

# Lifetime effects and cost-effectiveness of standard and higher-intensity statin therapy across population categories in the UK: a microsimulation modelling study

## SUPPLEMENTARY MATERIAL

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## Supplementary methods

### Handling missing values in UK Biobank

Following specification of participant characteristics, including those required for QRISK calculation, several characteristics, such as ethnicity, smoking status/cigarettes per day, BMI (including height, weight), total cholesterol, LDL cholesterol (LDL-C), HDL cholesterol, creatinine and blood pressure measures, and Townsend score, had some missing values (see Supplementary methods table 1). Missing ethnicities were imputed as white, the majority category. Missing smoking statuses were imputed with the majority smoking status by sex, age category and education level. Missing cigarettes per day were imputed with the majority level, i.e. 10-20. Missing Townsend scores were imputed by regressing on index of multiple deprivation (IMD) scores, years and sources (England, Wales or Scotland) if IMD scores were available, and imputed by looking up an average Townsend score according to the rounded ordnance survey coordinates if IMD scores were missing, or, finally, imputed by looking up an average Townsend score for the areas of the participant UK Biobank assessment centres if IMD scores and ordnance survey coordinates were both missing. The remaining continuous variables with missing values were imputed using multiple imputation by chained equations with 20 imputations and 10 iterations for each using the package “mice” in R, with weight, height, LDL-C, HDL cholesterol, triglycerides, creatinine, systolic blood pressure (two measures) and diastolic blood pressure (two measures), and with age, sex, (imputed) ethnicity, (imputed) smoking status, baseline cardiovascular diseases, treated hypertension, statin treatment status and diabetes added as auxiliary variables. Acknowledging the computational intensity of microsimulation model development and execution,<sup>1</sup> the missing values for continuous factors were replaced with the mean values across the 20 imputed values. After missing data imputation, participants’ QRISK3 scores were calculated using an external R package “QRISK3”.<sup>2</sup>

**Supplementary methods table 1 Participants with missing data at baseline in UK Biobank (N = 501,854)**

	<b>Number participants with missing values</b>	<b>Participants with missing values (%)</b>
Physical activity*	99,996	19.9%
HDL cholesterol	72,530	14.5%
LDL cholesterol	33,744	6.7%
Creatinine	33,092	6.6%
Diet quality	11,018	2.2%
Smoking	2,946	0.6%
Body mass index	3,087	0.6%
Ethnicity	2,771	0.6%
Systolic blood pressure	1,319	0.3%
Diastolic blood pressure	1,317	0.3%
Townsend score	622	0.1%
<i>For QRISK3 calculation only</i>		
Height (cm)	3,087	0.6%
Weight (kg)	2,757	0.5%
Total cholesterol/HDL	72,530	14.5%
Standard deviation of systolic blood pressure	1,826	0.4%

\*Missing values for physical activity level were not imputed but coded as a separate level.  
HDL, high-density lipoprotein; LDL, low-density lipoprotein

## Physical activity and diet specifications

The **physical activity** level is indicated by the International Physical Activity Questionnaire (IPAQ) activity group, the UK Biobank derived variable based on Metabolic Equivalent Task (MET) scores and categorised following the IPAQ guidelines into three levels<sup>3</sup>:

**Low:** no activity or not enough to meet moderate or high level;

**Moderate:** 3 or more days of vigorous-intensity activity of at least 20 min/day/week,  
or

5 or more days of moderate-intensity activity and/or walking of at least 30 min/day/week, or

5 or more days of any combination of walking, moderate or vigorous-intensity activities achieving a minimum of at least 600 MET-min/week;

**High:** vigorous-intensity activity on at least 3 days and accumulating at least 1500 MET-min/week, or

7 or more days of any combination of walking, moderate or vigorous-intensity activities achieving a minimum of at least 3000 MET-min/week.

About 20% of the IPAQ values at entry into UK Biobank were missing; these are used in analyses as a separate category.

**Daily diet** is considered to be healthy if it meets at least 4 of the following 7 components<sup>4</sup>, otherwise unhealthy:

### Component of food frequency

- 1) Fruits:  $\geq 3$  servings/day
- 2) Vegetables:  $\geq 3$  servings/day
- 3) Fish:  $\geq 2$  servings/week
- 4) Processed meats:  $\leq 1$  serving/week
- 5) Unprocessed red meats:  $\leq 1.5$  servings/week
- 6) Whole grains:  $\geq 3$  servings/day
- 7) Refined grains:  $\leq 1.5$  servings/day

The 11018 (2%) uncertain cases due to missing data in some categories of food intake were combined with the unhealthy diet category, as an early model indicated similar associations.

## Derivation of 10-year cardiovascular risk using QRISK3<sup>5</sup> for participants at entry into the UK Biobank

Further to participant characteristics previously defined or derived from UK Biobank, the following assumptions were made (**Supplementary methods table 2**). First, we assumed that all unspecified black ethnicity (n=171) were black Caribbean. Second, at the entry into UK Biobank (2006-2010) few histories of CKD were coded as CKD stages 3-5 and many were coded as unspecified CKD; the whole chronic renal failure category were used to mean "CKD stage 3-5" for calculation of QRISK3. Third, the categories of depressive episode and recurrent depressive disorder were used to mean "moderate/severe depression" required for calculation of QRISK3, because many were coded as unspecified depression in UK Biobank. Fourth, we used history of heart disease of father, mother and sibling to substitute angina or

heart attack in a 1st degree relative <60 required in QRISK3, as this is the closest information available in UK Biobank. The code lists of medications for antihypertension, erectile dysfunction treatment, regular steroid tablets and atypical antipsychotic treatment were sourced from a published study using UK Biobank data<sup>6</sup>.

**Supplementary methods table 2 QRISK3 risk factors' specification using UK Biobank data**

<b>QRISK3 risk factor</b>	<b>Risk factor specification in UK Biobank</b>
Sex	Original UK Biobank variable
Age	Must be 25-84. All UK Biobank participants are eligible at entry into UK Biobank.
Height (cm)	Original UK Biobank variable
Weight (kg)	Derived from BMI and height
Ethnicity	<ol style="list-style-type: none"> <li>1. White or not stated: white, British, Irish, any other white background, prefer not to answer, do not know</li> <li>2. Indian: Indian</li> <li>3. Pakistani: Pakistani</li> <li>4. Bangladeshi: Bangladeshi</li> <li>5. Chinese: Chinese</li> <li>6. Other Asian: Asian or Asian British, any other Asian background</li> <li>7. Black Caribbean: Caribbean, Black or Black British, any other Black background</li> <li>8. Black African: African</li> <li>9. Others: mixed, other ethnic group, white and black Caribbean, white and black African, white and Asian, any other mixed background</li> </ol>
Townsend score	Original UK Biobank variable
Smoking status	<ol style="list-style-type: none"> <li>1. Non-smoker</li> <li>2. Ex-smoker</li> <li>3. Light smoker: &lt;10 cigarettes/day</li> <li>4. Moderate smoker: 10-19 cigarettes/day, or did not report</li> <li>5. Heavy smoker: 20+ cigarettes/day</li> </ol>
Diabetes type 1	UK Biobank algorithm, ICD10: E10 insulin-dependent diabetes mellitus, E14 Unspecified diabetes mellitus (diagnosis age≤20 years)
Diabetes type 2	UK Biobank algorithm, ICD10: E11 Non-insulin-dependent diabetes mellitus; E12 Malnutrition-related diabetes mellitus; E13 Other specified diabetes mellitus; E14 Unspecified diabetes mellitus (diagnosis age>20 years)
Atrial fibrillation	UK Biobank algorithm, ICD10: I48 Atrial fibrillation and flutter
Chronic kidney disease (stage 3,4 or5)	ICD10: N18 Chronic renal failure
Rheumatoid arthritis	UK Biobank algorithm, ICD10: M05 Seropositive rheumatoid arthritis; M06 Other rheumatoid arthritis
Migraine	UK Biobank algorithm, ICD10: G43 Migraine
Systemic lupus erythematosus	UK Biobank algorithm, ICD10: M32 Systemic lupus erythematosus

Severe mental illness (schizophrenia, bipolar disorder and moderate/severe depression)	UK Biobank algorithm, ICD10: F20 Schizophrenia; F23 Acute and transient psychotic disorders; F31 Bipolar affective disorder; F32 Depressive episode; F33 Recurrent depressive disorder
Erectile dysfunction or treatment	Combination of nurse interview medical conditions and medications data. <sup>3</sup>
Angina or heart attack in a 1 <sup>st</sup> degree relative <60	Including history of “heart disease” of father, mother and siblings. There is no information about whether the disease happened before 60 years old. Therefore, there are two assumptions: 1) heart disease were angina or heart attack, and 2) all the diseases happened under 60.
Total cholesterol/HDL	Total cholesterol/HDL
Systolic blood pressure	Mean, if there are two successive measures
Standard deviation of systolic blood pressure	Standard deviation of two successive measures
Blood pressure treatment	As defined in the main text
Regular steroid tablets	From the nurse interview’s medications data <sup>6</sup>
Atypical antipsychotic medication	From the nurse interview’s medications data <sup>6</sup>

### Derivation of pre-treatment LDL-C levels for statin-treated UK Biobank participants

We adjusted upwards the LDL-C levels of participants who were on statin treatment at entry into UK Biobank to derive “pre-treatment” LDL-C levels using the potency of their statin regimen (see Supplementary Table 1).

Statin dosage information was not collected at UK Biobank baseline interview but for participants with linked primary care prescription records both type of statin and dosage were available. However, more than half of the UK Biobank participants did not have linked primary care data, and, therefore, no linked primary care prescription records. Additionally, there were some discrepancies between reported statin use at UK Biobank recruitment and available statin prescription records; for such cases a report of statin use in either source was accepted and, if more than one source available, the more intensive regimen was used.

Reports of statin treatment with an exact statin medication and dosage were directly associated with the proportional LDL-C reductions according to Supplementary Table 1. Statin medications with unknown dosage were assumed to have the average proportional LDL-C reduction according to weighted frequencies, separately for categories of participants without and with history of cardiovascular disease, from respective participant categories for which exact statin medication and dose were available. There were few cases with combinations of two statins, where for those with known dosages, the more potent regimen was retained (one case with simvastatin 40mg and atorvastatin 10mg, we keep the latter), and for those with unknown dosage, the statin regimen retained followed the following hierarchy in decreasing order of rosuvastatin, atorvastatin, simvastatin, pravastatin, fluvastatin.

The **pre-treatment LDL cholesterol (LDL-C<sub>pre-treatment</sub>)** of statin-treated participants was calculated as:

$$\text{LDL-C}_{\text{pre-treatment}} = \text{LDL-C}_{\text{entry}} / (1 - \% \text{LDL-C reduction on statin treatment})$$

## The cardiovascular disease microsimulation policy model

### *Model structure*

Details of the cardiovascular disease microsimulation policy model are reported elsewhere<sup>1</sup>. Briefly, this cardiovascular disease microsimulation model projects cardiovascular disease, and key competing risks of diabetes, cancer and nonvascular death, over peoples' lifetimes using a set of individual characteristics. The model simulates annually the first occurrences of seven disease endpoints: myocardial infarction (MI), stroke, coronary revascularisation (CRV), incident cancer, incident diabetes, vascular death, and nonvascular death (**Supplementary methods figure S1**). Risks of these endpoints are informed from parametric proportional hazards risk equations. These risk equations, except for diabetes, were initially estimated using individual participant data in the Cholesterol Treatment Trialists' (CTT) Collaboration.<sup>7</sup> Subsequently, the risk equations were calibrated using the contemporary UK Biobank population cohort,<sup>8</sup> comprising 501,854 participants followed up until March 2017. Separate risk equations were estimated for individuals without and with history of cardiovascular disease at baseline for model endpoints except for incident cancer and incident diabetes. These risk equations take into account baseline characteristics of individuals, including age, sex, ethnicity, body mass index (BMI), smoking status, blood pressure, lipids, Hemoglobin A1c (HbA1c) and creatinine levels, previous history of cardiovascular disease, treated hypertension, diabetes and cancer, mental illness, physical activity, diet quality, and socioeconomic deprivation.

In addition to the risk equations for the model's endpoints, the pooled data from the 2006, 2011, and 2017 Health Survey for England informed a linear regression model of the health-related quality of life (QoL) associated with participant characteristics, disease and event histories. The QoL was measured using the EuroQoL-5 Dimension (EQ-5D) utility, where a value of 0 represents death, a value of 1 perfect health and negative values represent health states worse than death. The linear regression model was integrated into the microsimulation model to annually assess QoL and, together with survival, inform quality-adjusted life years (QALYs).

Healthcare cost models, predicting annual primary and hospital care costs (2020£) associated with individual characteristics, disease histories and endpoints in the model, were integrated into the model to project long-term healthcare costs.<sup>9</sup>

### *Model validation*

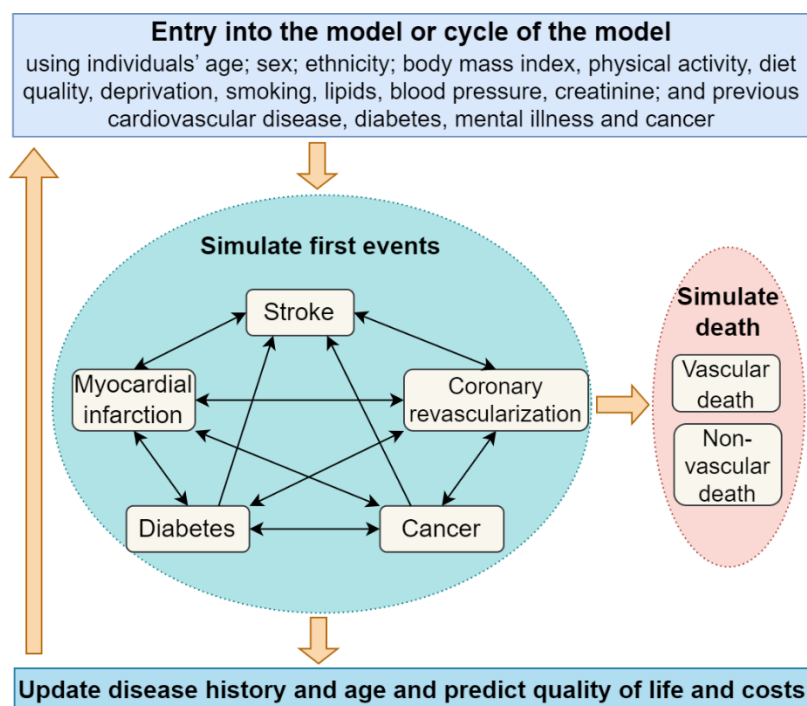
The cardiovascular disease policy model was validated using the UK Biobank cohort data, with about three further years of follow-up until February 2020, or up to 12 years of follow-up. Furthermore, the model was externally validated using the Whitehall II cohort (from phase 9 in the study), involving 6,761 individuals with about 10 years follow-up. In these validations, individual participant characteristics at baseline were used to simulate future disease risks and mortality. There was a generally strong agreement between the model's predicted cumulative incidence rates and the observed rates of endpoints across participant categories (**Supplementary methods figure S2**). While some overprediction of stroke risk is noted for the Whitehall II cohort, the overall microsimulation model performance, including of vascular and non-vascular mortality, was good. Whitehall II cohort was much smaller than UK Biobank and the identification of the stroke endpoint was exclusively based on linked hospital admissions and death registry data while a more comprehensive strategy, including some primary care data, was employed in UK Biobank. In view of the small cohort size, we did not consider further calibration of the stroke risk equation and the model was indicated.

