Lipid-lowering strategies for primary prevention of coronary heart disease in the United Kingdom: A cost-effectiveness analysis

Supplementary Appendix

Jedidiah I Morton, Clara Marquina, Melanie Lloyd, Gerald F Watts, Sophia Zoungas, Danny Liew, and Zanfina Ademi

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Abbreviations

- CHD: Coronary heart disease
- LDL-C: Low-density lipoprotein-cholesterol
- LLS: Lipid lowering strategy
- MI: Myocardial infarction
- MR: Mendelian randomisation
- NHS: National Health Service (of the United Kingdom)
- OSA: One-way sensitivity analysis
- PSA: Probabilistic sensitivity analysis
- QALY: Quality-adjusted life year
- RR: Relative risk
- SE: Standard error
- UK: United Kingdom
- YLL: Years of life lived

Supplementary Table 1: Model inputs

Input	Value	Distribution	Source
Incidence of non-fatal MI	Age and sex-specific	Log-normal See Figure 2	UK Biobank
Incidence of fatal MI	Age and sex-specific	Log-normal See Figure 3	UK Biobank
Non-CHD mortality rate for people without MI	Age and sex-specific	Log-normal See Figure 3	UK Biobank
All-cause mortality rate for people with MI	Age-, sex-, and time-since-MI-specific	Log-normal See Figure 4	UK Biobank
Effect of statins on LDL-C (control arm only)	45% (44, 46) reduction	Normal	[1]
Effect of interventions on LDL-C	Low/moderate intensity statins: 40% (39, 41) reduction	Normal	[1]
	High intensity statins: 50% (49, 51) reduction		[1]
	Low/moderate intensity statins and ezetimibe: 55% (54, 56) reduction		[2]
	Inclisiran: 51.5% (49.0, 53.9) reduction		[3]
Effect of cumulative LDL-C on the incidence of MI	RR: 0.48 (0.45, 0.50)	Log-normal	[4]
Utility for people without MI	Age and sex-specific (± 5%)	Modified normal See Figure 5	[5]
Chronic utility for people with MI	0.79 (0.73, 0.85)	Beta	[6]
Acute disutility for MI	-0.03 (± 50%)	Normal	[7]
Cost of acute MI	£2047.31 (± 15%)	Gamma	National Health Service Cost Schedule; See Table 3
Excess healthcare costs for people with MI	£4705.45 (SE: 112.71) for the first 6 months £1015.21 (SE: 171.23) per year thereafter	Gamma	[8]
Annual cost of statins (control arm only)	£19.00	Fixed	[9, 10]
Annual cost of interventions	Low/moderate intensity statins: £18.39	Fixed	[9]
	High intensity statins: £27.39		[9]
	low/moderate intensity statins and ezetimibe: £49.31		[9]
	Inclisiran: £3974.72		[11]

Supplementary Table 2: Proportion of primary prevention population in the control scenario on LLT at or before a given age, stratified by sex and LDL-C.

		LDL-C (mmol/L)			
Sex	Age	Overall	≥3.0	≥4.0	≥5.0
Females	40	0.17%	0.10%	0.08%	0.14%
	50	1.69%	1.04%	0.75%	1.00%
	60	13.46%	11.33%	13.14%	21.63%
	70	39.27%	40.38%	56.09%	81.71%
	80	54.85%	59.31%	79.88%	97.85%
Males	40	0.45%	0.30%	0.22%	0.33%
	50	3.45%	2.23%	1.80%	3.19%
	60	19.92%	15.85%	20.14%	38.58%
	70	46.60%	44.38%	61.03%	88.18%
	80	60.53%	62.17%	82.26%	98.73%

Supplementary Table 3: Calculation of acute MI costs

Code	Description	Number	Unit cost (£)	Weighted mean (£)
EB10A	Actual or Suspected Myocardial Infarction with CC Score 13+	19452	3312.25	
EB10B	Actual or Suspected Myocardial Infarction with CC Score 10-12	21042	2333.65	
EB10C	Actual or Suspected Myocardial Infarction with CC Score 7-9	23518	1867.01	2047.31
EB10D	Actual or Suspected Myocardial Infarction with CC Score 4-6	25523	1588.42	
EB10E	Actual or Suspected Myocardial Infarction with CC Score 0-3	19637	1299.82	

Supplementary Table 4: Mean; median (IQR) LDL-C by stratification group.

Sex	LDL-C (mmol/L)	Mean; median (IQR)
Females	Overall	3.63; 3.57 (3.01, 4.18)
	≥3.0	3.97; 3.85 (3.43, 4.38)
	≥4.0	4.63; 4.49 (4.22, 4.90)
	≥5.0	5.48; 5.35 (5.15, 5.68)
Males	Overall	3.51; 3.49 (2.92, 4.07)
	≥3.0	3.91; 3.80 (3.41, 4.28)
	≥4.0	4.56; 4.43 (4.19, 4.79)
	≥5.0	5.41; 5.30 (5.12, 5.57)

The results of the PSA for the overall population are shown here. For results stratified by sex and LDL-C, see the protocol, pages 223-254.

Supplementary Table 5: PSA results – Low/moderate intensity statins

Age of intervention	Outcome	Control	Intervention	
			Absolute value	Difference to control
30	N	458,692 (458,692, 458,692)	458,692 (458,692, 458,692)	0 (0, 0)
	Incident MIs	65,884 (59,047, 76,917)	40,446 (35,702, 47,759)	-25,478; -38.7% (-29,239, -22,985)
	Deaths	148,250 (135,515, 163,065)	141,189 (129,601, 154,270)	-6,942; -4.7% (-11,345, -3,948)
	YLL	10,961,655 (10,931,241, 10,988,973)	10,978,037 (10,948,815, 11,004,193)	16,060; 0.15% (10,939, 23,183)
	QALYs	9,463,645 (8,605,772, 10,402,795)	9,487,549 (8,627,452, 10,430,464)	23,856; 0.25% (18,875, 30,617)
	Medication costs (£, millions)	24,166,453 (23,773,203, 24,551,866)	202,307,875 (201,770,475, 202,788,872)	178,133,450; 737.1% (177,695,384, 178,539,932)
	Acute MI costs (£, millions)	30,912,201 (22,151,292, 42,011,453)	19,090,338 (13,590,477, 26,022,253)	-11,799,265; -38.2% (-16,072,621, -8,455,634)
	Chronic MI costs (£, millions)	236,411,076 (177,680,675, 310,583,139)	148,041,302 (111,014,232, 194,517,480)	-87,813,746; -37.1% (-116,166,402, -67,294,308)
	Total healthcare costs (£, millions)	291,595,992 (232,186,590, 368,806,912)	369,780,315 (331,905,304, 419,036,693)	78,319,864; 26.9% (48,471,005, 100,045,639)
	ICER (Δ £/ Δ QALY)			3,253 (1,951, 4,784)
40	N	456,016 (455,474, 456,463)	456,016 (455,474, 456,463)	0 (0, 0)
	Incident MIs	64,668 (58,176, 75,517)	45,685 (40,741, 53,488)	-19,084; -29.5% (-21,940, -17,147)
	Deaths	146,184 (133,833, 160,457)	140,787 (129,557, 153,670)	-5,364; -3.7% (-8,621, -3,128)
	YLL	9,974,590 (9,934,146, 10,011,467)	9,990,008 (9,950,316, 10,024,573)	15,400; 0.15% (10,103, 21,853)
	QALYs	8,367,720 (7,600,682, 9,226,820)	8,389,929 (7,619,553, 9,251,512)	22,215; 0.27% (17,008, 28,087)
	Medication costs (£, millions)	33,524,575 (33,084,085, 33,927,219)	184,135,447 (183,405,136, 184,771,432)	150,614,120; 449.3% (150,032,049, 151,138,528)
	Acute MI costs (£, millions)	41,081,469 (29,407,783, 55,720,978)	29,374,604 (21,067,225, 39,903,236)	-11,691,858; -28.5% (-16,020,128, -8,499,896)
	Chronic MI costs (£, millions)	300,337,994 (229,727,005, 390,169,572)	218,220,636 (166,174,293, 282,887,839)	-82,007,145; -27.3% (-107,018,600, -62,992,561)
	Total healthcare costs (£, millions)	375,240,733 (303,129,187, 470,321,391)	432,259,725 (379,048,534, 500,309,838)	56,430,806; 15.0% (29,699,978, 76,296,717)
	ICER (Δ £/ Δ QALY)			2,553 (1,270, 3,969)
50	N	449,476 (448,240, 450,535)	449,476 (448,240, 450,535)	0 (0, 0)
	Incident MIs	61,604 (55,417, 71,816)	49,920 (44,936, 58,174)	-11,777; -19.1% (-13,688, -10,352)
	Deaths	141,159 (129,584, 154,626)	137,856 (126,720, 149,854)	-3,405; -2.4% (-5,349, -1,880)
	YLL	8,599,242 (8,548,403, 8,643,411)	8,610,418 (8,558,926, 8,655,147)	11,297; 0.13% (6,762, 16,503)
	QALYs	6,985,205 (6,347,824, 7,705,302)	7,001,080 (6,362,782, 7,723,897)	15,465; 0.22% (11,362, 20,170)
	Medication costs (£, millions)	45,019,095 (44,545,200, 45,446,337)	158,758,710 (157,811,015, 159,581,643)	113,740,460; 252.6% (113,111,274, 114,300,188)
	Acute MI costs (£, millions)	51,257,486 (36,846,314, 69,315,522)	42,021,680 (30,108,029, 57,043,160)	-9,224,553; -18.0% (-12,631,421, -6,607,093)
	Chronic MI costs (£, millions)	346,705,291 (270,211,369, 445,572,288)	288,515,988 (223,597,015, 370,337,341)	-58,065,245; -16.7% (-75,107,806, -45,008,031)
	Total healthcare costs (£, millions)	443,047,023 (365,715,585, 546,622,032)	489,871,441 (423,278,953, 574,971,367)	46,476,579; 10.5% (28,596,754, 60,192,163)
	ICER (Δ £/ Δ QALY)			2,985 (1,669, 4,536)
60	N	434,024 (432,139, 435,752)	434,024 (432,139, 435,752)	0 (0, 0)
	Incident MIs	53,960 (48,221, 63,678)	48,819 (43,599, 57,608)	-5,161; -9.6% (-6,201, -4,507)
	Deaths	129,376 (118,856, 141,347)	127,884 (117,384, 139,240)	-1,547; -1.2% (-2,404, -1,006)
	YLL	6,718,611 (6,660,927, 6,769,209)	6,723,507 (6,666,687, 6,774,154)	5,097; 0.08% (3,958, 6,690)
	QALYs	5,271,297 (4,793,374, 5,815,845)	5,278,313 (4,799,087, 5,823,334)	6,558; 0.12% (5,268, 8,109)
	Medication costs (£, millions)	53,190,587 (52,633,497, 53,703,497)	124,044,710 (122,998,542, 124,976,847)	70,864,270; 133.2% (70,299,724, 71,365,919)
	Acute MI costs (£, millions)	55,833,348 (39,943,626, 75,360,416)	50,890,288 (36,550,704, 68,671,343)	-4,935,388; -8.8% (-6,730,638, -3,494,764)
	Chronic MI costs (£, millions)	324,908,701 (257,520,251, 413,036,814)	299,234,515 (235,821,837, 378,995,564)	-25,839,476; -8.0% (-33,082,922, -20,460,744)
	Total healthcare costs (£, millions)	434,303,614 (364,990,639, 527,226,971)	474,407,902 (410,413,036, 559,619,837)	40,042,832; 9.2% (32,288,964, 45,917,080)
	ICER (Δ £/ Δ QALY)			6,076 (4,447, 7,990)

