-primary TIA	0.78
Post-primary stroke	0.668
Secondary stable angina	0.541
Secondary unstable angina	0.489
Secondary AMI	0.431
Secondary TIA	0.760
Secondary stroke	0.479
Post-secondary stable angina	0.715
Post-secondary unstable angina	0.647
Post-secondary AMI	0.685
Post-secondary TIA	0.78
Post-secondary stroke	0.641

### Costs

A detailed discussion of the cost data used to model each state is provided in Salisbury et al.<sup>8</sup> Briefly, the costs of stable and unstable angina, of non-fatal acute myocardial infarction are based on Ward et al<sup>5</sup> and Ara et al.<sup>2</sup> The cost of fatal

acute myocardial infarction are based on Clarke et al.<sup>9</sup> The costs of non-fatal stroke and of transient ischaemic attack are based on Luengo-Fernandez et al.<sup>7</sup> The cost of fatal stroke is based on Youman et al.<sup>10</sup> In all cases, costs were adjusted to 2012/13 sterling prices as described in Salisbury et al.<sup>8</sup>

#### **A4 Health state costs**

<b>Health state</b>	<b>Mean cost in 2012/13 £ prices</b>
Stable angina	606
Stable angina in subsequent years	356
Unstable angina	4,324
Unstable angina in subsequent years	453
Non-fatal acute myocardial infarction	3,362
Post non-fatal acute myocardial infarction	356
Fatal acute myocardial infarction	1,846
Transient ischaemic attack	3,963
Transient ischaemic attack in subsequent years	1,380
Non-fatal stroke	8,989
Non-fatal stroke in subsequent years	1,976
Fatal stroke	9,493

## INCIDENCE RATES FOR PRIMARY EVENTS

Incidence rates for primary events are used to calculate the probability of one of stable angina, unstable angina, acute myocardial infarction (AMI), stroke, and transient ischaemic attack (TIA). These incidence rates are then used to disaggregate the risk of any such event, measured by the QRISK2 score, into the risk of a single event.

The data sources and adjustments made to data are described in more detail in Salisbury et al. <sup>8</sup> Here, we briefly describe these sources, and present in A5 and A6 the incidence data used in the simulation model.

The incidence of angina was taken from data for England reported British Heart Foundation Coronary Heart Disease Statistics 2012,<sup>11</sup> using the data reported for England. This was split into incidences of stable and unstable angina using incidences reported in Sutcliffe et al. <sup>12</sup> Incidence of fatal and non-fatal AMI was also taken from British Heart Foundation Coronary Heart Disease Statistics 2012.<sup>11</sup> Incidence of first ever stroke was based on Wang et al, <sup>13</sup> and incidence on mortality from strokes was based on Lee et al. <sup>14</sup>

Incidence of TIA is taken from British Heart Foundation Stroke Statistics 2009. <sup>15</sup>

### A5 Incidence rates of CVD events per 1,000 males per year

Age band	Stable angina	Unstable angina	Non-fatal AMI	Fatal AMI	TIA	Non-fatal stroke	Fatal stroke
55-64	0.84	0.25	0.28	0.04	0.74	0.65	0.08
65-74	1.16	0.35	0.42	0.11	1.45	1.27	0.16
75-84	0.75	0.23	0.73	0.29	3.27	2.73	0.35
85+	0.75	0.23	1.23	0.76	7.94	5.12	0.65

## A6 Incidence rates of CVD events per 1,000 females per year

Age band	Stable angina	Unstable angina	Non-fatal AMI	Fatal AMI	TIA	Non-fatal stroke	Fatal stroke
55-64	0.35	0.11	0.07	0.02	1.05	0.63	0.14
65-74	0.74	0.22	0.18	0.06	2.18	1.23	0.28
75-84	0.57	0.17	0.38	0.22	5.61	2.64	0.6
85+	0.57	0.17	0.75	0.64	9.14	4.95	1.13

### References

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