## Model simulations

For the purpose of model execution, the model inputs are provided in the form of individual patient baseline characteristics. Each individual is simulated on an annual basis, progressing through the model until they reach either death or the age of 110 years. Within each annual cycle, the model predicts in a random order the first occurrences of MI, stroke, CRV, incident diabetes and incident cancer, followed by the prediction in a random order of the vascular and nonvascular death endpoints. Age and event history are updated annually for each individual. The occurrence of events within the model influences the subsequent risks of events in a time-dependent manner. Individuals who have a history of cancer and/or diabetes at the beginning of the simulation are not considered at risk for incident cancer or diabetes in the model. To minimize the Monte Carlo error, we implemented 500 first-order simulations for each individual and averaged the outcomes across these simulations for each year.

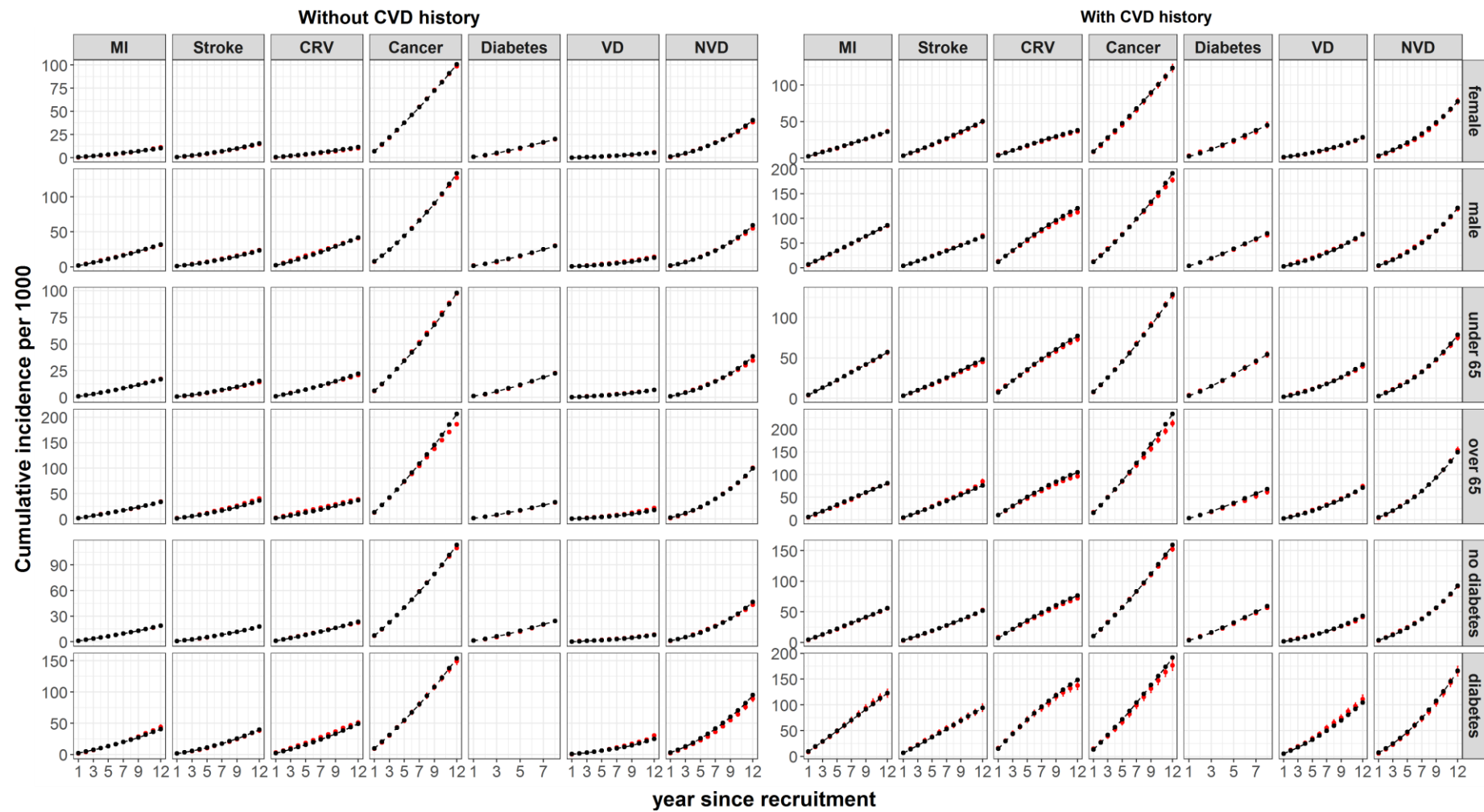
The model was implemented using R 4.2.1. The R code of the cardiovascular disease policy model (License: MIT License) are available at <http://www.herc.ox.ac.uk/downloads/supportingmaterial>. To enhance the usability of the cardiovascular disease policy model, we have developed a visual user interface. The interface, along with a user guide, can be accessed at [https://livedataoxford.shinyapps.io/shiny\\_ctt\\_ukb\\_model/](https://livedataoxford.shinyapps.io/shiny_ctt_ukb_model/). The model interface facilitates users to simulate long-term outcomes for individual profiles or a group of individuals.

## Supplementary methods figure S1 Schematic of the cardiovascular disease microsimulation model



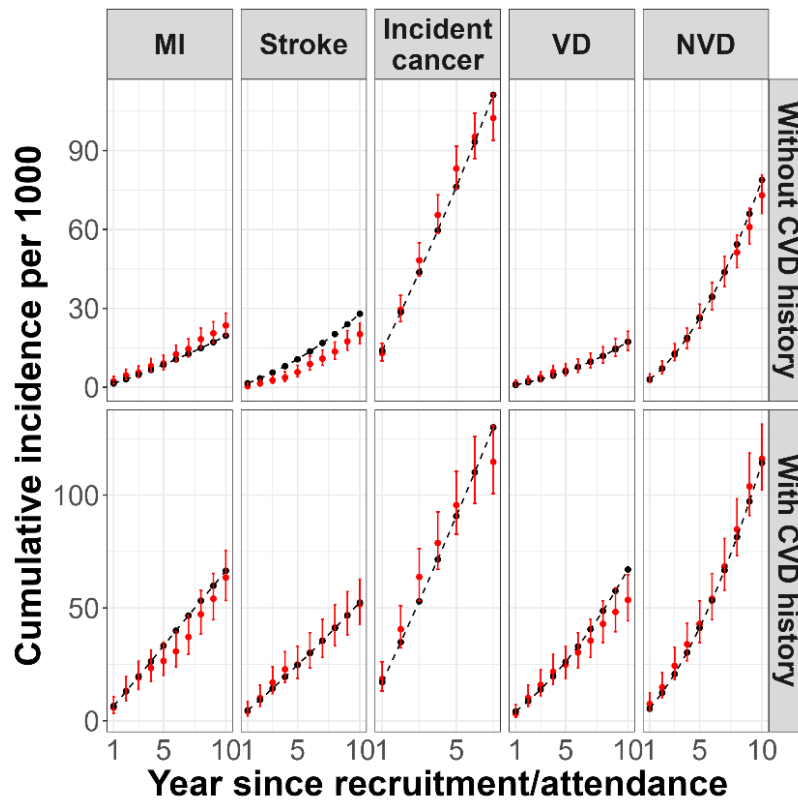
## Supplementary methods figure S2 Validation of the cardiovascular disease policy model

### A. In UK Biobank cohort





## B. In the Whitehall II cohort (Phase 9)



**RED=Observed; BLACK=model.** In the UK Biobank, validation covers 12 years including three extra years that were not used to calibrate the model. Follow-up of incident diabetes partly relies on primary care records, which ended earlier than other data types in the UK Biobank. In the Whitehall II Phase 9 data, validation covers 10 years (7 years for incidence cancer due to stopping follow-up earlier), and fewer categories were divided due to the relatively small number of this cohort. The endpoints of incident diabetes and CRV were not included in the validation in the Whitehall II data due to the lack of reliable follow-up data. MI, myocardial infarction; CRV, coronary revascularisation; VD, vascular death; NVD, non-vascular death.

### Integrating treatment effects of statin therapy in the cardiovascular disease microsimulation model

The rate ratios (RR (CI)) per 1mmol/L reduction in LDL-C with statin therapy, as reported by Cholesterol Treatment Trialists' Collaborative meta-analysis of individual participant data from large randomised controlled trials of statin therapy,<sup>10</sup> informed effects on cardiovascular events. It is of note that each of the trials in the meta-analysis had at least 1000 people and, therefore, the uncertainty in mean LDL-C reduction between arms is negligible. Further meta-analyses of randomised controlled trials of statin therapy informed effects of statin therapy on incident diabetes in the model<sup>11, 12</sup> (see Table 1 in the manuscript). In the base case analysis, it was assumed that statins do not affect cancer incidence and non-vascular death.

The transition probabilities (tp) of events in the absence of statin treatment in the model in each cycle are calculated as:

$$tp(t_u) = 1 - \exp[H(t-u) - H(t)], \text{ where}$$

u is the length of the cycle (i.e. 1 year),  $H(t-u)$  and  $H(t)$  are the cumulative hazards at time  $t-u$  and  $t$ , respectively, and  $t_u$  is the cycle from  $t-u$  to  $t$ .

The treatment effects of statin ( $tx$ ) are calculated as:  $tx = \exp[ALR * \ln(RR)]$ , where  $RR$  is the rate ratio per 1 mmol/L LDL-C reduction with statin (see Table 1 in the manuscript) and  $ALR$  is the absolute LDL-C reduction with the statin therapy, which is product of pre-treatment LDL-C level and the proportional reduction in LDL-C with corresponding statin regimen (see Supplementary Table 1). It has been previously shown that the absolute reductions in LDL-C (in mmol/l) were greater in individuals with higher pre-treatment LDL-C concentrations and the percentage reductions were independent of pre-treatment concentrations and therefore more generalizable.<sup>13</sup>

The transition probabilities for events with statin treatment ( $tp_{tx}$ ) in each cycle of the model is calculated as:

$$tp_{tx}(t_u) = 1 - \exp[H(t-u) - H(t)]^{tx}$$

The excess rates on myopathy and rhabdomyolysis of statin treatment (see Table 1 in the manuscript) were applied as constant annual rate each year on statin treatment in the model.

## Specification of sensitivity and scenario analyses

**Supplementary methods table 3: Sensitivity analyses parameterisation in the model**

Scenario	Parameters
<b>Relative risk reduction in cardiovascular events with statin therapy increase/decrease annually</b>	Increase: further 1.5% relative risk reduction per 1 mmol/L reduction of LDL-C <sup>14</sup> added each year from year 6 onwards. Decrease: Relative risk reduction (RRR) reduced by 5% each year from year 6 onwards. Lifetime statin use and statin costs retained in simulations.
<b>Reduced statin treatment effects on cardiovascular events in the elderly</b>	Rate ratios (RR) per 1mmol/L LDL-C reduction based on effects only among participants >75 years of age in the Cholesterol Treatment Trialists' individual participant data meta-analysis <sup>10</sup> were applied in people from 76 years of age onward in model simulation. The applied effects were: Myocardial infarction: Major coronary event RR 0.82 (99% confidence interval (CI) 0.70–0.96) Stroke: RR 0.89 (99% CI 0.71, 1.10) Coronary revascularisation procedure: RR 1.02 (99% CI 0.75, 1.40) Vascular death: RR 0.95 (99% CI 0.83, 1.07)
<b>LDL reduction with statin therapy lower than expected</b>	Proportional reduction in LDL-C with statin therapy assumed 80% of expected reduction described in Supplementary table 1.
<b>Vary statin treatment effect on cancer incidence</b>	Rate ratio (RR) of 0.96 or 1.05, respectively, applied for incident cancer with statin therapy based on 95% confidence interval of the Cholesterol Treatment

	Trialists' individual participant data meta-analysis reporting RR of 1.00 [95% CI 0.96-1.05]. <sup>15</sup>
<b>Real-world compliance with statin therapy</b>	Using observed statin discontinuation and restarting rates for the first discontinuation and first restarting <sup>16</sup> , the derived probabilities of complying with statin therapy (Supplementary methods table 3) were applied to each individual in the respective years in model simulation. Both statin effects and costs discontinued with no statin use.
<b>Quality of life disutilities of daily statin pill</b>	0.001, 0.002 or 0.003 QALYs were deducted each year in the model <sup>17</sup>
<b>Quality of life disutilities of cardiovascular events</b>	50% or 150% of base-case decrements in quality of life related to cardiovascular events were applied
<b>Quality of life disutilities of diabetes</b>	Apply 50% of basecase decrement in quality of life related to diabetes
<b>Discount rates for costs and outcomes of 1.5%</b>	Annual discount rates to 1.5% were used for costs and QALYs (instead of the 3.5% base-case rates) <sup>18</sup>
<b>Include healthcare costs only for cardiovascular disease and incident diabetes</b>	Healthcare costs associated with cardiovascular disease and incident diabetes only included (i.e., unrelated healthcare costs were excluded).
<b>Increased cost of statin therapy</b>	The base-case costs of statin therapy increased 1.5, 2 or 5 times.
<b>Including variability around the proportional reductions in LDL-C with statin therapies</b>	The % LDL-C reductions sampled from normal distributions with mean 43% (standard deviation 14.5%) for standard statin and mean 55% (standard deviation 17.3%) for higher intensity statin therapy with standard deviations sourced from meta-analysis <sup>19</sup> .

**Supplementary methods table 4: Probabilities for first discontinuation and first restarting of statin treatment and the derived probabilities of compliance with statin therapy over the first 10 years**

Year	Cumulative probability (%)		On statin treatment (%)	
	Discontinuation	Restarting	On	Off
1	30%	50%	70%	30%
2	38%	59%	77%	23%
3	43%	64%	79%	21%
4	47%	68%	80%	20%
5	50%	70%	81%	19%
6	52%	72%	81%	19%
7	54%	74%	82%	18%
8	56%	76%	82%	18%
9	58%	77%	83%	17%
10	60%	79%	83%	17%

The first two columns present cumulative probabilities for the first discontinuation and first restarting of statin treatment<sup>16</sup>, followed by the derived compliance with statin treatment in first 10 years of treatment.