Supplementary Table 6: PSA results – High intensity statins

Age of intervention	Outcome	Control	Intervention	
			Absolute value	Difference to control
30	N	458,692 (458,692, 458,692)	458,692 (458,692, 458,692)	0 (0, 0)
	Incident MIs	65,884 (59,047, 76,917)	34,634 (30,550, 40,626)	-31,332; -47.6% (-36,013, -28,208)
	Deaths	148,250 (135,515, 163,065)	139,546 (127,828, 152,814)	-8,538; -5.8% (-13,959, -4,924)
	YLL	10,961,655 (10,931,241, 10,988,973)	10,981,411 (10,952,236, 11,007,313)	19,409; 0.18% (13,428, 27,501)
	QALYs	9,463,645 (8,605,772, 10,402,795)	9,492,583 (8,632,538, 10,435,855)	28,716; 0.30% (22,757, 36,251)
	Medication costs (£, millions)	24,166,453 (23,773,203, 24,551,866)	301,409,025 (300,609,931, 302,118,485)	277,225,262; 1147.1% (276,557,266, 277,800,740)
	Acute MI costs (£, millions)	30,912,201 (22,151,292, 42,011,453)	16,622,895 (11,734,329, 22,745,565)	-14,318,354; -46.3% (-19,413,154, -10,309,837)
	Chronic MI costs (£, millions)	236,411,076 (177,680,675, 310,583,139)	130,007,604 (96,882,927, 171,924,937)	-105,842,028; -44.8% (-137,939,119, -81,034,370)
	Total healthcare costs (£, millions)	291,595,992 (232,186,590, 368,806,912)	448,170,790 (415,408,073, 491,562,777)	156,996,676; 53.8% (122,561,426, 182,938,490)
	ICER (Δ £/ Δ QALY)			5,429 (3,907, 7,355)
40	N	456,016 (455,474, 456,463)	456,016 (455,474, 456,463)	0 (0, 0)
	Incident MIs	64,668 (58,176, 75,517)	40,540 (36,077, 47,423)	-24,276; -37.5% (-27,995, -21,739)
	Deaths	146,184 (133,833, 160,457)	139,388 (128,070, 152,044)	-6,794; -4.6% (-11,032, -4,073)
	YLL	9,974,590 (9,934,146, 10,011,467)	9,993,746 (9,953,454, 10,028,669)	19,140; 0.19% (13,128, 26,737)
	QALYs	8,367,720 (7,600,682, 9,226,820)	8,395,307 (7,625,262, 9,257,509)	27,383; 0.33% (21,417, 34,394)
	Medication costs (£, millions)	33,524,575 (33,084,085, 33,927,219)	274,353,296 (273,248,904, 275,310,092)	240,826,964; 718.4% (239,917,777, 241,632,602)
	Acute MI costs (£, millions)	41,081,469 (29,407,783, 55,720,978)	26,417,344 (18,896,047, 35,861,624)	-14,692,567; -35.8% (-20,077,700, -10,599,583)
	Chronic MI costs (£, millions)	300,337,994 (229,727,005, 390,169,572)	198,609,428 (150,069,000, 258,600,732)	-101,502,610; -33.8% (-132,575,023, -78,439,926)
	Total healthcare costs (£, millions)	375,240,733 (303,129,187, 470,321,391)	500,146,091 (450,543,840, 560,786,804)	124,373,408; 33.1% (92,407,530, 148,655,967)
	ICER (Δ £/ Δ QALY)			4,511 (3,138, 6,401)
50	N	449,476 (448,240, 450,535)	449,476 (448,240, 450,535)	0 (0, 0)
	Incident MIs	61,604 (55,417, 71,816)	45,856 (41,257, 53,514)	-15,856; -25.7% (-18,487, -13,967)
	Deaths	141,159 (129,584, 154,626)	136,614 (125,654, 148,899)	-4,572; -3.2% (-7,181, -2,729)
	YLL	8,599,242 (8,548,403, 8,643,411)	8,613,751 (8,562,021, 8,658,148)	14,869; 0.17% (9,771, 20,835)
	QALYs	6,985,205 (6,347,824, 7,705,302)	7,005,405 (6,366,830, 7,729,081)	20,135; 0.29% (15,470, 25,796)
	Medication costs (£, millions)	45,019,095 (44,545,200, 45,446,337)	236,546,049 (235,127,946, 237,763,849)	191,526,254; 425.4% (190,461,194, 192,457,870)
	Acute MI costs (£, millions)	51,257,486 (36,846,314, 69,315,522)	39,046,802 (27,923,744, 52,920,365)	-12,228,953; -23.9% (-16,506,193, -8,818,126)
	Chronic MI costs (£, millions)	346,705,291 (270,211,369, 445,572,288)	270,685,299 (209,669,477, 347,091,806)	-75,777,237; -21.9% (-97,300,252, -59,228,415)
	Total healthcare costs (£, millions)	443,047,023 (365,715,585, 546,622,032)	546,418,348 (485,251,503, 625,104,465)	103,306,739; 23.3% (81,228,996, 121,070,609)
	ICER (Δ £/ Δ QALY)			5,106 (3,611, 6,982)
60	N	434,024 (432,139, 435,752)	434,024 (432,139, 435,752)	0 (0, 0)
	Incident MIs	53,960 (48,221, 63,678)	46,186 (41,225, 54,385)	-7,808; -14.5% (-9,381, -6,861)
	Deaths	129,376 (118,856, 141,347)	127,100 (116,646, 138,390)	-2,333; -1.8% (-3,665, -1,549)
	YLL	6,718,611 (6,660,927, 6,769,209)	6,725,919 (6,669,304, 6,776,589)	7,511; 0.11% (5,905, 9,719)
	QALYs	5,271,297 (4,793,374, 5,815,845)	5,281,079 (4,801,866, 5,827,255)	9,639; 0.18% (7,855, 11,836)
	Medication costs (£, millions)	53,190,587 (52,633,497, 53,703,497)	184,817,300 (183,265,275, 186,207,239)	131,630,785; 247.5% (130,579,399, 132,613,608)
	Acute MI costs (£, millions)	55,833,348 (39,943,626, 75,360,416)	48,432,006 (34,673,084, 65,624,877)	-7,371,641; -13.2% (-10,104,153, -5,273,226)
	Chronic MI costs (£, millions)	324,908,701 (257,520,251, 413,036,814)	286,938,159 (225,956,368, 362,811,212)	-38,134,574; -11.7% (-48,367,558, -30,243,114)
	Total healthcare costs (£, millions)	434,303,614 (364,990,639, 527,226,971)	520,614,001 (458,979,957, 601,877,565)	86,026,051; 19.8% (75,066,611, 94,884,552)
	ICER (Δ £/ Δ QALY)			8,911 (6,808, 11,277)