**Supplementary Table 1: Proportional reductions in LDL cholesterol with statin regimens**

<b>Dose (mg/day)</b>	<b>% reduction in LDL cholesterol<sup>1</sup></b>				
	<b>5mg</b>	<b>10mg</b>	<b>20mg</b>	<b>40mg</b>	<b>80mg</b>
Fluvastatin	10%	15%	21%	27%	33%
Pravastatin	15%	20%	24%	29%	33%
Simvastatin	23%	27%	32%	37%	42%
Atorvastatin	31%	37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	58%

<sup>1</sup>Based on Law et al.<sup>13</sup>

**Supplementary Table 2: Number of UK Biobank participants, by sex, age, history of cardiovascular disease, 10-year cardiovascular risk and LDL cholesterol**

A. By sex, age, history of CVD and 10-year CVD risk

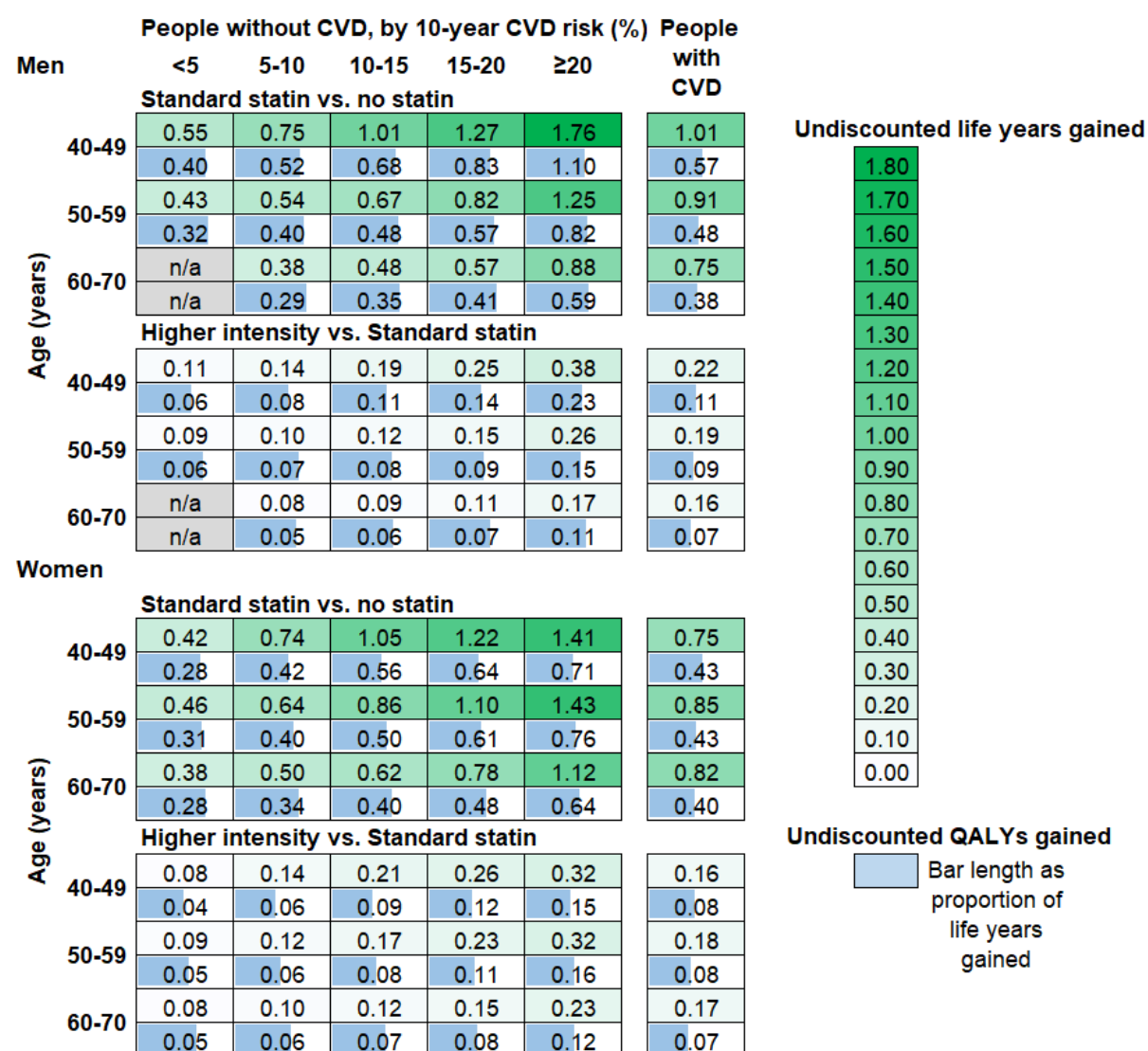
	Without CVD, by 10-year CVD risk (%)					with CVD
	<5	5-10	10-15	15-20	≥20	
Men						
40-49	29,556	14,976	3,415	1,216	1,177	2,798
50-59	3,959	24,290	18,565	8,970	9,035	8,161
60-70	n/a	2,703	14,883	20,150	42,101	22,775
Women						
40-49	57,059	3,447	619	247	419	2,814
50-59	46,336	30,155	6,579	2,128	2,120	6,622
60-70	3,394	36,730	31,390	15,194	13,763	14,108

B. By sex, age, LDL cholesterol, history of CVD and 10-year CVD risk

LDL cholesterol (mmol/L)																		
<3.4							3.4-4.1						≥4.1					
Without CVD, by 10-year CVD risk (%)						with CVD	Without CVD, by 10-year CVD risk (%)					with CVD	Without CVD, by 10-year CVD risk (%)					with CVD
<5	5-10	10-15	15-20	≥20	<5		5-10	10-15	15-20	≥20	<5		5-10	10-15	15-20	≥20		
Men																		
40-49	13,497	4,037	711	239	228	939	10,436	5,629	1,099	332	289	853	5,623	5,310	1,605	645	660	1,006
50-59	2,281	9,055	4,759	1,847	1,622	2,263	1,255	9,445	7,190	3,079	2,408	2,317	423	5,790	6,616	4,044	5,005	3,581
60-70	n/a	1,535	6,073	6,513	9,113	6,218	n/a	908	5,919	8,003	14,028	6,607	n/a	260 <sup>1</sup>	2,891	5,634	18,960	9,950
Women																		
40-49	32,831	986	146	60	119	1,430	17,285	1,214	178	59	86	827	6,943	1,247	295	128	214	557
50-59	18,843	6,707	1,025	308	366	1,868	17,471	11,228	1,980	540	454	2,109	10,022	12,220	3,574	1,280	1,300	2,645
60-70	1,522	9,822	5,742	1,994	1,589	2,956	1,304	14,829	11,580	4,693	3,039	4,298	568	12,079	14,068	8,507	9,135	6,854

CVD, cardiovascular disease. Categories of participants 40-49 years old at estimated 10-year CVD risk ≥10% combined for the presentation of results. n/a, not applicable.

**Supplementary Figure 1 Life years and QALYs gained with long-term statin therapy, by sex, age and 10-year cardiovascular risk**



QALY, quality-adjusted life year; CVD, cardiovascular disease; n/a, not applicable.

**Supplementary Figure 2 (a) Incremental cost-effectiveness ratios and (b) intervention with the highest probability of being cost-effective in categories of UK Biobank participants by sex, age, and 10-year cardiovascular risk**

**(a) Incremental cost-effectiveness ratios (£/QALY gained)**

		People without CVD, by 10-year CVD risk (%)					with CVD	ICER (£/QALY gained)
		<5	5-10	10-15	15-20	≥20		
<b>Men</b>		<b>Standard statin vs. no statin</b>						
Age (years)	40-49	£2,960	£1,700	£1,200	£1,160	£1,560	£2,820	
	50-59	£3,290	£2,020	£1,380	£1,090	£1,300	£1,990	
	60-70	NA	£2,580	£1,760	£1,360	£1,300	£1,230	£0
		<b>Higher intensity vs. Standard statin</b>						£5,000
Age (years)	40-49	£13,750	£9,560	£6,540	£4,600	£2,890	£6,050	£10,000
	50-59	£11,650	£8,890	£7,220	£5,620	£3,280	£5,110	£15,000
	60-70	NA	£8,540	£6,810	£5,610	£3,560	£3,870	£20,000
<b>Women</b>		<b>Standard statin vs. no statin</b>						£30,000
Age (years)	40-49	£6,390	£4,010	£3,170	£2,820	£3,680	£5,330	
	50-59	£4,330	£3,140	£2,660	£2,410	£2,590	£4,100	
	60-70	£3,690	£2,760	£2,190	£1,890	£1,910	£2,760	
		<b>Higher intensity vs. Standard statin</b>						
Age (years)	40-49	£25,220	£21,780	£11,390	£7,110	£5,950	£9,970	
	50-59	£15,070	£13,450	£11,140	£7,970	£4,850	£8,980	
	60-70	£10,720	£9,600	£8,470	£7,280	£4,940	£7,160	

**(b) Intervention with the highest probability of being cost-effective at £20,000/QALY**

		People without CVD, by 10-year CVD risk (%)					with CVD	Intervention (probability cost-effective shown)
		<5	5-10	10-15	15-20	≥20		
<b>Men</b>								
Age (years)	40-49	0.76	0.87	0.97	1.00	1.00	1.00	
	50-59	0.87	0.93	0.96	0.99	1.00	1.00	
	60-70	n/a	0.98	0.99	0.99	1.00	1.00	
<b>Women</b>								
Age (years)	40-49	0.69	0.54	0.88	1.00	1.00	0.96	
	50-59	0.76	0.78	0.86	0.98	1.00	0.97	
	60-70	0.96	0.96	0.96	0.99	1.00	0.99	

CVD, cardiovascular disease; ICER, Incremental Cost-Effectiveness Ratio (with costs and QALYs discounted at 3.5% per year); QALY, quality-adjusted life years; n/a, not applicable.

**Supplementary Table 3 Undiscounted and discounted life years and QALYs gained with statin therapy and incremental discounted healthcare costs (£)**

LDL-C	Sex	Statin therapy	Age	10-year CVD risk/ with CVD	Life years gained, discounted	Life years gained, undiscounted	QALYs gained, undiscounted	QALYs gained, discounted	Total cost (£), discounted	Incremental hospital care costs (£), discounted	Incremental primary care costs (£), discounted	Statin cost (£), discounted	Statin initiation and monitoring cost (£), discounted
<3.4	men	Standard	40-49	<5	0.38	0.09	0.28	0.07	331	-65	29	304	64
<3.4	men	Standard	40-49	[5,10)	0.46	0.13	0.32	0.09	310	-99	54	288	66
<3.4	men	Standard	40-49	[10,15)	0.64	0.20	0.40	0.13	361	-123	141	273	70
<3.4	men	Standard	40-49	with CVD	0.64	0.22	0.38	0.14	539	-169	158	271	279
<3.4	men	Standard	50-59	<5	0.33	0.09	0.25	0.07	322	-50	23	286	63
<3.4	men	Standard	50-59	[5,10)	0.36	0.11	0.26	0.08	285	-84	31	273	65
<3.4	men	Standard	50-59	[10,15)	0.41	0.13	0.28	0.10	265	-112	50	260	67
<3.4	men	Standard	50-59	[15,20)	0.49	0.17	0.32	0.12	273	-131	84	251	69
<3.4	men	Standard	50-59	≥20	0.62	0.24	0.39	0.16	367	-127	182	239	72
<3.4	men	Standard	50-59	with CVD	0.60	0.26	0.33	0.14	494	-198	213	233	246
<3.4	men	Standard	60-70	[5,10)	0.29	0.10	0.22	0.08	277	-63	23	253	64
<3.4	men	Standard	60-70	[10,15)	0.33	0.12	0.24	0.09	257	-85	34	243	65
<3.4	men	Standard	60-70	[15,20)	0.37	0.15	0.26	0.11	249	-101	51	233	67
<3.4	men	Standard	60-70	≥20	0.47	0.20	0.31	0.14	290	-112	116	216	70
<3.4	men	Standard	60-70	with CVD	0.54	0.27	0.28	0.14	432	-213	230	199	216
<3.4	men	Higher intensity	40-49	<5	0.07	0.02	0.04	0.01	191	-7	37	161	-1
<3.4	men	Higher intensity	40-49	[5,10)	0.09	0.02	0.04	0.01	199	-9	56	153	-1
<3.4	men	Higher intensity	40-49	≥10	0.12	0.04	0.06	0.02	194	-21	71	145	-1
<3.4	men	Higher intensity	40-49	with CVD	0.14	0.05	0.07	0.02	207	-13	76	144	1
<3.4	men	Higher intensity	50-59	<5	0.07	0.02	0.04	0.01	176	-4	29	151	-0
<3.4	men	Higher intensity	50-59	[5,10)	0.07	0.02	0.04	0.01	169	-11	36	144	-1
<3.4	men	Higher intensity	50-59	[10,15)	0.07	0.02	0.04	0.01	169	-16	48	138	-1



<3.4	men	Higher intensity	50-59	[15,20)	0.09	0.03	0.05	0.02	171	-19	58	133	-1
<3.4	men	Higher intensity	50-59	≥20	0.13	0.05	0.08	0.03	165	-26	65	127	-1
<3.4	men	Higher intensity	50-59	with CVD	0.13	0.06	0.06	0.03	191	-17	84	124	1
<3.4	men	Higher intensity	60-70	[5,10)	0.06	0.02	0.04	0.01	151	-8	25	134	-0
<3.4	men	Higher intensity	60-70	[10,15)	0.06	0.02	0.04	0.01	148	-12	32	129	-1
<3.4	men	Higher intensity	60-70	[15,20)	0.07	0.03	0.04	0.02	147	-16	40	123	-1
<3.4	men	Higher intensity	60-70	≥20	0.10	0.04	0.06	0.02	146	-21	53	115	-1
<3.4	men	Higher intensity	60-70	with CVD	0.12	0.06	0.05	0.03	164	-27	83	106	1
<3.4	women	Standard	40-49	<5	0.31	0.06	0.21	0.05	393	-14	31	315	61
<3.4	women	Standard	40-49	[5,10)	0.45	0.11	0.25	0.07	441	-12	95	294	64
<3.4	women	Standard	40-49	≥10	0.53	0.15	0.28	0.09	512	-1	162	286	65
<3.4	women	Standard	40-49	with CVD	0.58	0.16	0.35	0.10	670	-25	109	291	296
<3.4	women	Standard	50-59	<5	0.32	0.08	0.22	0.06	362	-28	33	295	62
<3.4	women	Standard	50-59	[5,10)	0.38	0.11	0.24	0.07	378	-28	63	281	63
<3.4	women	Standard	50-59	[10,15)	0.46	0.14	0.26	0.08	419	-25	112	267	65
<3.4	women	Standard	50-59	[15,20)	0.57	0.18	0.30	0.10	445	-43	154	268	67
<3.4	women	Standard	50-59	≥20	0.61	0.20	0.32	0.11	516	-26	216	259	68
<3.4	women	Standard	50-59	with CVD	0.61	0.21	0.33	0.12	661	-41	165	265	273
<3.4	women	Standard	60-70	<5	0.28	0.08	0.20	0.06	314	-49	24	277	62
<3.4	women	Standard	60-70	[5,10)	0.32	0.10	0.22	0.07	319	-53	42	267	63
<3.4	women	Standard	60-70	[10,15)	0.36	0.12	0.23	0.08	330	-56	66	255	64
<3.4	women	Standard	60-70	[15,20)	0.42	0.15	0.26	0.10	351	-58	98	246	66
<3.4	women	Standard	60-70	≥20	0.51	0.19	0.28	0.12	398	-72	166	235	68
<3.4	women	Standard	60-70	with CVD	0.61	0.25	0.30	0.12	628	-70	216	235	248
<3.4	women	Higher intensity	40-49	<5	0.06	0.01	0.03	0.01	199	4	29	167	-0
<3.4	women	Higher intensity	40-49	[5,10)	0.08	0.02	0.03	0.01	240	16	68	155	-0
<3.4	women	Higher intensity	40-49	≥10	0.12	0.03	0.06	0.02	221	11	59	151	-0
<3.4	women	Higher intensity	40-49	with CVD	0.13	0.04	0.07	0.02	214	9	50	154	0
<3.4	women	Higher intensity	50-59	<5	0.06	0.01	0.04	0.01	187	1	30	156	-0
<3.4	women	Higher intensity	50-59	[5,10)	0.07	0.02	0.03	0.01	206	8	51	148	-0

<3.4	women	Higher intensity	50-59	[10,15)	0.09	0.03	0.04	0.01	224	13	71	141	-1
<3.4	women	Higher intensity	50-59	[15,20)	0.13	0.04	0.06	0.02	208	1	65	142	-1
<3.4	women	Higher intensity	50-59	≥20	0.15	0.05	0.08	0.03	198	1	60	137	-1
<3.4	women	Higher intensity	50-59	with CVD	0.14	0.04	0.06	0.02	227	15	70	141	1
<3.4	women	Higher intensity	60-70	<5	0.06	0.02	0.04	0.01	162	-6	22	147	-0
<3.4	women	Higher intensity	60-70	[5,10)	0.06	0.02	0.04	0.01	174	-2	35	141	-0
<3.4	women	Higher intensity	60-70	[10,15)	0.07	0.02	0.04	0.01	187	3	50	135	-0
<3.4	women	Higher intensity	60-70	[15,20)	0.08	0.03	0.04	0.01	197	6	62	130	-1
<3.4	women	Higher intensity	60-70	≥20	0.11	0.04	0.06	0.02	178	-6	60	125	-1
<3.4	women	Higher intensity	60-70	with CVD	0.14	0.05	0.06	0.02	230	17	87	125	1
3.4-4.1	men	Standard	40-49	<5	0.58	0.14	0.43	0.11	287	-116	32	306	65
3.4-4.1	men	Standard	40-49	[5,10)	0.67	0.18	0.46	0.13	266	-154	60	293	67
3.4-4.1	men	Standard	40-49	≥10	0.89	0.28	0.58	0.19	328	-180	160	277	71
3.4-4.1	men	Standard	40-49	with CVD	0.89	0.32	0.52	0.19	556	-223	234	269	276
3.4-4.1	men	Standard	50-59	<5	0.50	0.14	0.38	0.11	284	-95	26	289	64
3.4-4.1	men	Standard	50-59	[5,10)	0.54	0.16	0.40	0.12	249	-130	36	277	66
3.4-4.1	men	Standard	50-59	[10,15)	0.60	0.19	0.42	0.14	233	-158	57	266	68
3.4-4.1	men	Standard	50-59	[15,20)	0.68	0.24	0.46	0.17	237	-180	91	257	69
3.4-4.1	men	Standard	50-59	≥20	0.86	0.33	0.54	0.22	355	-172	211	243	73
3.4-4.1	men	Standard	50-59	with CVD	0.78	0.33	0.43	0.18	416	-321	250	238	249
3.4-4.1	men	Standard	60-70	[5,10)	0.45	0.15	0.34	0.12	252	-98	28	258	64
3.4-4.1	men	Standard	60-70	[10,15)	0.50	0.18	0.37	0.14	227	-127	39	249	66
3.4-4.1	men	Standard	60-70	[15,20)	0.54	0.21	0.39	0.16	212	-150	56	239	67
3.4-4.1	men	Standard	60-70	≥20	0.67	0.28	0.45	0.20	278	-145	130	223	70
3.4-4.1	men	Standard	60-70	with CVD	0.68	0.34	0.36	0.18	313	-365	255	203	219
3.4-4.1	men	Higher intensity	40-49	<5	0.11	0.03	0.07	0.02	188	-16	43	162	-1
3.4-4.1	men	Higher intensity	40-49	[5,10)	0.12	0.03	0.07	0.02	193	-22	61	155	-1
3.4-4.1	men	Higher intensity	40-49	≥10	0.17	0.05	0.09	0.03	197	-31	82	147	-1
3.4-4.1	men	Higher intensity	40-49	with CVD	0.20	0.07	0.10	0.04	224	-16	96	143	1
3.4-4.1	men	Higher intensity	50-59	<5	0.10	0.03	0.07	0.02	172	-13	33	153	-1

3.4-4.1	men	Higher intensity	50-59	[5,10)	0.10	0.03	0.07	0.02	168	-18	40	147	-1
3.4-4.1	men	Higher intensity	50-59	[10,15)	0.11	0.03	0.06	0.02	169	-24	53	141	-1
3.4-4.1	men	Higher intensity	50-59	[15,20)	0.12	0.04	0.07	0.02	172	-28	65	136	-1
3.4-4.1	men	Higher intensity	50-59	≥20	0.18	0.07	0.10	0.04	179	-34	85	130	-1
3.4-4.1	men	Higher intensity	50-59	with CVD	0.17	0.07	0.08	0.03	191	-36	100	127	1
3.4-4.1	men	Higher intensity	60-70	[5,10)	0.09	0.03	0.06	0.02	150	-12	26	137	-1
3.4-4.1	men	Higher intensity	60-70	[10,15)	0.10	0.03	0.06	0.02	146	-19	34	132	-1
3.4-4.1	men	Higher intensity	60-70	[15,20)	0.10	0.04	0.07	0.02	144	-23	42	127	-1
3.4-4.1	men	Higher intensity	60-70	≥20	0.13	0.05	0.08	0.03	151	-28	61	119	-1
3.4-4.1	men	Higher intensity	60-70	with CVD	0.14	0.07	0.07	0.03	146	-55	91	109	1
3.4-4.1	women	Standard	40-49	<5	0.49	0.10	0.32	0.07	398	-27	49	316	61
3.4-4.1	women	Standard	40-49	[5,10)	0.64	0.16	0.35	0.09	455	-27	123	296	64
3.4-4.1	women	Standard	40-49	≥10	0.87	0.24	0.44	0.13	603	1	247	289	66
3.4-4.1	women	Standard	40-49	with CVD	0.77	0.22	0.45	0.14	668	-65	150	289	294
3.4-4.1	women	Standard	50-59	<5	0.47	0.12	0.32	0.08	359	-45	45	297	62
3.4-4.1	women	Standard	50-59	[5,10)	0.54	0.15	0.34	0.10	377	-50	80	284	64
3.4-4.1	women	Standard	50-59	[10,15)	0.65	0.20	0.37	0.12	435	-40	138	271	65
3.4-4.1	women	Standard	50-59	[15,20)	0.76	0.24	0.41	0.14	485	-37	192	264	67
3.4-4.1	women	Standard	50-59	≥20	0.89	0.30	0.45	0.16	618	-21	311	259	69
3.4-4.1	women	Standard	50-59	with CVD	0.77	0.26	0.41	0.15	631	-108	201	265	273
3.4-4.1	women	Standard	60-70	<5	0.42	0.12	0.30	0.09	314	-64	35	281	62
3.4-4.1	women	Standard	60-70	[5,10)	0.46	0.14	0.31	0.10	313	-76	54	272	63
3.4-4.1	women	Standard	60-70	[10,15)	0.52	0.18	0.34	0.12	320	-85	80	260	65
3.4-4.1	women	Standard	60-70	[15,20)	0.59	0.21	0.36	0.14	351	-82	117	251	66
3.4-4.1	women	Standard	60-70	≥20	0.71	0.27	0.40	0.16	437	-76	207	239	68
3.4-4.1	women	Standard	60-70	with CVD	0.74	0.29	0.37	0.15	546	-175	229	240	252
3.4-4.1	women	Higher intensity	40-49	<5	0.10	0.02	0.05	0.01	213	5	41	167	-0
3.4-4.1	women	Higher intensity	40-49	[5,10)	0.11	0.03	0.04	0.01	254	14	84	157	-1
3.4-4.1	women	Higher intensity	40-49	≥10	0.19	0.05	0.08	0.02	272	19	100	153	-1
3.4-4.1	women	Higher intensity	40-49	with CVD	0.17	0.05	0.09	0.02	231	11	66	153	1

3.4-4.1	women	Higher intensity	50-59	<5	0.10	0.02	0.06	0.01	194	1	37	157	-0
3.4-4.1	women	Higher intensity	50-59	[5,10)	0.10	0.03	0.05	0.01	216	7	59	151	-1
3.4-4.1	women	Higher intensity	50-59	[10,15)	0.12	0.04	0.05	0.01	240	14	83	144	-1
3.4-4.1	women	Higher intensity	50-59	[15,20)	0.16	0.05	0.07	0.02	245	14	92	140	-1
3.4-4.1	women	Higher intensity	50-59	≥20	0.20	0.06	0.10	0.03	228	-0	92	138	-1
3.4-4.1	women	Higher intensity	50-59	with CVD	0.17	0.05	0.08	0.03	233	9	83	141	1
3.4-4.1	women	Higher intensity	60-70	<5	0.09	0.03	0.06	0.02	166	-7	25	149	-0
3.4-4.1	women	Higher intensity	60-70	[5,10)	0.09	0.03	0.05	0.02	178	-5	40	144	-1
3.4-4.1	women	Higher intensity	60-70	[10,15)	0.10	0.03	0.06	0.02	191	-1	54	138	-1
3.4-4.1	women	Higher intensity	60-70	[15,20)	0.12	0.04	0.06	0.02	205	2	70	133	-1
3.4-4.1	women	Higher intensity	60-70	≥20	0.15	0.06	0.08	0.03	205	-2	80	127	-1
3.4-4.1	women	Higher intensity	60-70	with CVD	0.16	0.06	0.07	0.03	214	-6	91	128	1
≥4.1	men	Standard	40-49	<5	0.89	0.22	0.65	0.16	228	-183	37	308	66
≥4.1	men	Standard	40-49	[5,10)	1.05	0.29	0.74	0.21	190	-240	66	296	69
≥4.1	men	Standard	40-49	≥10	1.64	0.54	1.09	0.37	353	-267	266	279	74
≥4.1	men	Standard	40-49	with CVD	1.45	0.58	0.78	0.31	717	-319	507	260	269
≥4.1	men	Standard	50-59	<5	0.73	0.20	0.55	0.16	254	-132	30	292	65
≥4.1	men	Standard	50-59	[5,10)	0.82	0.25	0.60	0.19	196	-195	43	281	67
≥4.1	men	Standard	50-59	[10,15)	0.94	0.31	0.67	0.23	178	-232	70	271	69
≥4.1	men	Standard	50-59	[15,20)	1.09	0.37	0.76	0.27	188	-256	111	262	71
≥4.1	men	Standard	50-59	≥20	1.65	0.65	1.09	0.44	491	-193	360	248	76
≥4.1	men	Standard	50-59	with CVD	1.19	0.54	0.60	0.27	381	-547	453	231	244
≥4.1	men	Standard	60-70	[5,10)	0.67	0.23	0.50	0.18	265	-105	44	261	65
≥4.1	men	Standard	60-70	[10,15)	0.75	0.27	0.55	0.20	199	-173	52	254	67
≥4.1	men	Standard	60-70	[15,20)	0.84	0.32	0.60	0.23	198	-191	74	246	68
≥4.1	men	Standard	60-70	≥20	1.23	0.53	0.83	0.37	409	-130	239	227	73
≥4.1	men	Standard	60-70	with CVD	0.92	0.46	0.46	0.23	66	-697	342	202	219
≥4.1	men	Higher intensity	40-49	<5	0.17	0.04	0.11	0.02	184	-26	48	163	-1
≥4.1	men	Higher intensity	40-49	[5,10)	0.20	0.05	0.12	0.03	184	-37	65	157	-1
≥4.1	men	Higher intensity	40-49	≥10	0.33	0.10	0.20	0.06	211	-47	111	149	-2

≥4.1	men	Higher intensity	40-49	with CVD	0.31	0.12	0.15	0.06	279	-27	165	140	2
≥4.1	men	Higher intensity	50-59	<5	0.15	0.04	0.10	0.03	170	-16	32	155	-1
≥4.1	men	Higher intensity	50-59	[5,10)	0.16	0.05	0.10	0.03	163	-29	44	149	-1
≥4.1	men	Higher intensity	50-59	[10,15)	0.18	0.06	0.11	0.04	164	-37	58	144	-1
≥4.1	men	Higher intensity	50-59	[15,20)	0.20	0.07	0.13	0.04	164	-45	71	140	-2
≥4.1	men	Higher intensity	50-59	≥20	0.33	0.12	0.20	0.08	208	-42	119	133	-2
≥4.1	men	Higher intensity	50-59	with CVD	0.25	0.11	0.11	0.05	197	-75	146	124	1
≥4.1	men	Higher intensity	60-70	[5,10)	0.14	0.05	0.10	0.03	155	-13	30	139	-1
≥4.1	men	Higher intensity	60-70	[10,15)	0.15	0.05	0.10	0.04	143	-29	38	135	-1
≥4.1	men	Higher intensity	60-70	[15,20)	0.16	0.06	0.10	0.04	141	-35	46	131	-1
≥4.1	men	Higher intensity	60-70	≥20	0.24	0.10	0.15	0.06	175	-30	85	122	-2
≥4.1	men	Higher intensity	60-70	with CVD	0.19	0.10	0.08	0.04	110	-115	115	109	1
≥4.1	women	Standard	40-49	<5	0.76	0.16	0.49	0.11	384	-64	71	316	62
≥4.1	women	Standard	40-49	[5,10)	1.08	0.28	0.61	0.16	445	-83	164	299	65
≥4.1	women	Standard	40-49	≥10	1.71	0.52	0.89	0.28	716	-67	427	288	69
≥4.1	women	Standard	40-49	with CVD	1.18	0.39	0.59	0.20	881	-52	372	277	284
≥4.1	women	Standard	50-59	<5	0.70	0.18	0.48	0.13	346	-78	62	299	63
≥4.1	women	Standard	50-59	[5,10)	0.86	0.24	0.54	0.16	355	-104	107	288	64
≥4.1	women	Standard	50-59	[10,15)	1.10	0.33	0.65	0.20	420	-108	184	277	66
≥4.1	women	Standard	50-59	[15,20)	1.37	0.44	0.77	0.26	507	-108	277	269	68
≥4.1	women	Standard	50-59	≥20	1.85	0.66	0.99	0.37	825	-54	547	260	72
≥4.1	women	Standard	50-59	with CVD	1.09	0.40	0.52	0.20	659	-228	359	259	268
≥4.1	women	Standard	60-70	<5	0.59	0.17	0.43	0.13	303	-87	44	284	62
≥4.1	women	Standard	60-70	[5,10)	0.70	0.22	0.47	0.16	297	-115	73	276	64
≥4.1	women	Standard	60-70	[10,15)	0.81	0.27	0.53	0.18	297	-142	108	266	65
≥4.1	women	Standard	60-70	[15,20)	0.97	0.34	0.60	0.22	330	-152	158	258	67
≥4.1	women	Standard	60-70	≥20	1.36	0.52	0.78	0.31	525	-122	331	246	69
≥4.1	women	Standard	60-70	with CVD	0.96	0.40	0.45	0.19	336	-456	303	238	250
≥4.1	women	Higher intensity	40-49	<5	0.15	0.03	0.08	0.02	226	4	55	167	-1
≥4.1	women	Higher intensity	40-49	[5,10)	0.21	0.05	0.09	0.02	267	11	99	159	-1