Supplementary Table 7: PSA results – Low/moderate intensity statins and ezetimibe

Age of intervention	Outcome	Control	Intervention	
			Absolute value	Difference to control
30	N	458,692 (458,692, 458,692)	458,692 (458,692, 458,692)	0 (0, 0)
	Incident MIs	65,884 (59,047, 76,917)	31,932 (28,164, 37,697)	-33,988; -51.6% (-39,394, -30,589)
	Deaths	148,250 (135,515, 163,065)	138,746 (127,022, 151,884)	-9,246; -6.2% (-15,073, -5,374)
	YLL	10,961,655 (10,931,241, 10,988,973)	10,982,874 (10,953,716, 11,008,670)	20,847; 0.19% (14,614, 29,639)
	QALYs	9,463,645 (8,605,772, 10,402,795)	9,495,173 (8,634,753, 10,439,257)	30,898; 0.33% (24,625, 39,276)
	Medication costs (£, millions)	24,166,453 (23,773,203, 24,551,866)	542,696,422 (541,258,656, 543,968,418)	518,545,040; 2145.7% (517,275,089, 519,630,422)
	Acute MI costs (£, millions)	30,912,201 (22,151,292, 42,011,453)	15,502,783 (11,016,377, 21,195,622)	-15,404,474; -49.8% (-20,958,904, -11,133,694)
	Chronic MI costs (£, millions)	236,411,076 (177,680,675, 310,583,139)	121,911,170 (90,763,304, 162,099,335)	-113,934,073; -48.2% (-149,406,881, -87,079,870)
	Total healthcare costs (£, millions)	291,595,992 (232,186,590, 368,806,912)	680,104,555 (648,842,988, 721,702,544)	388,808,057; 133.3% (351,115,941, 417,327,962)
	ICER (Δ £/ Δ QALY)			12,567 (9,810, 16,055)
40	N	456,016 (455,474, 456,463)	456,016 (455,474, 456,463)	0 (0, 0)
	Incident MIs	64,668 (58,176, 75,517)	38,128 (33,913, 44,725)	-26,652; -41.2% (-30,829, -23,936)
	Deaths	146,184 (133,833, 160,457)	138,668 (127,426, 151,476)	-7,474; -5.1% (-11,966, -4,493)
	YLL	9,974,590 (9,934,146, 10,011,467)	9,995,562 (9,955,095, 10,030,444)	20,873; 0.21% (14,563, 29,012)
	QALYs	8,367,720 (7,600,682, 9,226,820)	8,398,019 (7,627,593, 9,261,267)	29,885; 0.36% (23,584, 37,460)
	Medication costs (£, millions)	33,524,575 (33,084,085, 33,927,219)	494,005,360 (492,008,687, 495,726,109)	460,489,243; 1373.6% (458,679,873, 462,027,621)
	Acute MI costs (£, millions)	41,081,469 (29,407,783, 55,720,978)	25,055,596 (17,889,434, 34,097,748)	-16,005,912; -39.0% (-21,796,707, -11,619,716)
	Chronic MI costs (£, millions)	300,337,994 (229,727,005, 390,169,572)	189,376,443 (143,940,527, 246,901,840)	-110,790,258; -36.9% (-144,107,945, -85,446,399)
	Total healthcare costs (£, millions)	375,240,733 (303,129,187, 470,321,391)	708,820,168 (663,172,809, 768,299,730)	332,937,762; 88.7% (299,125,474, 359,711,103)
	ICER (Δ £/ Δ QALY)			11,107 (8,655, 14,508)
50	N	449,476 (448,240, 450,535)	449,476 (448,240, 450,535)	0 (0, 0)
	Incident MIs	61,604 (55,417, 71,816)	43,946 (39,481, 51,150)	-17,759; -28.8% (-20,792, -15,715)
	Deaths	141,159 (129,584, 154,626)	136,016 (125,344, 148,430)	-5,111; -3.6% (-8,063, -3,074)
	YLL	8,599,242 (8,548,403, 8,643,411)	8,615,506 (8,563,475, 8,660,008)	16,536; 0.19% (11,231, 22,847)
	QALYs	6,985,205 (6,347,824, 7,705,302)	7,007,446 (6,368,810, 7,732,430)	22,414; 0.32% (17,430, 28,271)
	Medication costs (£, millions)	45,019,095 (44,545,200, 45,446,337)	425,938,266 (423,370,649, 428,136,053)	380,922,901; 846.1% (378,739,819, 382,806,507)
	Acute MI costs (£, millions)	51,257,486 (36,846,314, 69,315,522)	37,648,900 (26,949,070, 51,163,664)	-13,609,940; -26.6% (-18,402,896, -9,855,626)
	Chronic MI costs (£, millions)	346,705,291 (270,211,369, 445,572,288)	262,041,396 (204,200,959, 336,044,769)	-84,395,679; -24.3% (-108,123,858, -65,926,575)
	Total healthcare costs (£, millions)	443,047,023 (365,715,585, 546,622,032)	726,097,355 (666,617,818, 802,660,414)	282,805,369; 63.8% (256,909,957, 302,714,878)
	ICER (Δ £/ Δ QALY)			12,584 (9,820, 16,491)
60	N	434,024 (432,139, 435,752)	434,024 (432,139, 435,752)	0 (0, 0)
	Incident MIs	53,960 (48,221, 63,678)	44,888 (40,012, 52,711)	-9,086; -16.8% (-10,906, -8,035)
	Deaths	129,376 (118,856, 141,347)	126,740 (116,281, 138,095)	-2,712; -2.1% (-4,205, -1,805)
	YLL	6,718,611 (6,660,927, 6,769,209)	6,727,166 (6,670,881, 6,777,758)	8,672; 0.13% (6,850, 11,336)
	QALYs	5,271,297 (4,793,374, 5,815,845)	5,282,788 (4,802,966, 5,828,846)	11,128; 0.21% (9,099, 13,848)
	Medication costs (£, millions)	53,190,587 (52,633,497, 53,703,497)	332,787,256 (330,008,756, 335,285,707)	279,596,113; 525.6% (277,293,341, 281,675,164)
	Acute MI costs (£, millions)	55,833,348 (39,943,626, 75,360,416)	47,295,206 (33,816,226, 63,898,003)	-8,535,376; -15.3% (-11,704,058, -6,095,452)
	Chronic MI costs (£, millions)	324,908,701 (257,520,251, 413,036,814)	280,819,049 (221,872,888, 356,177,029)	-44,087,966; -13.6% (-55,799,474, -34,791,851)
	Total healthcare costs (£, millions)	434,303,614 (364,990,639, 527,226,971)	661,246,813 (601,090,398, 741,056,253)	226,875,556; 52.2% (213,864,070, 236,914,075)
	ICER (Δ £/ Δ QALY)			20,335 (16,273, 25,299)