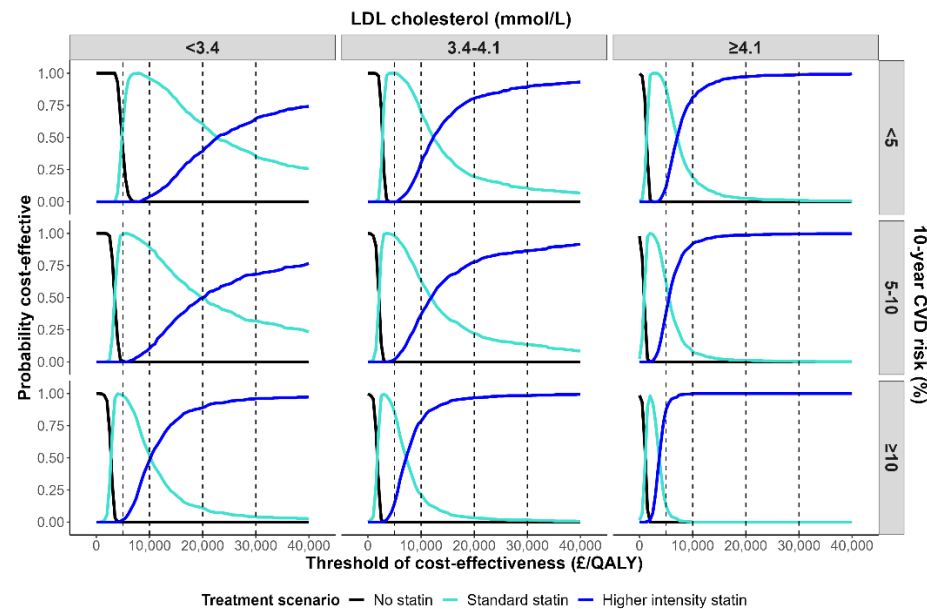
≥4.1	women	Higher intensity	40-49	≥10	0.36	0.10	0.17	0.05	291	8	131	154	-2
≥4.1	women	Higher intensity	40-49	with CVD	0.24	0.08	0.11	0.04	309	33	127	148	1
≥4.1	women	Higher intensity	50-59	<5	0.14	0.03	0.08	0.02	200	-2	44	158	-1
≥4.1	women	Higher intensity	50-59	[5,10)	0.17	0.04	0.09	0.02	222	0	69	153	-1
≥4.1	women	Higher intensity	50-59	[10,15)	0.21	0.06	0.11	0.03	255	7	101	148	-1
≥4.1	women	Higher intensity	50-59	[15,20)	0.27	0.08	0.13	0.04	277	12	123	144	-1
≥4.1	women	Higher intensity	50-59	≥20	0.40	0.13	0.20	0.07	293	3	151	140	-2
≥4.1	women	Higher intensity	50-59	with CVD	0.22	0.08	0.09	0.03	260	-3	124	138	1
≥4.1	women	Higher intensity	60-70	<5	0.13	0.04	0.08	0.02	172	-6	28	150	-1
≥4.1	women	Higher intensity	60-70	[5,10)	0.14	0.04	0.09	0.03	182	-9	46	146	-1
≥4.1	women	Higher intensity	60-70	[10,15)	0.16	0.05	0.09	0.03	196	-9	64	141	-1
≥4.1	women	Higher intensity	60-70	[15,20)	0.19	0.07	0.10	0.04	211	-7	82	137	-1
≥4.1	women	Higher intensity	60-70	≥20	0.28	0.10	0.15	0.06	240	-6	116	132	-1
≥4.1	women	Higher intensity	60-70	with CVD	0.19	0.08	0.08	0.03	182	-56	109	127	1

CVD, cardiovascular disease; LDL-C, low density lipoprotein cholesterol; QALY, Quality Adjusted Life Year

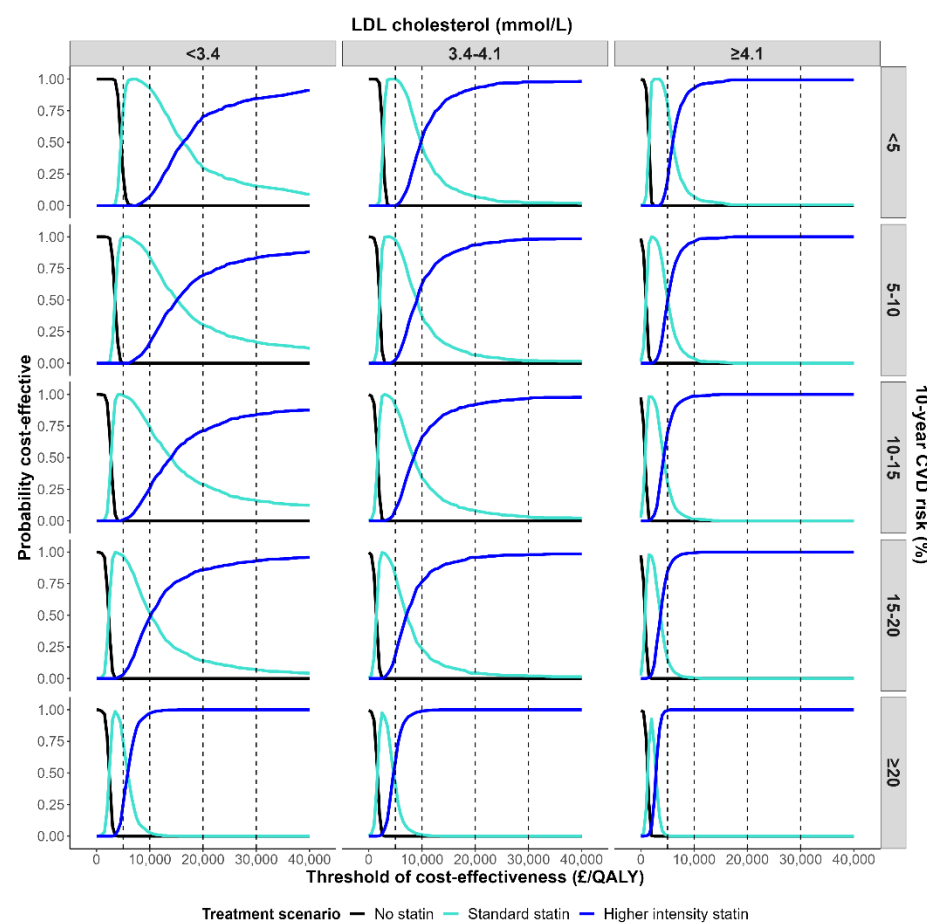
## Supplementary Figure 3 Probability of statin therapy being cost-effective at different thresholds of cost-effectiveness (£/QALY)

### A. People without history of cardiovascular disease

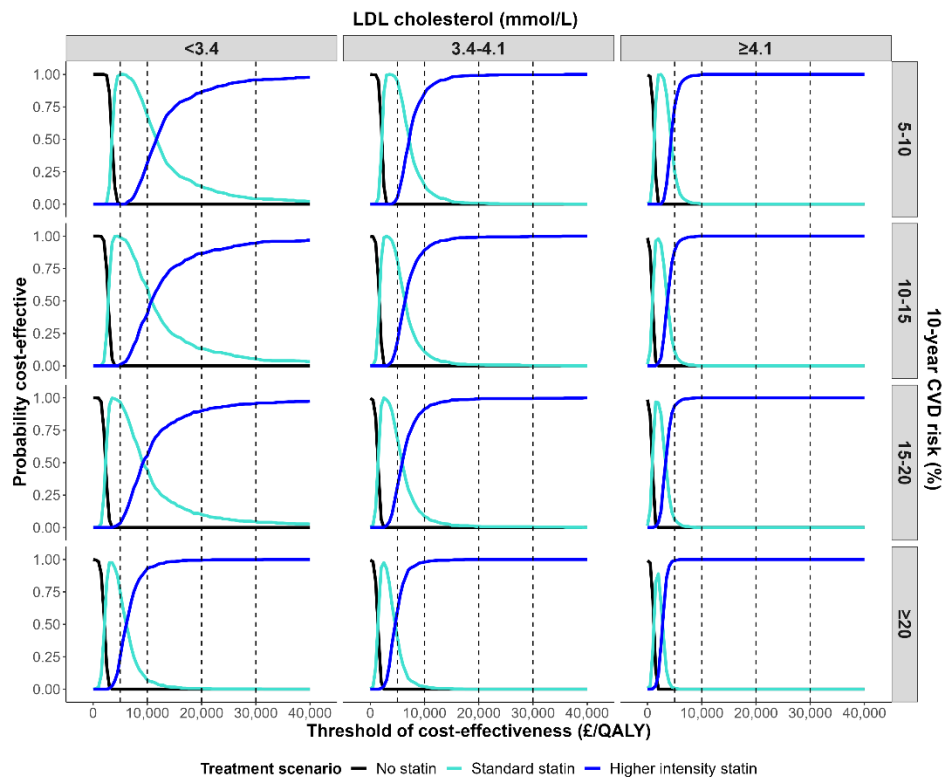
#### A1. Men 40-49 years old



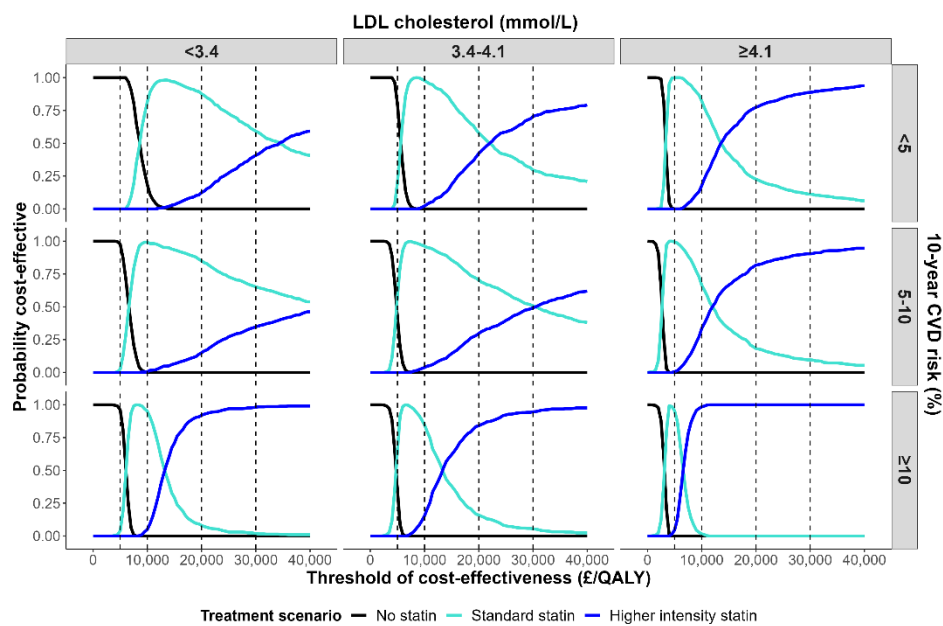
#### A2. Men 50-59 years old



### A3. Men 60-70 years old

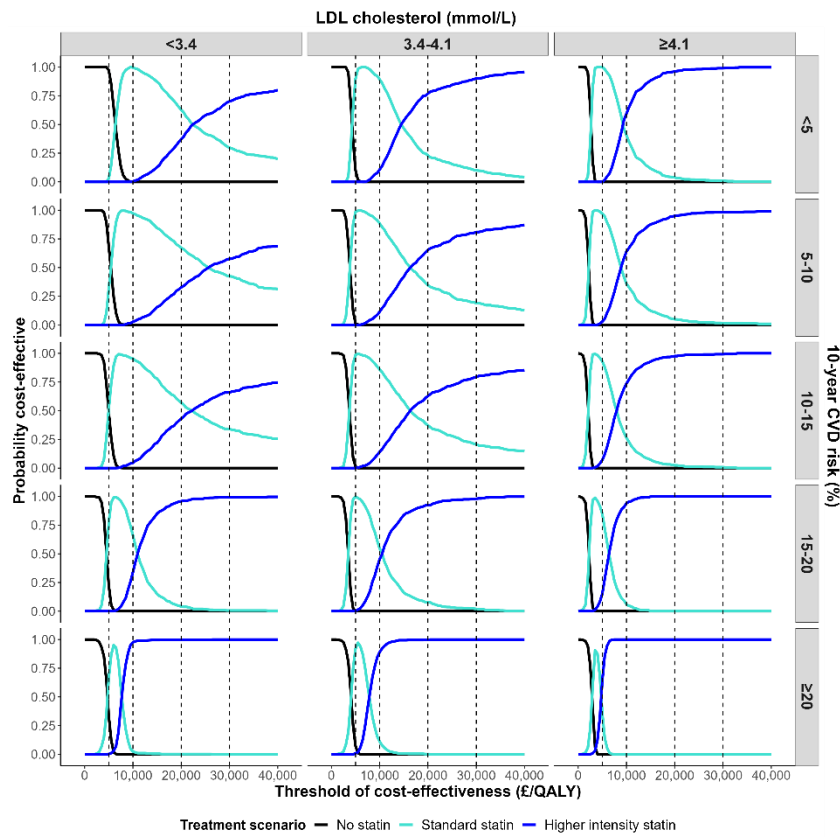


### A4. Women 40-49 years old

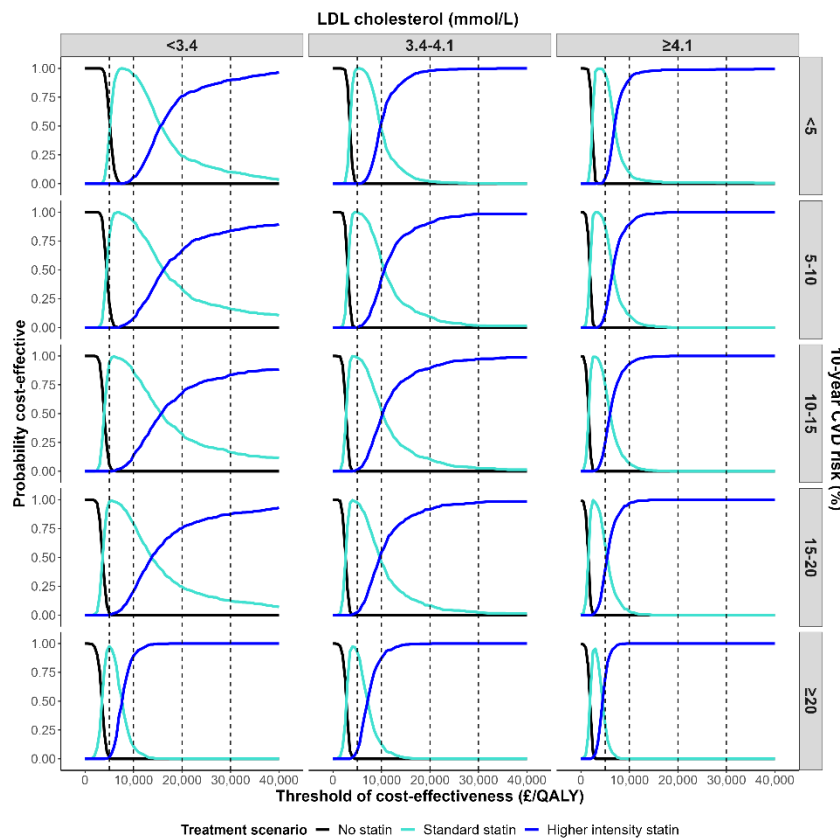




## A5. Women 50-59 years old

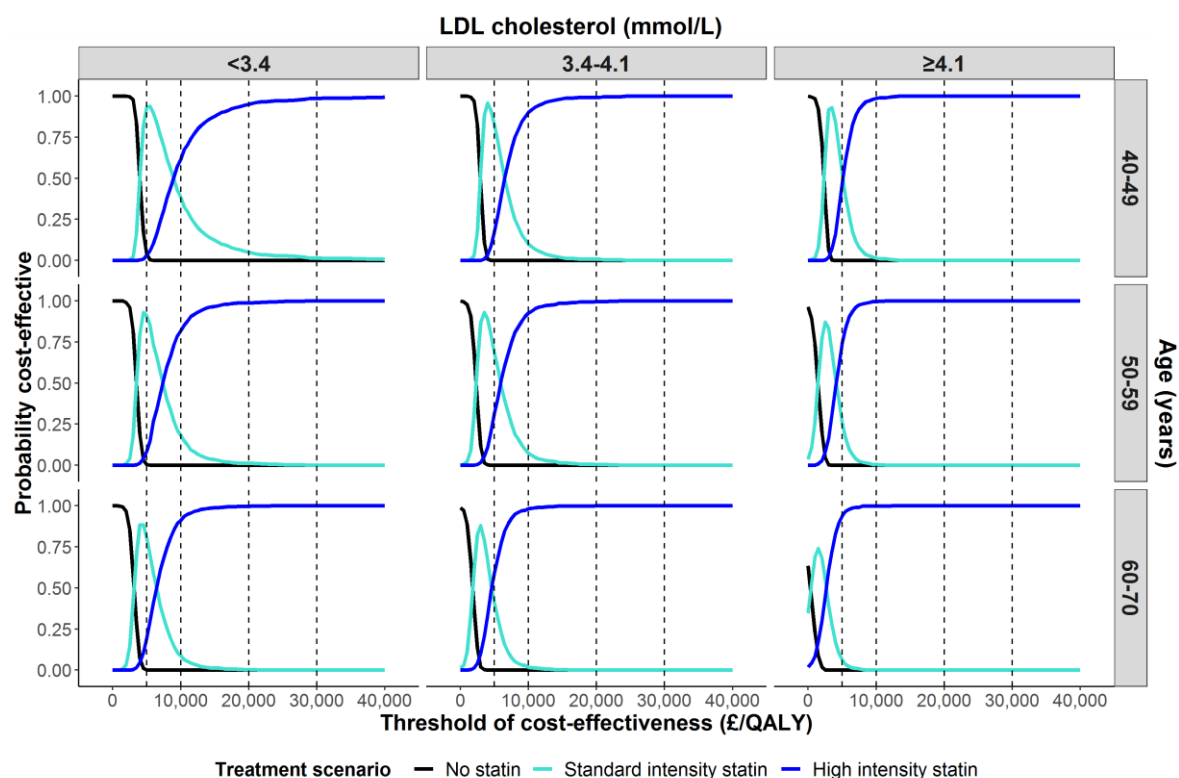


## A6. Women 60-70 years old

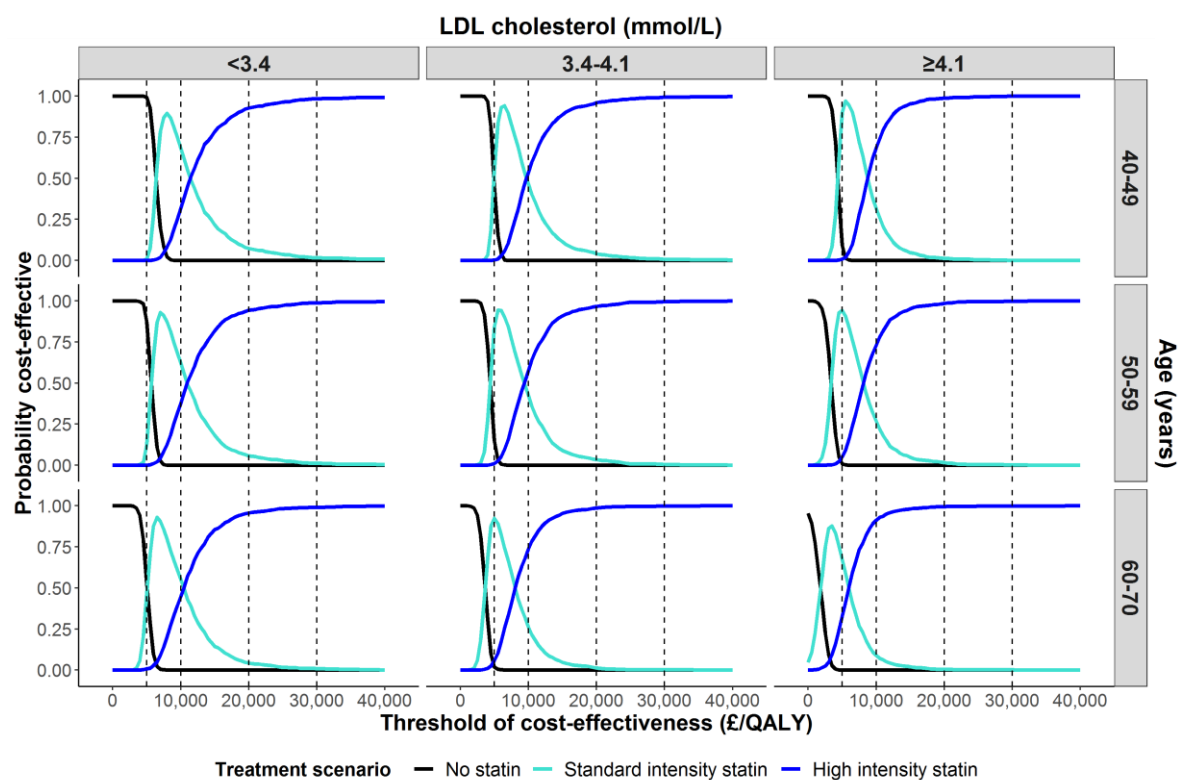


## B. People with history of CVD

### B1. Men



### B2. Women



LDL, low density lipoprotein; CVD, cardiovascular disease; QALY, quality-adjusted life year.

**Supplementary Table 4 Impact of excess new diabetes due to statin therapy on QALYs gained**

**A. In people without history of cardiovascular disease and without diabetes at baseline**

Sex, CVD risk	Men, high	Men, moderate	Women, high	Women, moderate
Age (years)	60-70	40-49	60-70	40-49
10-year CVD (%)	15-20	5-10	15-20	5-10
LDL cholesterol (mmol/L)	≥4.1	<3.4	≥4.1	<3.4
<b>QALYs gained (undiscounted) with Standard statin vs No statin</b>				
Base-case (with excess diabetes)	0.60	0.31	0.60	0.24
Without excess diabetes	0.62	0.34	0.63	0.27
<b>QALYs lost due to excess diabetes with statin</b>	<b>-0.02</b>	<b>-0.03</b>	<b>-0.02</b>	<b>-0.03</b>
<b>QALYs gained (undiscounted) with Higher intensity vs Standard statin</b>				
Base-case (with excess diabetes)	0.10	0.04	0.10	0.02
Without excess diabetes	0.14	0.09	0.14	0.07
<b>QALYs lost due to excess diabetes with statin</b>	<b>-0.03</b>	<b>-0.05</b>	<b>-0.03</b>	<b>-0.05</b>

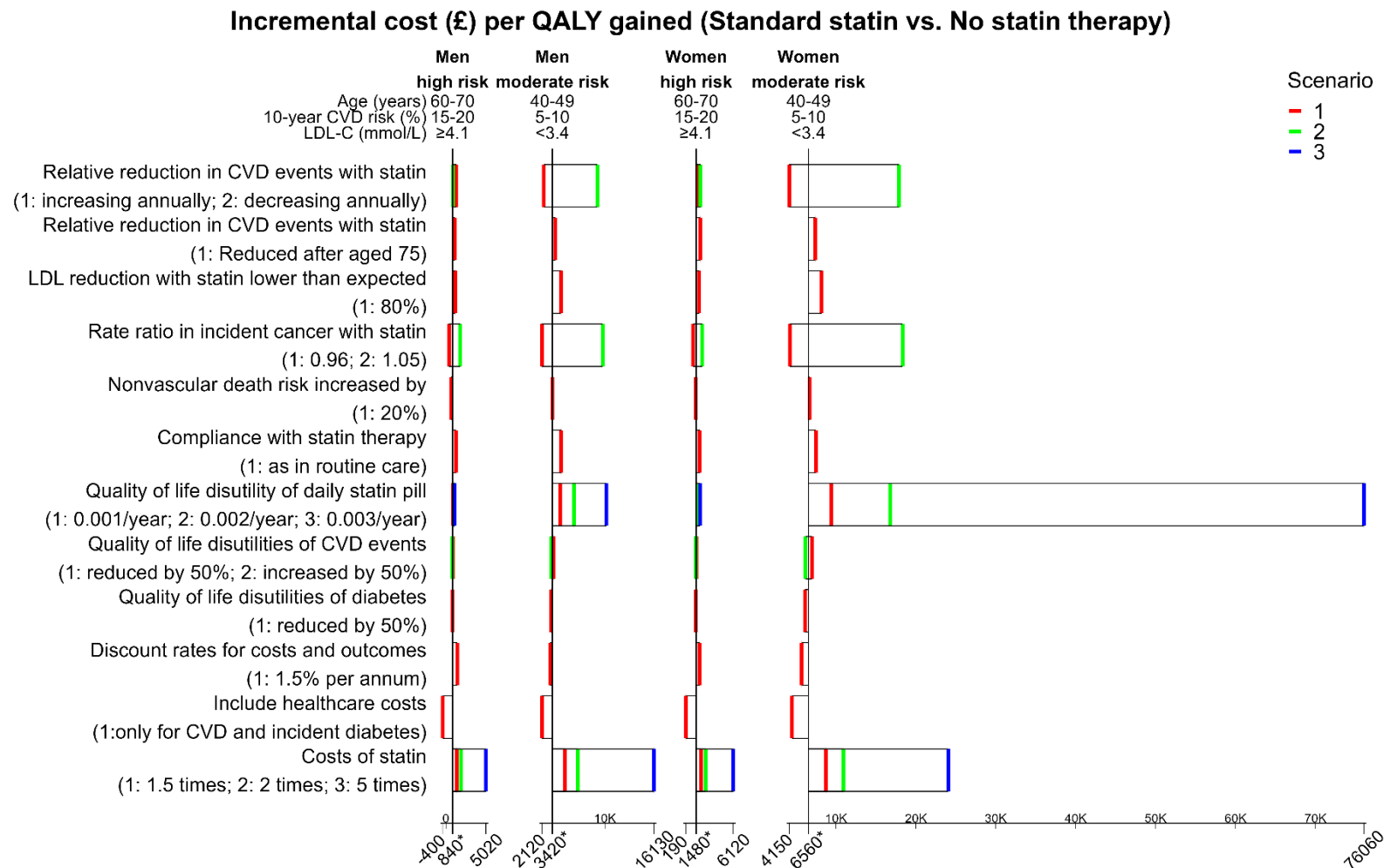
**B. In people with history of cardiovascular disease and without diabetes at baseline**

Sex, CVD risk	Men, very high	Men, high	Women, very high	Women, high
Age (years)	60-70	40-49	60-70	40-49
LDL cholesterol (mmol/L)	≥4.1	<3.4	≥4.1	<3.4
<b>QALYs gained (undiscounted) with Standard statin vs No statin</b>				
Base-case (with excess diabetes)	0.46	0.38	0.46	0.35
Without excess diabetes	0.48	0.41	0.48	0.37
<b>QALYs lost due to excess diabetes with statin</b>	<b>-0.02</b>	<b>-0.03</b>	<b>-0.02</b>	<b>-0.02</b>
<b>QALYs gained (undiscounted) with Higher intensity vs Standard statin</b>				
Base-case (with excess diabetes)	0.08	0.07	0.07	0.07
Without excess diabetes	0.11	0.11	0.11	0.10
<b>QALYs lost due to excess diabetes with statin</b>	<b>-0.03</b>	<b>-0.04</b>	<b>-0.04</b>	<b>-0.03</b>

LDL, low density lipoprotein; QALY, quality-adjusted life year.

## Supplementary Figure 4 Sensitivity analyses of cost-effectiveness of standard statin versus no statin therapy

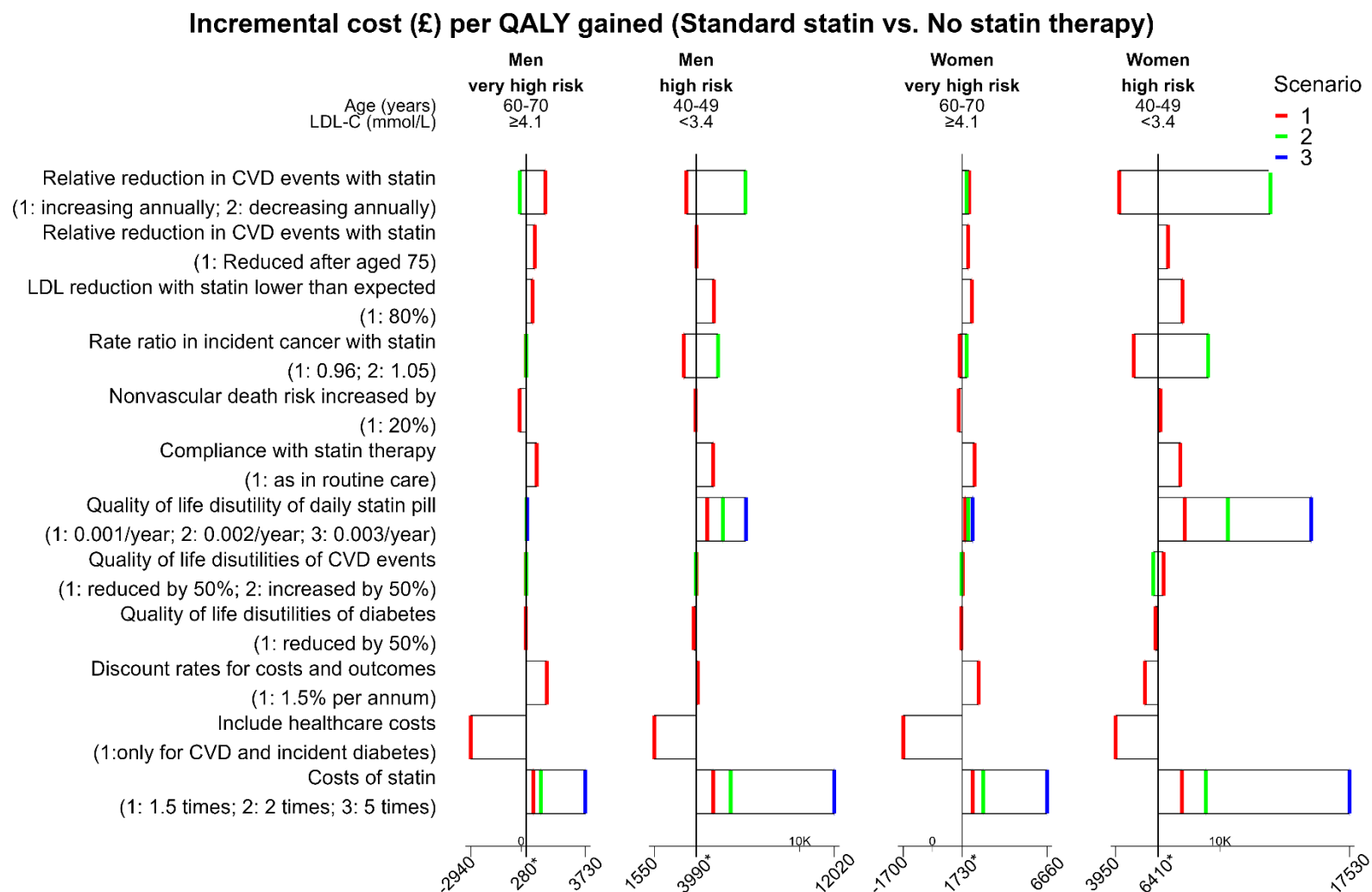
(a) People without history of cardiovascular disease



\*Incremental cost per QALY in base-case cost-effectiveness analysis.

CVD, cardiovascular disease; LDL-C, low density lipoprotein cholesterol; QALY, Quality-Adjusted Life Year.