Supplementary Table 8: PSA results – Inclisiran

Age of intervention	Outcome	Control	Intervention	
			Absolute value	Difference to control
30	N	458,692 (458,692, 458,692)	458,692 (458,692, 458,692)	0 (0, 0)
	Incident MIs	65,884 (59,047, 76,917)	33,690 (29,766, 39,714)	-32,242; -48.9% (-37,354, -28,650)
	Deaths	148,250 (135,515, 163,065)	139,254 (127,649, 152,486)	-8,738; -5.9% (-14,489, -5,002)
	YLL	10,961,655 (10,931,241, 10,988,973)	10,982,009 (10,952,616, 11,007,814)	19,794; 0.18% (13,743, 28,370)
	QALYs	9,463,645 (8,605,772, 10,402,795)	9,493,566 (8,633,617, 10,437,793)	29,406; 0.31% (23,242, 37,749)
	Medication costs (£, millions)	24,166,453 (23,773,203, 24,551,866)	43,741,569,402 (43,624,740,406, 43,844,135,502)	43,717,378,445; 180901.1% (43,600,639,086, 43,819,865,783)
	Acute MI costs (£, millions)	30,912,201 (22,151,292, 42,011,453)	16,280,522 (11,541,031, 22,364,139)	-14,716,535; -47.6% (-19,981,216, -10,531,838)
	Chronic MI costs (£, millions)	236,411,076 (177,680,675, 310,583,139)	127,601,851 (94,895,239, 168,608,598)	-108,019,556; -45.7% (-143,154,656, -82,252,199)
	Total healthcare costs (£, millions)	291,595,992 (232,186,590, 368,806,912)	43,884,948,991 (43,763,429,340, 43,996,857,052)	43,594,316,062; 14950.2% (43,470,087,337, 43,696,689,150)
	ICER (Δ £/ Δ QALY)			1,482,023 (1,153,300, 1,873,878)
40	N	456,016 (455,474, 456,463)	456,016 (455,474, 456,463)	0 (0, 0)
	Incident MIs	64,668 (58,176, 75,517)	39,737 (35,432, 46,456)	-25,054; -38.7% (-29,302, -22,180)
	Deaths	146,184 (133,833, 160,457)	139,180 (127,989, 151,873)	-7,000; -4.8% (-11,300, -4,209)
	YLL	9,974,590 (9,934,146, 10,011,467)	9,994,373 (9,954,183, 10,029,037)	19,602; 0.20% (13,530, 27,518)
	QALYs	8,367,720 (7,600,682, 9,226,820)	8,395,712 (7,626,257, 9,259,677)	28,217; 0.34% (22,068, 35,373)
	Medication costs (£, millions)	33,524,575 (33,084,085, 33,927,219)	39,815,478,119 (39,655,605,708, 39,953,316,711)	39,781,975,831; 118665.1% (39,622,223,742, 39,919,602,897)
	Acute MI costs (£, millions)	41,081,469 (29,407,783, 55,720,978)	26,094,072 (18,620,306, 35,564,824)	-15,106,474; -36.8% (-20,599,930, -10,896,565)
	Chronic MI costs (£, millions)	300,337,994 (229,727,005, 390,169,572)	196,065,931 (148,277,720, 253,804,861)	-104,324,276; -34.7% (-137,783,526, -80,016,831)
	Total healthcare costs (£, millions)	375,240,733 (303,129,187, 470,321,391)	40,036,055,620 (39,876,591,305, 40,179,553,607)	39,662,620,818; 10569.9% (39,495,908,930, 39,804,842,380)
	ICER (Δ £/ Δ QALY)			1,406,296 (1,121,775, 1,796,281)
50	N	449,476 (448,240, 450,535)	449,476 (448,240, 450,535)	0 (0, 0)
	Incident MIs	61,604 (55,417, 71,816)	45,288 (40,712, 52,544)	-16,432; -26.7% (-19,491, -14,307)
	Deaths	141,159 (129,584, 154,626)	136,397 (125,542, 148,722)	-4,746; -3.4% (-7,518, -2,862)
	YLL	8,599,242 (8,548,403, 8,643,411)	8,614,235 (8,562,788, 8,658,431)	15,320; 0.18% (10,258, 21,581)
	QALYs	6,985,205 (6,347,824, 7,705,302)	7,006,173 (6,367,532, 7,730,383)	20,826; 0.30% (15,985, 26,603)
	Medication costs (£, millions)	45,019,095 (44,545,200, 45,446,337)	34,328,491,835 (34,123,813,696, 34,504,403,552)	34,283,456,602; 76153.1% (34,079,162,221, 34,459,201,386)
	Acute MI costs (£, millions)	51,257,486 (36,846,314, 69,315,522)	38,697,416 (27,851,400, 52,450,754)	-12,633,136; -24.6% (-17,146,232, -8,984,222)
	Chronic MI costs (£, millions)	346,705,291 (270,211,369, 445,572,288)	267,792,217 (206,616,798, 342,034,938)	-78,601,215; -22.7% (-102,809,693, -60,472,759)
	Total healthcare costs (£, millions)	443,047,023 (365,715,585, 546,622,032)	34,632,504,627 (34,436,892,171, 34,813,862,256)	34,193,924,724; 7717.9% (33,985,504,445, 34,371,271,220)
	ICER (Δ £/ Δ QALY)			1,638,818 (1,283,226, 2,140,728)
60	N	434,024 (432,139, 435,752)	434,024 (432,139, 435,752)	0 (0, 0)
	Incident MIs	53,960 (48,221, 63,678)	45,806 (40,992, 53,710)	-8,217; -15.2% (-10,033, -7,047)
	Deaths	129,376 (118,856, 141,347)	126,948 (116,574, 138,244)	-2,440; -1.9% (-3,946, -1,622)
	YLL	6,718,611 (6,660,927, 6,769,209)	6,726,486 (6,669,616, 6,776,827)	7,826; 0.12% (6,093, 10,490)
	QALYs	5,271,297 (4,793,374, 5,815,845)	5,281,688 (4,801,550, 5,827,429)	10,081; 0.19% (8,130, 12,678)
	Medication costs (£, millions)	53,190,587 (52,633,497, 53,703,497)	26,822,213,091 (26,595,913,227, 27,022,475,949)	26,769,017,372; 50326.6% (26,543,361,451, 26,968,748,023)
	Acute MI costs (£, millions)	55,833,348 (39,943,626, 75,360,416)	48,097,122 (34,688,895, 65,193,370)	-7,737,962; -13.9% (-10,595,013, -5,403,219)
	Chronic MI costs (£, millions)	324,908,701 (257,520,251, 413,036,814)	284,819,867 (225,157,753, 359,471,856)	-39,881,785; -12.3% (-51,327,853, -31,299,814)
	Total healthcare costs (£, millions)	434,303,614 (364,990,639, 527,226,971)	27,151,868,915 (26,940,026,090, 27,357,835,146)	26,721,314,566; 6152.7% (26,492,336,503, 26,924,391,304)
	ICER (Δ £/ Δ QALY)			2,650,674 (2,106,068, 3,298,793)

Supplementary Table 9: PSA results – Summary of all interventions – All females.