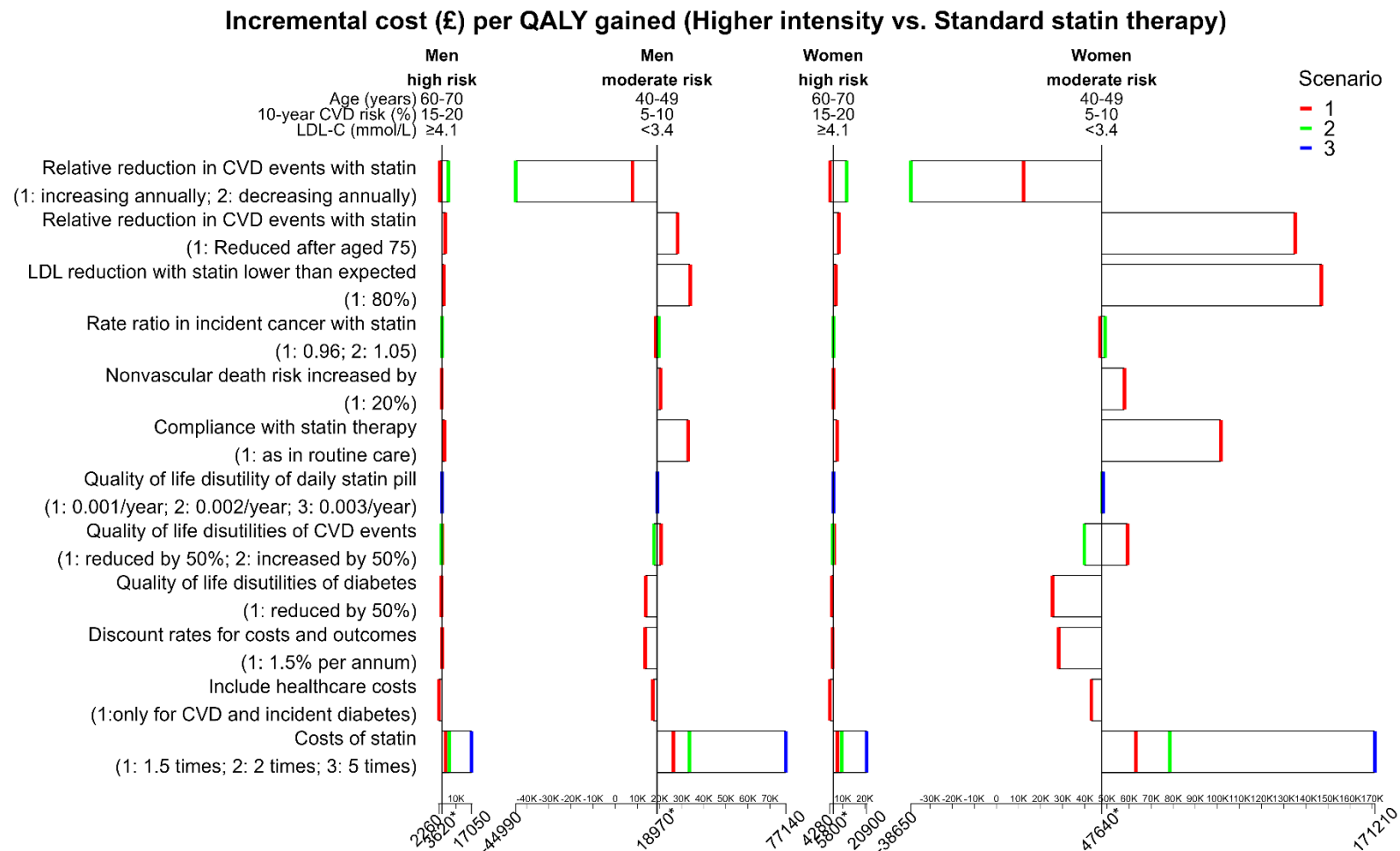
(b) people with history of cardiovascular disease



\*Incremental cost per QALY in base-case cost-effectiveness analysis.

CVD, cardiovascular disease; LDL-C, low density lipoprotein cholesterol; QALY, Quality-Adjusted Life Year.

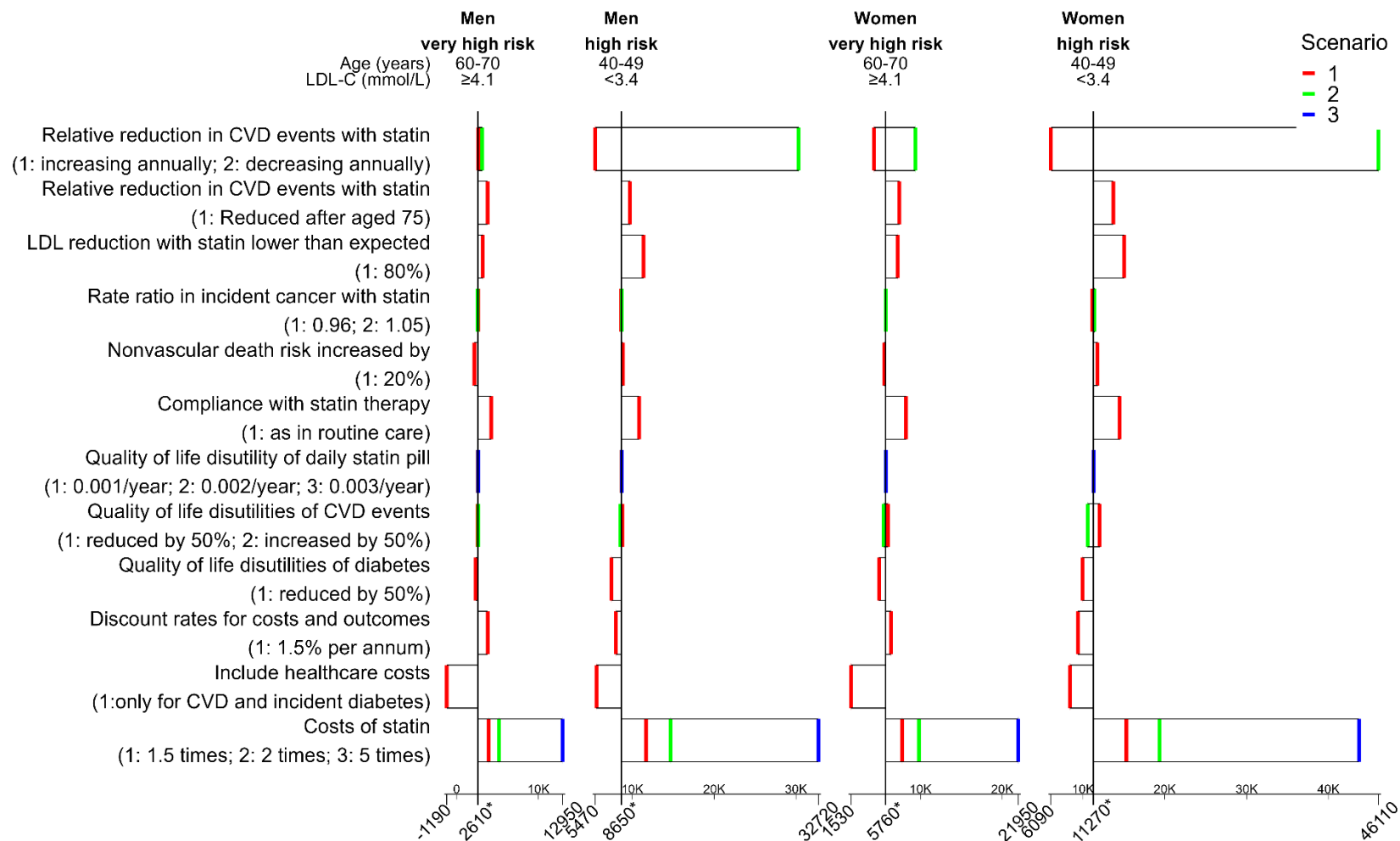
**Supplementary Figure 5 Sensitivity analyses of cost-effectiveness of higher intensity versus standard statin therapy**  
**(a) People without history of cardiovascular disease**



\*Incremental cost per QALY in base-case cost-effectiveness analysis. CVD, cardiovascular disease; LDL-C, low density lipoprotein cholesterol; QALY, Quality-Adjusted Life Year. In the scenario analysis with decreasing relative reductions in CVD events with statin therapy over time, negative incremental discounted QALYs in patient categories with LDL<3.4mmol/L and negative incremental cost per QALY are projected.

**(b) People with history of cardiovascular disease**

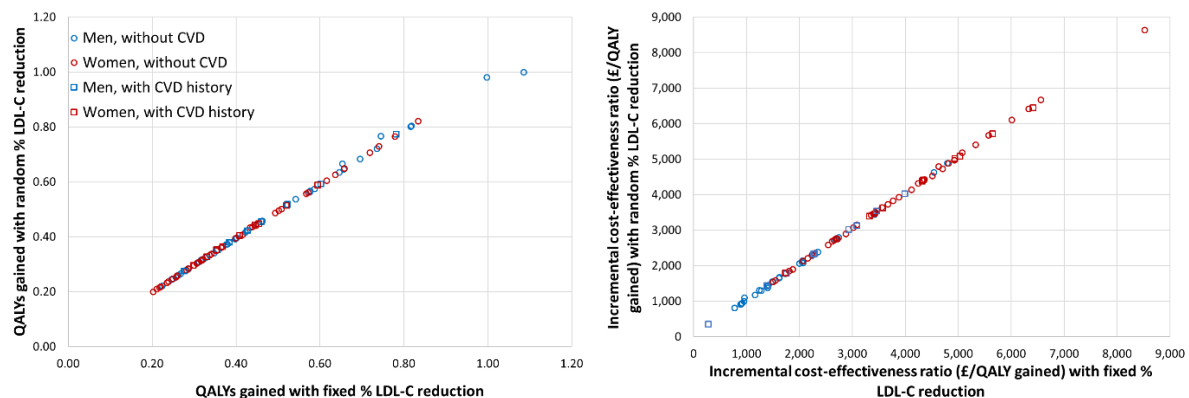
**Incremental cost (£) per QALY gained (Higher intensity vs. Standard statin therapy)**



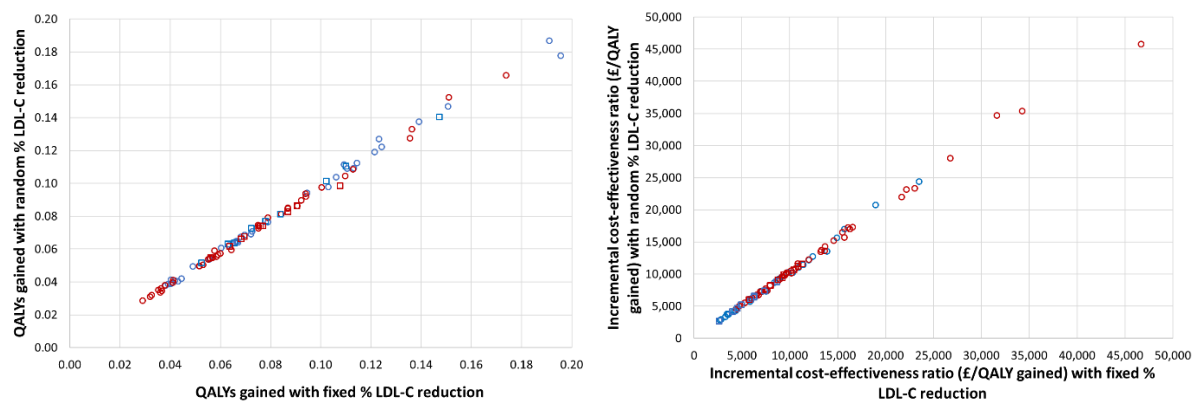
\*Incremental cost per QALY in base-case cost-effectiveness analysis. CVD, cardiovascular disease; LDL-C, low density lipoprotein cholesterol; QALY, Quality-Adjusted Life Year.

**Supplementary Figure 6 QALYs gained per person and cost-effectiveness of long-term statin therapy in categories by sex, age, pre-treatment LDL cholesterol level and cardiovascular risk: comparison of basecase and scenario analysis with variability around the proportional reduction in LDL-C with statin therapy**

**(a) Standard statin therapy**



**(b) Higher intensity statin therapy**



Results presented in participant categories by sex (men, women), age (40-49, 50-59, 60-70 years), pre-treatment LDL-C level (<3.4, 3.4-4.1,  $\geq 4.1$  mmol/L) and cardiovascular risk (10-year cardiovascular risk <5%, 5%-10%, 10%-15%, 15%-20%,  $\geq 20\%$ ) or history of cardiovascular disease history at statin initiation. % LDL-C reduction at 43% for standard statin and 55% for higher intensity statin therapy (basecase) and sampled (as part of the 500 microsimulations) from normal distributions with mean 43% (standard deviation 14.5%) for standard statin and mean 55% (standard deviation 17.3%) for higher intensity statin therapy.



# Supplementary Table 5 Sensitivity analyses for cost-effectiveness (£/QALY) of statin therapy

## A. People without history of cardiovascular disease: Standard statin vs. No statin therapy

Sex, cardiovascular risk	Men, high	Men, moderate	Women, high	Women, moderate	Men, low risk	Men, low risk	Women, low risk	Women, low risk
Age (years)	60-70	40-49	60-70	40-49	50-59	40-49	50-59	40-49
10-year cardiovascular risk (%)	15-20	5-10	15-20	5-10	<5	<5	<5	<5
LDL cholesterol (mmol/L)	≥4.1	<3.4	≥4.1	<3.4	<3.4	<3.4	<3.4	<3.4
<b>Base-case</b>	£840	£3,420	£1,480	£6,560	£4,540	£4,790	£6,340	£8,530
Relative reduction in CVD events with statin therapy increasing annually	£1,300	£2,360	£1,640	£4,150	£2,550	£2,520	£2,970	£3,620
Relative reduction in CVD events with statin therapy decreasing annually	£920	£9,050	£2,010	£17,880	£11,960	£16,520	£18,860	£34,650
Relative reduction in CVD events with statin therapy reduced in elderly	£1,120	£3,790	£1,990	£7,410	£5,690	£5,710	£8,440	£10,960
LDL reduction with statin 80% from expected	£1,160	£4,500	£1,850	£8,200	£5,820	£6,220	£8,030	£10,800
Rate ratio in incident cancer with statin therapy of 0.96	£390	£2,120	£1,090	£4,230	£2,160	£2,620	£3,240	£4,320
Rate ratio in incident cancer with statin therapy of 1.05	£1,790	£9,720	£2,230	£18,340	£242,270	£31,410	£131,210	-£923,710*
Risk of nonvascular death increased by 20%	£650	£3,420	£1,400	£6,700	£4,650	£4,930	£6,630	£9,020
Compliance with statin therapy as in routine care	£1,260	£4,520	£1,920	£7,480	£5,410	£5,760	£7,540	£10,210
With quality of life disutility of daily statin pill of 0.001/year	£910	£4,390	£1,610	£9,440	£6,310	£6,920	£9,910	£16,270
With quality of life disutility of daily statin pill of 0.002/year	£980	£6,130	£1,770	£16,790	£10,360	£12,400	£22,730	£178,620
With quality of life disutility of daily statin pill of 0.003/year	£1,080	£10,180	£1,960	£76,060	£28,760	£60,050	-£77,460*	-£19,900*

Quality of life disutilities of CVD events reduced by 50%	£870	£3,550	£1,540	£6,990	£4,740	£4,960	£6,760	£9,030
Quality of life disutilities of CVD events increased by 50%	£820	£3,300	£1,430	£6,190	£4,360	£4,630	£5,960	£8,080
Quality of life disutilities of diabetes reduced by 50%	£830	£3,280	£1,450	£6,130	£4,440	£4,640	£6,170	£8,250
Discount rates for costs and outcomes at 1.5% per annum	£1,420	£3,140	£1,910	£5,700	£3,700	£3,740	£4,790	£5,960
Include only healthcare costs for CVD and incident diabetes	[-£400]	£2,120	£190	£4,490	£3,410	£3,710	£5,150	£7,230
Cost of statin x1.5	£1,360	£5,010	£2,060	£8,750	£6,560	£6,990	£8,920	£11,940
Cost of statin x2	£1,890	£6,590	£2,640	£10,930	£8,570	£9,200	£11,510	£15,360
Cost of statin x5	£5,020	£16,130	£6,120	£24,040	£20,650	£22,400	£27,040	£35,860
With variability around the % reduction in LDL-C with statin therapy	£910	£3,440	£1,540	£6,670	£4,630	£4,880	£6,410	£8,640

CVD, cardiovascular disease. Negative values in brackets represent cost savings. \*Negative values indicate result due to decrease in QALYs.