Age of intervention	Outcome	Absolute value	Difference to control			
		Control	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	N	252,531 (252,531, 252,531)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	22,634 (19,273, 28,938)	-9,399; -41.5% (-11,785, -8,040)	-11,472; -50.7% (-14,452, -9,831)	-12,409; -54.8% (-15,572, -10,612)	-11,766; -52.0% (-14,820, -9,968)
	Deaths	63,670 (57,736, 71,031)	-3,219; -5.1% (-5,511, -1,728)	-3,914; -6.1% (-6,730, -2,158)	-4,219; -6.6% (-7,232, -2,365)	-4,028; -6.3% (-7,045, -2,224)
	YLL	6,073,022 (6,057,744, 6,086,650)	5,158; 0.08% (1,853, 8,621)	6,097; 0.10% (2,685, 10,113)	6,565; 0.11% (3,020, 10,536)	6,237; 0.10% (2,792, 10,253)
	QALYs	5,180,100 (4,710,153, 5,709,383)	7,310; 0.14% (4,833, 10,279)	8,750; 0.17% (6,027, 12,040)	9,348; 0.18% (6,504, 12,744)	8,927; 0.17% (6,156, 12,263)
	Medication costs (£, millions)	12 (12, 12)	100; 840.8% (100, 100)	155; 1301.4% (155, 155)	289; 2423.2% (288, 289)	24,202; 203273.0% (24,145, 24,252)
	Acute MI costs (£, millions)	10 (7, 14)	-4; -40.9% (-6, -3)	-5; -49.1% (-7, -3)	-5; -52.8% (-7, -4)	-5; -50.3% (-7, -4)
	Chronic MI costs (£, millions)	70 (52, 94)	-28; -39.8% (-37, -21)	-33; -47.5% (-45, -25)	-36; -51.0% (-48, -27)	-34; -48.6% (-46, -26)
	Total healthcare costs (£, millions)	92 (74, 117)	68; 73.9% (58, 75)	117; 126.5% (105, 125)	247; 268.5% (234, 257)	24,163; 26224.9% (24,102, 24,213)
	ICER (Δ £/ Δ QALY)		9,283 (6,437, 14,329)	13,315 (9,503, 19,615)	26,376 (19,310, 37,842)	2,706,488 (1,969,551, 3,926,770)
40	N	251,456 (251,210, 251,654)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	22,317 (19,037, 28,481)	-7,251; -32.5% (-9,071, -6,163)	-9,120; -40.9% (-11,439, -7,762)	-9,968; -44.7% (-12,565, -8,436)	-9,390; -42.1% (-11,949, -7,855)
	Deaths	62,715 (57,026, 69,899)	-2,468; -3.9% (-4,295, -1,260)	-3,114; -5.0% (-5,440, -1,679)	-3,401; -5.4% (-5,981, -1,902)	-3,211; -5.1% (-5,566, -1,763)
	YLL	5,551,019 (5,531,278, 5,569,124)	4,826; 0.09% (1,820, 8,172)	5,970; 0.11% (2,819, 9,367)	6,469; 0.12% (3,238, 10,212)	6,130; 0.11% (2,943, 9,667)
	QALYs	4,601,636 (4,181,089, 5,073,736)	6,879; 0.15% (4,439, 9,668)	8,451; 0.18% (5,754, 11,391)	9,150; 0.20% (6,414, 12,273)	8,675; 0.19% (5,944, 11,680)
	Medication costs (£, millions)	17 (16, 17)	86; 515.3% (85, 86)	136; 816.6% (135, 136)	258; 1550.2% (257, 259)	22,122; 132913.8% (22,044, 22,188)
	Acute MI costs (£, millions)	13 (9, 18)	-4; -31.4% (-6, -3)	-5; -38.9% (-7, -4)	-6; -42.3% (-8, -4)	-5; -39.9% (-7, -4)
	Chronic MI costs (£, millions)	91 (69, 120)	-27; -29.9% (-36, -21)	-34; -36.8% (-44, -26)	-36; -40.0% (-48, -28)	-34; -37.8% (-46, -26)
	Total healthcare costs (£, millions)	121 (98, 152)	54; 44.9% (45, 61)	97; 80.4% (86, 106)	216; 178.6% (203, 225)	22,082; 18268.6% (22,003, 22,150)
	ICER (Δ £/ Δ QALY)		7,858 (5,237, 12,661)	11,505 (8,171, 17,059)	23,551 (17,473, 34,269)	2,545,380 (1,887,241, 3,726,175)
50	N	248,932 (248,399, 249,393)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	21,489 (18,320, 27,408)	-4,642; -21.6% (-5,866, -3,849)	-6,187; -28.8% (-7,863, -5,147)	-6,910; -32.2% (-8,731, -5,791)	-6,416; -29.9% (-8,220, -5,275)
	Deaths	60,522 (55,181, 67,438)	-1,596; -2.6% (-2,858, -753)	-2,126; -3.5% (-3,729, -1,106)	-2,393; -4.0% (-4,150, -1,263)	-2,212; -3.7% (-3,887, -1,181)
	YLL	4,826,271 (4,802,422, 4,846,945)	3,718; 0.08% (816, 6,588)	4,794; 0.10% (1,837, 7,964)	5,331; 0.11% (2,187, 8,715)	4,974; 0.10% (1,957, 8,166)
	QALYs	3,874,808 (3,521,035, 4,274,674)	5,038; 0.13% (2,808, 7,454)	6,520; 0.17% (4,093, 9,084)	7,226; 0.19% (4,688, 9,940)	6,685; 0.17% (4,220, 9,351)
	Medication costs (£, millions)	23 (23, 23)	66; 290.8% (66, 67)	110; 482.3% (109, 110)	216; 948.3% (215, 217)	19,231; 84402.4% (19,131, 19,313)
	Acute MI costs (£, millions)	17 (12, 23)	-3; -20.5% (-5, -2)	-5; -26.9% (-6, -3)	-5; -29.9% (-7, -4)	-5; -27.8% (-6, -3)
	Chronic MI costs (£, millions)	108 (84, 141)	-21; -19.1% (-28, -16)	-27; -24.8% (-35, -21)	-30; -27.4% (-39, -23)	-28; -25.5% (-37, -21)
	Total healthcare costs (£, millions)	148 (123, 182)	42; 28.4% (35, 48)	78; 52.9% (69, 86)	181; 122.2% (171, 189)	19,197; 12942.4% (19,097, 19,282)
	ICER (Δ £/ Δ QALY)		8,289 (5,382, 15,390)	11,995 (8,443, 19,451)	25,135 (18,214, 38,610)	2,874,104 (2,047,217, 4,553,995)
60	N	243,128 (242,279, 243,873)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	19,525 (16,548, 25,222)	-2,164; -11.1% (-2,867, -1,806)	-3,224; -16.5% (-4,282, -2,706)	-3,736; -19.1% (-4,918, -3,128)	-3,387; -17.3% (-4,525, -2,766)
	Deaths	55,576 (50,536, 62,245)	-748; -1.3% (-1,357, -454)	-1,110; -2.0% (-2,041, -673)	-1,294; -2.3% (-2,344, -782)	-1,158; -2.1% (-2,158, -725)
	YLL	3,834,043 (3,806,741, 3,858,245)	1,855; 0.05% (1,341, 2,756)	2,706; 0.07% (1,934, 3,931)	3,102; 0.08% (2,230, 4,576)	2,816; 0.07% (2,013, 4,309)
	QALYs	2,973,414 (2,703,787, 3,280,042)	2,414; 0.08% (1,880, 3,125)	3,491; 0.12% (2,740, 4,541)	4,009; 0.13% (3,151, 5,182)	3,631; 0.12% (2,832, 4,767)
	Medication costs (£, millions)	28 (28, 28)	43; 152.3% (42, 43)	77; 275.8% (77, 78)	162; 576.7% (161, 163)	15,271; 54440.3% (15,164, 15,367)
	Acute MI costs (£, millions)	19 (14, 27)	-2; -10.3% (-3, -1)	-3; -15.2% (-4, -2)	-3; -17.5% (-5, -2)	-3; -15.9% (-4, -2)
	Chronic MI costs (£, millions)	110 (86, 142)	-10; -9.3% (-13, -8)	-15; -13.6% (-19, -12)	-17; -15.6% (-22, -13)	-16; -14.2% (-20, -12)
	Total healthcare costs (£, millions)	158 (133, 191)	30; 19.3% (27, 33)	59; 37.7% (55, 63)	141; 89.6% (136, 146)	15,253; 9681.7% (15,145, 15,347)
	ICER (Δ £/ Δ QALY)		12,564 (9,196, 16,779)	17,049 (12,767, 22,241)	35,275 (26,881, 45,193)	4,195,768 (3,183,393, 5,397,560)

Supplementary Table 10: PSA results – Summary of all interventions – All males.

Age of intervention	Outcome	Absolute value	Difference to control			
		Control	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	N	206,161 (206,161, 206,161)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	43,271 (39,778, 48,051)	-16,080; -37.2% (-17,664, -14,801)	-19,908; -46.0% (-21,745, -18,306)	-21,596; -49.9% (-23,688, -19,888)	-20,458; -47.3% (-22,562, -18,634)
	Deaths	84,461 (77,680, 92,333)	-3,706; -4.4% (-5,926, -2,061)	-4,584; -5.4% (-7,236, -2,614)	-5,010; -5.9% (-7,863, -2,874)	-4,728; -5.6% (-7,522, -2,666)
	YLL	4,888,657 (4,872,621, 4,902,511)	11,015; 0.23% (7,737, 15,437)	13,300; 0.27% (9,698, 18,332)	14,351; 0.29% (10,523, 19,473)	13,660; 0.28% (9,887, 18,887)
	QALYs	4,284,290 (3,894,835, 4,692,361)	16,568; 0.39% (13,110, 21,012)	20,041; 0.47% (15,980, 25,165)	21,567; 0.50% (17,243, 26,812)	20,447; 0.48% (16,366, 25,853)
	Medication costs (£, millions)	12 (12, 12)	78; 636.3% (78, 78)	122; 997.2% (122, 123)	230; 1875.8% (229, 231)	19,515; 159136.6% (19,456, 19,568)
	Acute MI costs (£, millions)	21 (15, 28)	-8; -36.9% (-11, -6)	-9; -45.0% (-13, -7)	-10; -48.6% (-14, -7)	-10; -46.2% (-13, -7)
	Chronic MI costs (£, millions)	165 (126, 217)	-60; -36.2% (-79, -46)	-72; -43.7% (-95, -56)	-78; -47.1% (-102, -60)	-74; -44.6% (-98, -56)
	Total healthcare costs (£, millions)	199 (158, 252)	10; 5.2% (-9, 25)	40; 20.3% (18, 58)	142; 71.3% (116, 161)	19,432; 9771.9% (19,367, 19,485)
	ICER (Δ £/ Δ QALY)		622 (-562, 1,590)	1,986 (820, 3,194)	6,566 (4,864, 8,698)	950,312 (751,702, 1,186,725)
40	N	204,562 (204,256, 204,824)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	42,422 (39,098, 46,946)	-11,856; -27.9% (-13,044, -10,855)	-15,156; -35.7% (-16,683, -13,877)	-16,696; -39.4% (-18,315, -15,364)	-15,652; -36.9% (-17,371, -14,240)
	Deaths	83,414 (76,842, 90,990)	-2,834; -3.4% (-4,393, -1,566)	-3,652; -4.4% (-5,540, -2,131)	-4,022; -4.8% (-6,084, -2,360)	-3,780; -4.5% (-5,797, -2,201)
	YLL	4,423,442 (4,401,853, 4,442,531)	10,595; 0.24% (7,183, 14,690)	13,139; 0.30% (9,496, 17,759)	14,412; 0.33% (10,526, 19,243)	13,541; 0.31% (9,797, 18,369)
	QALYs	3,768,069 (3,419,774, 4,153,084)	15,301; 0.41% (11,754, 19,267)	18,952; 0.50% (14,860, 23,752)	20,652; 0.55% (16,417, 25,809)	19,501; 0.52% (15,214, 24,500)
	Medication costs (£, millions)	17 (17, 17)	65; 384.2% (65, 65)	105; 621.6% (104, 105)	202; 1199.4% (202, 203)	17,660; 104616.3% (17,577, 17,731)
	Acute MI costs (£, millions)	28 (20, 38)	-8; -27.2% (-10, -6)	-10; -34.2% (-13, -7)	-10; -37.5% (-14, -8)	-10; -35.4% (-13, -7)
	Chronic MI costs (£, millions)	209 (161, 272)	-55; -26.2% (-71, -42)	-68; -32.6% (-88, -52)	-75; -35.7% (-96, -57)	-70; -33.4% (-92, -54)
	Total healthcare costs (£, millions)	254 (205, 318)	2; 1.0% (-15, 15)	27; 10.6% (6, 43)	117; 46.2% (95, 135)	17,580; 6919.4% (17,490, 17,655)
	ICER (Δ £/ Δ QALY)		169 (-981, 1,051)	1,433 (288, 2,511)	5,658 (4,132, 7,590)	901,580 (716,602, 1,154,873)
50	N	200,554 (199,824, 201,172)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	40,144 (37,059, 44,324)	-7,095; -17.7% (-7,946, -6,359)	-9,660; -24.1% (-10,731, -8,712)	-10,843; -27.0% (-12,001, -9,879)	-10,008; -24.9% (-11,247, -8,943)
	Deaths	80,636 (74,579, 87,628)	-1,816; -2.3% (-2,762, -902)	-2,466; -3.1% (-3,629, -1,400)	-2,766; -3.4% (-4,084, -1,622)	-2,552; -3.2% (-3,819, -1,475)
	YLL	3,772,703 (3,745,500, 3,796,471)	7,701; 0.20% (4,075, 11,228)	10,144; 0.27% (6,377, 13,843)	11,261; 0.30% (7,409, 15,080)	10,434; 0.28% (6,638, 14,156)
	QALYs	3,110,452 (2,825,946, 3,430,587)	10,471; 0.34% (7,389, 13,783)	13,718; 0.44% (10,346, 17,354)	15,245; 0.49% (11,649, 19,109)	14,116; 0.45% (10,713, 17,939)
	Medication costs (£, millions)	22 (22, 22)	47; 213.5% (47, 48)	82; 367.3% (81, 82)	165; 741.5% (164, 166)	15,054; 67716.6% (14,945, 15,146)
	Acute MI costs (£, millions)	34 (25, 46)	-6; -16.7% (-8, -4)	-8; -22.4% (-10, -6)	-9; -25.0% (-12, -6)	-8; -23.2% (-11, -6)
	Chronic MI costs (£, millions)	238 (186, 304)	-37; -15.7% (-49, -29)	-49; -20.6% (-63, -38)	-55; -23.0% (-69, -43)	-51; -21.4% (-66, -39)
	Total healthcare costs (£, millions)	295 (242, 363)	4; 1.5% (-7, 13)	25; 8.4% (11, 36)	102; 34.4% (86, 114)	14,995; 5075.9% (14,885, 15,092)
	ICER (Δ £/ Δ QALY)		422 (-698, 1,353)	1,809 (729, 2,959)	6,631 (4,920, 8,961)	1,060,317 (833,271, 1,398,079)
60	N	190,902 (189,759, 191,953)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	34,446 (31,652, 38,338)	-2,996; -8.7% (-3,379, -2,671)	-4,584; -13.3% (-5,147, -4,124)	-5,348; -15.5% (-5,983, -4,855)	-4,823; -14.0% (-5,552, -4,232)
	Deaths	73,781 (68,258, 79,882)	-790; -1.1% (-1,098, -528)	-1,220; -1.7% (-1,677, -833)	-1,430; -1.9% (-1,975, -981)	-1,277; -1.7% (-1,825, -879)
	YLL	2,884,350 (2,853,471, 2,911,267)	3,228; 0.11% (2,565, 4,001)	4,801; 0.17% (3,888, 5,908)	5,572; 0.19% (4,527, 6,840)	5,015; 0.17% (4,033, 6,341)
	QALYs	2,298,592 (2,090,807, 2,535,982)	4,150; 0.18% (3,373, 5,097)	6,145; 0.27% (5,077, 7,411)	7,115; 0.31% (5,859, 8,625)	6,440; 0.28% (5,253, 7,982)
	Medication costs (£, millions)	25 (25, 25)	28; 112.0% (28, 28)	54; 215.9% (54, 55)	118; 468.8% (117, 119)	11,497; 45738.7% (11,376, 11,606)
	Acute MI costs (£, millions)	36 (26, 49)	-3; -8.0% (-4, -2)	-4; -12.2% (-6, -3)	-5; -14.1% (-7, -4)	-5; -12.8% (-6, -3)
	Chronic MI costs (£, millions)	215 (171, 271)	-16; -7.3% (-20, -12)	-23; -10.8% (-29, -19)	-27; -12.6% (-34, -21)	-24; -11.3% (-31, -19)
	Total healthcare costs (£, millions)	277 (232, 334)	10; 3.5% (5, 13)	27; 9.6% (20, 32)	86; 31.0% (78, 92)	11,469; 4143.4% (11,344, 11,579)
	ICER (Δ £/ Δ QALY)		2,330 (1,153, 3,468)	4,320 (3,050, 5,694)	12,015 (9,651, 14,910)	1,781,228 (1,438,102, 2,184,265)

Supplementary Table 11: PSA results – Summary of all interventions – Females with LDL-C ≥3.0 mmol/L.