#### B. People without history of cardiovascular disease: Higher intensity vs standard statin therapy

Sex, cardiovascular risk	Men, high	Men, moderate	Women, high	Women, moderate	Men, low risk	Men, low risk	Women, low risk	Women, low risk
Age (years)	60-70	40-49	60-70	40-49	50-59	40-49	50-59	40-49
10-year cardiovascular risk (%)	15-20	5-10	15-20	5-10	<5	<5	<5	<5
LDL cholesterol (mmol/L)	≥4.1	<3.4	≥4.1	<3.4	<3.4	<3.4	<3.4	<3.4
<b>Base-case</b>	£3,620	£18,970	£5,800	£47,640	£15,570	£23,490	£23,050	£34,290
Relative reduction in CVD events with statin therapy increasing annually	£2,750	£7,800	£4,320	£12,370	£7,070	£8,060	£9,090	£11,410
Relative reduction in CVD events with statin therapy decreasing annually	£6,580	-£44,990*	£11,880	-£38,650*	£411,880	-£54,160*	-£185,710*	-£71,380*

Relative reduction in CVD events with statin therapy reduced in elderly	£5,170	£28,220	£8,370	£135,170	£23,810	£39,040	£42,510	£65,690
LDL reduction with statin 80% from expected	£4,450	£33,890	£7,030	£147,070	£23,110	£38,700	£33,770	£54,030
Rate ratio in incident cancer with statin therapy of 0.96	£3,590	£18,360	£5,750	£47,000	£15,020	£22,730	£22,620	£33,550
Rate ratio in incident cancer with statin therapy of 1.05	£3,660	£19,680	£5,850	£49,190	£16,050	£24,610	£23,560	£35,210
Risk of nonvascular death increased by 20%	£3,550	£20,560	£5,840	£57,920	£16,170	£25,420	£25,150	£38,900
Compliance with statin therapy as in routine care	£4,800	£33,030	£7,500	£101,540	£22,570	£31,820	£30,380	£46,700
With quality of life disutility of daily statin pill of 0.001/year	£3,630	£19,010	£5,810	£47,830	£15,600	£23,540	£23,090	£34,360
With quality of life disutility of daily statin pill of 0.002/year	£3,630	£19,060	£5,820	£48,020	£15,620	£23,590	£23,130	£34,430
With quality of life disutility of daily statin pill of 0.003/year	£3,640	£19,100	£5,830	£48,210	£15,650	£23,640	£23,170	£34,510
Quality of life disutilities of CVD events reduced by 50%	£3,790	£20,690	£6,150	£59,350	£16,590	£25,460	£25,960	£38,670
Quality of life disutilities of CVD events increased by 50%	£3,470	£17,520	£5,490	£39,790	£14,670	£21,810	£20,720	£30,800
Quality of life disutilities of diabetes reduced by 50%	£3,360	£13,760	£5,160	£25,390	£13,250	£17,670	£18,610	£25,730
Discount rates for costs and outcomes at 1.5% per annum	£3,710	£13,500	£5,420	£28,210	£11,280	£15,000	£15,530	£20,480
Include only healthcare costs for CVD and incident diabetes	£2,260	£17,040	£4,280	£42,940	£14,250	£21,960	£21,480	£32,420
Cost of statin x1.5	£5,300	£26,240	£7,680	£63,090	£22,260	£33,390	£32,680	£48,600
Cost of statin x2	£6,980	£33,510	£9,570	£78,530	£28,950	£43,280	£42,310	£62,920
Cost of statin x5	£17,050	£77,140	£20,900	£171,210	£69,070	£102,630	£100,100	£148,800
With variability around the % reduction in LDL-C with statin therapy	£3,350	£20,780	£5,540	£45,780	£16,980	£24,420	£23,350	£35,360

CVD, cardiovascular disease. Negative values in brackets represent cost savings. \*Negative values indicate result due to decrease in QALYs.

### C. People with history of cardiovascular disease

Sex, cardiovascular risk Age (years) LDL cholesterol (mmol/L)	Standard statin vs. No statin therapy				Higher intensity vs standard statin therapy			
	Men, very high 60-70 ≥4.1	Men, high 40-49 <3.4	Women, very high 60-70 ≥4.1	Women, high 40-49 <3.4	Men, very high 60-70 ≥4.1	Men, high 40-49 <3.4	Women, very high 60-70 ≥4.1	Women, high 40-49 <3.4
<b>Base-case</b>	£280	£3,990	£1,730	£6,410	£2,610	£8,650	£5,760	£11,270
Relative reduction in CVD events with statin therapy increasing annually	£1,400	£3,420	£2,140	£4,140	£2,630	£5,470	£4,330	£6,090
Relative reduction in CVD events with statin therapy decreasing annually	[-£70]	£6,860	£1,980	£12,930	£3,140	£30,320	£9,380	£46,110
Relative reduction in CVD events with statin therapy reduced in elderly	£790	£4,020	£2,080	£6,980	£3,790	£9,710	£7,440	£13,710
LDL reduction with statin 80% from expected	£660	£5,030	£2,290	£7,830	£3,220	£11,370	£7,240	£15,050
Rate ratio in incident cancer with statin therapy of 0.96	£270	£3,270	£1,580	£5,000	£2,640	£8,610	£5,760	£11,170
Rate ratio in incident cancer with statin therapy of 1.05	£290	£5,260	£2,000	£9,320	£2,570	£8,730	£5,770	£11,430
Risk of nonvascular death increased by 20%	[-£100]	£3,950	£1,530	£6,540	£2,170	£8,840	£5,570	£11,790
Compliance with statin therapy as in routine care	£900	£4,980	£2,450	£7,710	£4,240	£10,830	£8,250	£14,500
With quality of life disutility of daily statin pill of 0.001/year	£300	£4,640	£1,900	£7,950	£2,610	£8,670	£5,780	£11,290
With quality of life disutility of daily statin pill of 0.002/year	£320	£5,540	£2,090	£10,470	£2,620	£8,690	£5,790	£11,310
With quality of life disutility of daily statin pill of 0.003/year	£340	£6,880	£2,340	£15,310	£2,630	£8,700	£5,810	£11,330
Quality of life disutilities of CVD events reduced by 50%	£270	£4,010	£1,770	£6,720	£2,550	£8,760	£6,040	£12,050

Quality of life disutilities of CVD events increased by 50%	£290	£3,970	£1,700	£6,130	£2,670	£8,550	£5,520	£10,580
Quality of life disutilities of diabetes reduced by 50%	£270	£3,850	£1,670	£6,250	£2,340	£7,450	£4,950	£9,940
Discount rates for costs and outcomes at 1.5% per annum	£1,480	£4,080	£2,680	£5,640	£3,800	£7,990	£6,410	£9,380
Include only healthcare costs for CVD and incident diabetes	[-£2,940]	£1,550	[-£1,700]	£3,950	[-£1,190]	£5,610	£1,530	£8,420
Cost of statin x1.5	£710	£4,990	£2,350	£7,800	£3,900	£11,660	£7,790	£15,320
Cost of statin x2	£1,140	£6,000	£2,960	£9,190	£5,190	£14,670	£9,810	£19,380
Cost of statin x5	£3,730	£12,020	£6,660	£17,530	£12,950	£32,720	£21,950	£43,720
With variability around the % reduction in LDL-C with statin therapy	£360	£4,030	£1,790	£6,450	£2,710	£8,820	£6,040	£11,590

LDL, low density lipoprotein; CVD, cardiovascular disease. Negative values in brackets represent cost savings.

**Supplementary Figure 7 Scenario analysis of QALYs gained and cost-effectiveness with long-term standard statin therapy in categories by sex, age, pre-treatment LDL cholesterol level and 10-year cardiovascular risk with added hypothetical disutility of daily pill of 0.002 QALYs/year**

**A. Undiscounted QALYs gained per person**

		LDL cholesterol (mmol/L)																			
		<3.4					3.4-4.1					≥4.1									
		Without CVD, by 10-year CVD risk (%)					with CVD	Without CVD, by 10-year CVD risk (%)							with CVD	Without CVD, by 10-year CVD risk (%)					with CVD
		<5	5-10	10-15	15-20	≥20		<5	5-10	10-15	15-20	≥20		<5	5-10	10-15	15-20	≥20			
Men	Age (years)																			QALYs	
	40-49	0.20	0.25		0.34		0.32	0.35	0.39		0.51		0.46	0.57	0.67		1.02		0.72		
	50-59	0.18	0.20	0.23	0.27	0.34	0.28	0.31	0.33	0.36	0.40	0.49	0.38	0.48	0.54	0.61	0.70	1.03	0.55		1.00
	60-70	n/a	0.16	0.19	0.22	0.27	0.24	n/a	0.28	0.31	0.34	0.40	0.31	n/a	0.44	0.49	0.55	0.78	0.42	0.80	
Women	Age (years)																			0.60	
	40-49	0.13	0.18		0.21		0.28	0.24	0.28		0.37		0.37	0.40	0.54		0.82		0.53	0.40	
	50-59	0.14	0.17	0.19	0.24	0.26	0.27	0.24	0.27	0.30	0.34	0.39	0.35	0.40	0.47	0.58	0.70	0.93	0.46	0.20	
	60-70	0.14	0.16	0.18	0.20	0.23	0.25	0.23	0.25	0.28	0.31	0.35	0.32	0.36	0.41	0.47	0.54	0.73	0.40	0.00	

**B. Incremental cost-effectiveness ratios (£/QALY gained)**

		LDL cholesterol (mmol/L)																		
		<3.4					3.4-4.1					≥4.1								
		Without CVD, by 10-year CVD risk (%)					Without CVD, by 10-year CVD risk (%)					Without CVD, by 10-year CVD risk (%)								
		<5	5-10	10-15	15-20	≥20	with CVD	<5	5-10	10-15	15-20	≥20	with CVD	<5	5-10	10-15	15-20	≥20	with CVD	ICER (£/QALY gained)
Men	Age (years)																			
	40-49	£12,400	£6,130	£3,790		£5,540	£4,510	£2,980	£2,180		£3,650	£1,900	£1,120	£1,080		£2,590				
	50-59	£10,360	£6,360	£4,270	£3,220	£2,950	£4,480	£4,170	£2,930	£2,200	£1,800	£1,920	£2,770	£2,180	£1,320	£950	£810	£1,200	£1,570	0
	60-70	n/a	£6,140	£4,350	£3,310	£2,640	£3,840	n/a	£2,950	£2,190	£1,740	£1,670	£2,090	n/a	£1,860	£1,180	£980	£1,220	£320	5,000
Women	Age (years)																			
	40-49	£178,620	£16,790	£11,280		£10,470	£14,510	£8,620	£6,750		£7,020	£5,790	£3,650	£2,990		£5,320				
	50-59	£22,730	£11,900	£9,030	£6,790	£6,750	£8,250	£8,340	£6,250	£5,390	£4,770	£4,900	£5,810	£4,080	£2,980	£2,540	£2,310	£2,480	£4,060	20,000
	60-70	£13,560	£8,960	£6,700	£5,510	£4,810	£6,820	£5,990	£4,770	£3,830	£3,440	£3,390	£4,580	£3,350	£2,550	£2,020	£1,770	£1,880	£2,090	30,000
																			50,000	

QALY, quality-adjusted life year; LDL, low density lipoprotein; CVD, cardiovascular disease; ICER, incremental cost-effectiveness ratio with costs and QALYs discounted at 3.5% per year. For the category of women 40-49 years old with 10-year cardiovascular risk<5% and LDL cholesterol<3.4mmol/L, small discounted QALYs are projected as gains in QALYs accrue later in life.

**Supplementary Table 6 A scenario analysis of stopping statin treatment at 80 years of age**

**A. People without history of cardiovascular disease**

Sex, cardiovascular risk		Men, high	Men, moderate	Women, high	Women, moderate
Age (years)		60-70	40-49	60-70	40-49
10-year cardiovascular risk (%)		15-20	5-10	15-20	5-10
LDL cholesterol (mmol/L)		≥4.1	<3.4	≥4.1	<3.4
<b>Standard statin therapy</b>					
Standard statin until 80 years of age vs No statin	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.21 [£485]	0.19 £3,499	0.16 £849	0.13 £7,637
Lifetime Standard statin vs Standard statin until 80 years of age	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.39 £1,893	0.13 £3,215	0.45 £1,808	0.12 £4,617
<b>Higher intensity statin therapy</b>					
Higher intensity statin until 80 years of age vs No statin	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.23 £215	0.20 £5,814	0.16 £2,400	0.13 £12,641
Lifetime higher intensity statin vs Higher intensity statin until 80 years of age	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.47 £1,975	0.16 £3,374	0.55 £1,952	0.15 £4,905

**B. People with CVD**

Sex, cardiovascular risk		Men, very high	Men, high	Women, very high	Women, high
Age (years)		60-70	40-49	60-70	40-49
LDL cholesterol (mmol/L)		≥4.1	<3.4	≥4.1	<3.4
<b>Standard statin</b>					
Standard statin until 80 years of age vs No statin	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.25 [£1220]	0.30 £3,810	0.18 £230	0.22 £6,810
Lifetime Standard statin vs Standard statin until 80 years of age	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.20 £3,020	0.08 £5,160	0.27 £3,290	0.13 £5,230
<b>Higher intensity statin</b>					
Higher intensity statin until 80 years of age vs No statin	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.29 [£780]	0.36 £4,600	0.20 £1,140	0.26 £7,830

Lifetime higher intensity statin vs Higher intensity statin until 80 years of age	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.25 £3,050	0.10 £5,210	0.33 £3,370	0.16 £5,320
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<sup>1</sup>Costs and outcomes discounted at 3.5%/year.

Values in brackets represent cost savings. LDL, low density lipoprotein; QALY, quality-adjusted life year.



**Supplementary Table 7 A scenario analysis of delaying statin treatment in 40 to 44 years old people without history of cardiovascular disease**

		Men 40-44 years old, by 10-year CVD risk (%)			Women 40-44 years old, by 10-year CVD risk (%)		
		<5	5-10	≥10	<5	5-10	≥10
Immediate initiation vs Delayed by 5 years lifetime standard statin	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.01 £10,384	0.02 £239	0.05 [£2,582]	0.00 £33,948	0.01 £5,907	0.03 £1,624
Immediate initiation vs Delayed by 5 years lifetime higher intensity statin therapy	Undiscounted QALYs gained £/QALY <sup>1</sup>	0.01 £14,536	0.02 £2,043	0.06 [£1,979]	0.01 £41,888	0.01 £9,279	0.03 £3,054

<sup>1</sup>With costs and outcomes discounted at 3.5%/year.

Values in brackets represent cost savings. CVD, cardiovascular disease; LDL, low density lipoprotein; QALY, quality-adjusted life year.

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