Age of intervention	Outcome	Absolute value	Difference to control			
		Control	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	N	190,859 (190,859, 190,859)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	19,580 (16,690, 25,006)	-8,422; -43.0% (-10,483, -7,200)	-10,242; -52.3% (-12,907, -8,749)	-11,050; -56.4% (-13,905, -9,470)	-10,522; -53.7% (-13,214, -8,923)
	Deaths	49,000 (44,282, 55,066)	-2,914; -5.9% (-4,932, -1,498)	-3,520; -7.2% (-5,906, -1,899)	-3,798; -7.8% (-6,493, -2,074)	-3,620; -7.4% (-6,128, -1,971)
	YLL	4,588,513 (4,576,834, 4,598,845)	4,597; 0.10% (1,841, 7,634)	5,426; 0.12% (2,590, 8,909)	5,792; 0.13% (2,906, 9,426)	5,564; 0.12% (2,674, 9,141)
	QALYs	3,912,651 (3,557,939, 4,312,983)	6,547; 0.17% (4,299, 9,287)	7,802; 0.20% (5,478, 10,862)	8,365; 0.21% (5,908, 11,506)	7,975; 0.20% (5,599, 11,027)
	Medication costs (£, millions)	9 (9, 9)	76; 839.2% (75, 76)	117; 1299.2% (117, 117)	218; 2419.2% (218, 218)	18,290; 202957.7% (18,245, 18,328)
	Acute MI costs (£, millions)	9 (6, 12)	-4; -42.2% (-5, -3)	-4; -50.7% (-6, -3)	-5; -54.5% (-6, -3)	-4; -51.9% (-6, -3)
	Chronic MI costs (£, millions)	61 (45, 82)	-25; -41.2% (-34, -19)	-30; -49.1% (-40, -22)	-32; -52.7% (-42, -24)	-31; -50.3% (-41, -23)
	Total healthcare costs (£, millions)	79 (63, 100)	47; 59.6% (37, 53)	83; 105.3% (72, 90)	181; 230.5% (170, 190)	18,254; 23232.6% (18,207, 18,293)
	ICER (Δ £/ Δ QALY)		7,108 (4,835, 11,147)	10,512 (7,462, 15,690)	21,602 (15,635, 30,967)	2,290,220 (1,652,351, 3,262,681)
40	N	190,012 (189,816, 190,170)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	19,300 (16,483, 24,602)	-6,503; -33.7% (-8,091, -5,494)	-8,155; -42.3% (-10,207, -6,946)	-8,898; -46.1% (-11,176, -7,578)	-8,383; -43.4% (-10,690, -7,075)
	Deaths	48,213 (43,699, 54,133)	-2,220; -4.6% (-3,850, -1,169)	-2,797; -5.8% (-4,844, -1,543)	-3,038; -6.3% (-5,338, -1,712)	-2,863; -5.9% (-4,970, -1,596)
	YLL	4,192,850 (4,177,601, 4,206,457)	4,344; 0.10% (1,678, 7,244)	5,309; 0.13% (2,510, 8,453)	5,757; 0.14% (2,866, 9,026)	5,479; 0.13% (2,627, 8,675)
	QALYs	3,474,711 (3,157,150, 3,831,429)	6,151; 0.18% (4,024, 8,577)	7,533; 0.22% (5,199, 10,158)	8,203; 0.24% (5,837, 10,917)	7,768; 0.22% (5,442, 10,421)
	Medication costs (£, millions)	13 (12, 13)	65; 514.5% (65, 65)	103; 815.4% (102, 103)	195; 1548.3% (194, 195)	16,713; 132758.3% (16,652, 16,766)
	Acute MI costs (£, millions)	11 (8, 16)	-4; -32.6% (-5, -3)	-5; -40.2% (-6, -3)	-5; -43.7% (-7, -4)	-5; -41.2% (-7, -3)
	Chronic MI costs (£, millions)	79 (59, 104)	-25; -31.0% (-32, -18)	-30; -38.1% (-40, -23)	-33; -41.4% (-43, -25)	-31; -39.1% (-41, -23)
	Total healthcare costs (£, millions)	103 (83, 130)	36; 35.3% (28, 43)	68; 65.7% (58, 76)	157; 152.2% (146, 165)	16,677; 16163.6% (16,614, 16,728)
	ICER (Δ £/ Δ QALY)		5,891 (3,822, 9,348)	8,932 (6,466, 13,257)	19,173 (14,317, 27,283)	2,147,789 (1,600,091, 3,066,778)
50	N	188,018 (187,571, 188,386)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	18,581 (15,844, 23,666)	-4,181; -22.5% (-5,261, -3,460)	-5,546; -29.9% (-7,038, -4,639)	-6,177; -33.2% (-7,807, -5,178)	-5,742; -30.9% (-7,371, -4,746)
	Deaths	46,527 (42,230, 52,154)	-1,448; -3.1% (-2,579, -639)	-1,924; -4.1% (-3,379, -986)	-2,134; -4.6% (-3,720, -1,113)	-1,988; -4.3% (-3,530, -1,041)
	YLL	3,643,106 (3,624,472, 3,659,861)	3,300; 0.09% (752, 5,929)	4,288; 0.12% (1,643, 7,168)	4,760; 0.13% (1,969, 7,798)	4,422; 0.12% (1,778, 7,447)
	QALYs	2,923,315 (2,655,529, 3,224,875)	4,567; 0.16% (2,522, 6,729)	5,902; 0.20% (3,730, 8,273)	6,507; 0.22% (4,211, 8,992)	6,074; 0.21% (3,904, 8,608)
	Medication costs (£, millions)	17 (17, 17)	50; 288.2% (50, 50)	83; 478.3% (82, 83)	163; 941.3% (162, 164)	14,518; 83820.4% (14,439, 14,582)
	Acute MI costs (£, millions)	15 (10, 20)	-3; -21.4% (-4, -2)	-4; -28.0% (-6, -3)	-5; -30.9% (-6, -3)	-4; -28.7% (-6, -3)
	Chronic MI costs (£, millions)	94 (72, 122)	-19; -20.0% (-25, -14)	-24; -25.8% (-32, -19)	-27; -28.5% (-35, -20)	-25; -26.5% (-33, -19)
	Total healthcare costs (£, millions)	126 (104, 155)	28; 22.2% (21, 33)	55; 43.2% (46, 61)	132; 104.3% (122, 138)	14,489; 11472.3% (14,411, 14,557)
	ICER (Δ £/ Δ QALY)		6,059 (3,823, 11,639)	9,169 (6,464, 15,067)	20,096 (14,528, 31,155)	2,383,131 (1,681,769, 3,708,045)
60	N	183,402 (182,723, 184,029)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	16,888 (14,311, 21,760)	-1,938; -11.5% (-2,556, -1,618)	-2,884; -17.1% (-3,821, -2,422)	-3,344; -19.8% (-4,390, -2,802)	-3,026; -17.9% (-4,028, -2,478)
	Deaths	42,724 (38,745, 48,101)	-670; -1.6% (-1,206, -411)	-997; -2.3% (-1,804, -609)	-1,156; -2.7% (-2,074, -709)	-1,038; -2.4% (-1,917, -640)
	YLL	2,890,072 (2,868,596, 2,909,268)	1,678; 0.06% (1,213, 2,474)	2,448; 0.08% (1,743, 3,571)	2,804; 0.10% (1,989, 4,148)	2,538; 0.09% (1,804, 3,866)
	QALYs	2,240,077 (2,035,996, 2,470,317)	2,190; 0.10% (1,699, 2,829)	3,150; 0.14% (2,477, 4,078)	3,627; 0.16% (2,828, 4,658)	3,293; 0.15% (2,551, 4,306)
	Medication costs (£, millions)	22 (22, 22)	32; 145.2% (31, 32)	58; 265.2% (57, 58)	121; 557.6% (120, 122)	11,512; 52903.0% (11,427, 11,590)
	Acute MI costs (£, millions)	17 (12, 23)	-2; -10.7% (-2, -1)	-3; -15.7% (-4, -2)	-3; -18.1% (-4, -2)	-3; -16.5% (-4, -2)
	Chronic MI costs (£, millions)	95 (74, 123)	-9; -9.7% (-12, -7)	-13; -14.1% (-17, -10)	-15; -16.2% (-20, -12)	-14; -14.7% (-18, -11)
	Total healthcare costs (£, millions)	134 (113, 163)	20; 15.3% (17, 23)	42; 31.0% (37, 45)	103; 76.6% (98, 107)	11,496; 8566.0% (11,410, 11,573)
	ICER (Δ £/ Δ QALY)		9,318 (6,688, 12,637)	13,178 (9,818, 17,354)	28,440 (21,619, 36,735)	3,488,957 (2,663,533, 4,507,392)

Supplementary Table 12: PSA results – Summary of all interventions – Females with LDL-C ≥4.0 mmol/L.

Age of intervention	Outcome	Absolute value	Difference to control			
		Control	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	N	79,921 (79,921, 79,921)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	10,980 (9,421, 13,870)	-4,934; -44.9% (-6,060, -4,251)	-6,032; -54.9% (-7,458, -5,184)	-6,500; -59.2% (-8,082, -5,580)	-6,178; -56.3% (-7,680, -5,270)
	Deaths	21,500 (19,249, 24,673)	-1,709; -7.9% (-2,844, -872)	-2,074; -9.6% (-3,453, -1,122)	-2,228; -10.4% (-3,756, -1,229)	-2,118; -9.9% (-3,607, -1,156)
	YLL	1,919,657 (1,914,162, 1,924,401)	2,744; 0.14% (1,065, 4,734)	3,261; 0.17% (1,471, 5,449)	3,500; 0.18% (1,651, 5,784)	3,341; 0.17% (1,565, 5,568)
	QALYs	1,635,740 (1,486,934, 1,803,485)	4,028; 0.25% (2,629, 5,707)	4,788; 0.29% (3,258, 6,642)	5,090; 0.31% (3,533, 7,078)	4,882; 0.30% (3,343, 6,798)
	Medication costs (£, millions)	5 (5, 5)	31; 621.4% (30, 31)	48; 974.8% (48, 48)	90; 1835.1% (90, 90)	7,655; 155877.8% (7,636, 7,671)
	Acute MI costs (£, millions)	5 (3, 7)	-2; -44.9% (-3, -2)	-3; -53.9% (-4, -2)	-3; -57.8% (-4, -2)	-3; -55.0% (-4, -2)
	Chronic MI costs (£, millions)	35 (26, 47)	-15; -44.2% (-21, -11)	-18; -52.5% (-25, -14)	-20; -56.2% (-26, -15)	-19; -53.6% (-25, -14)
	Total healthcare costs (£, millions)	45 (36, 57)	13; 28.7% (7, 17)	27; 60.1% (20, 32)	68; 151.1% (61, 73)	7,633; 17032.9% (7,613, 7,650)
	ICER (Δ £/ Δ QALY)		3,212 (1,701, 5,394)	5,612 (3,721, 8,720)	13,181 (9,516, 19,386)	1,563,320 (1,122,363, 2,283,469)
40	N	79,525 (79,428, 79,603)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	10,818 (9,306, 13,646)	-3,768; -34.8% (-4,593, -3,191)	-4,765; -44.0% (-5,892, -4,068)	-5,220; -48.2% (-6,457, -4,429)	-4,904; -45.3% (-6,114, -4,142)
	Deaths	21,153 (18,992, 24,243)	-1,290; -6.1% (-2,213, -647)	-1,628; -7.7% (-2,790, -851)	-1,777; -8.4% (-3,069, -947)	-1,672; -7.9% (-2,889, -868)
	YLL	1,752,536 (1,745,524, 1,759,083)	2,615; 0.15% (944, 4,514)	3,248; 0.19% (1,433, 5,321)	3,518; 0.20% (1,682, 5,632)	3,326; 0.19% (1,520, 5,394)
	QALYs	1,450,655 (1,317,234, 1,600,457)	3,795; 0.26% (2,385, 5,318)	4,636; 0.32% (3,126, 6,297)	5,026; 0.35% (3,467, 6,745)	4,756; 0.33% (3,234, 6,470)
	Medication costs (£, millions)	7 (7, 7)	25; 371.7% (25, 26)	41; 602.8% (41, 41)	80; 1165.4% (80, 80)	6,988; 101891.7% (6,961, 7,012)
	Acute MI costs (£, millions)	7 (5, 9)	-2; -34.0% (-3, -2)	-3; -42.4% (-4, -2)	-3; -46.1% (-4, -2)	-3; -43.7% (-4, -2)
	Chronic MI costs (£, millions)	45 (34, 60)	-15; -32.9% (-20, -11)	-18; -40.6% (-24, -14)	-20; -44.2% (-26, -15)	-19; -41.7% (-25, -14)
	Total healthcare costs (£, millions)	59 (47, 74)	8; 14.0% (3, 12)	20; 34.2% (14, 25)	57; 96.9% (50, 62)	6,966; 11874.9% (6,938, 6,991)
	ICER (Δ £/ Δ QALY)		2,174 (772, 4,216)	4,309 (2,677, 6,898)	11,275 (8,122, 16,897)	1,464,046 (1,075,493, 2,157,394)
50	N	78,576 (78,344, 78,762)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	10,409 (8,942, 13,133)	-2,338; -22.5% (-2,909, -1,912)	-3,179; -30.5% (-3,991, -2,669)	-3,572; -34.3% (-4,486, -3,007)	-3,301; -31.7% (-4,157, -2,725)
	Deaths	20,377 (18,337, 23,278)	-816; -4.0% (-1,441, -336)	-1,103; -5.4% (-1,907, -534)	-1,238; -6.1% (-2,186, -634)	-1,135; -5.6% (-1,980, -575)
	YLL	1,519,940 (1,511,259, 1,527,874)	2,002; 0.13% (272, 3,688)	2,602; 0.17% (818, 4,402)	2,892; 0.19% (1,057, 4,737)	2,707; 0.18% (862, 4,603)
	QALYs	1,218,105 (1,107,316, 1,344,159)	2,771; 0.23% (1,379, 4,217)	3,580; 0.29% (2,117, 5,121)	3,947; 0.32% (2,450, 5,617)	3,689; 0.30% (2,228, 5,293)
	Medication costs (£, millions)	9 (9, 10)	19; 196.3% (18, 19)	32; 341.5% (32, 32)	66; 694.9% (65, 66)	6,058; 63966.9% (6,023, 6,087)
	Acute MI costs (£, millions)	8 (6, 11)	-2; -21.8% (-2, -1)	-2; -28.9% (-3, -2)	-3; -32.1% (-4, -2)	-2; -29.9% (-3, -2)
	Chronic MI costs (£, millions)	54 (41, 70)	-11; -20.8% (-15, -8)	-15; -27.0% (-19, -11)	-16; -30.1% (-21, -12)	-15; -27.9% (-20, -11)
	Total healthcare costs (£, millions)	72 (59, 89)	6; 7.8% (2, 9)	15; 21.3% (10, 19)	47; 65.2% (41, 51)	6,041; 8405.4% (6,005, 6,071)
	ICER (Δ £/ Δ QALY)		2,034 (581, 4,737)	4,262 (2,627, 7,986)	11,792 (8,325, 19,776)	1,634,746 (1,139,990, 2,713,538)
60	N	76,367 (76,001, 76,671)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	9,420 (8,020, 11,994)	-959; -10.2% (-1,214, -796)	-1,541; -16.4% (-1,982, -1,296)	-1,827; -19.4% (-2,346, -1,527)	-1,628; -17.3% (-2,136, -1,329)
	Deaths	18,610 (16,776, 21,256)	-328; -1.8% (-572, -197)	-527; -2.8% (-949, -330)	-627; -3.4% (-1,114, -391)	-552; -3.0% (-1,002, -348)
	YLL	1,200,802 (1,190,973, 1,209,635)	886; 0.07% (623, 1,272)	1,363; 0.11% (974, 1,989)	1,589; 0.13% (1,146, 2,331)	1,425; 0.12% (1,004, 2,139)
	QALYs	929,421 (845,177, 1,025,355)	1,172; 0.13% (891, 1,501)	1,777; 0.19% (1,375, 2,279)	2,074; 0.22% (1,626, 2,647)	1,860; 0.20% (1,424, 2,422)
	Medication costs (£, millions)	12 (12, 12)	10; 83.6% (10, 10)	21; 173.6% (21, 21)	47; 392.6% (47, 48)	4,782; 39605.0% (4,743, 4,817)
	Acute MI costs (£, millions)	10 (7, 13)	-1; -9.7% (-1, -1)	-1; -15.3% (-2, -1)	-2; -17.8% (-2, -1)	-2; -16.0% (-2, -1)
	Chronic MI costs (£, millions)	54 (42, 70)	-5; -9.1% (-6, -4)	-8; -13.9% (-10, -6)	-9; -16.2% (-11, -7)	-8; -14.6% (-10, -6)
	Total healthcare costs (£, millions)	76 (64, 92)	4; 5.6% (3, 5)	12; 15.7% (10, 14)	37; 48.7% (34, 39)	4,772; 6295.9% (4,732, 4,807)
	ICER (Δ £/ Δ QALY)		3,600 (2,014, 5,594)	6,708 (4,723, 9,419)	17,706 (13,702, 23,275)	2,565,053 (1,977,680, 3,346,184)

Supplementary Table 13: PSA results – Summary of all interventions – Females with LDL-C ≥5.0 mmol/L.

Age of intervention	Outcome	Absolute value	Difference to control			
		Control	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	N	16,646 (16,646, 16,646)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	3,365 (2,898, 4,202)	-1,540; -45.8% (-1,856, -1,309)	-1,910; -56.7% (-2,314, -1,635)	-2,064; -61.3% (-2,518, -1,771)	-1,960; -58.3% (-2,401, -1,667)
	Deaths	4,846 (4,235, 5,708)	-525; -10.8% (-913, -223)	-647; -13.4% (-1,114, -311)	-704; -14.5% (-1,201, -350)	-666; -13.7% (-1,163, -334)
	YLL	399,125 (397,601, 400,359)	965; 0.24% (194, 1,789)	1,145; 0.29% (342, 2,046)	1,227; 0.31% (396, 2,153)	1,175; 0.29% (358, 2,076)
	QALYs	339,721 (308,382, 374,420)	1,412; 0.42% (798, 2,113)	1,666; 0.49% (1,040, 2,439)	1,780; 0.52% (1,138, 2,594)	1,698; 0.50% (1,069, 2,515)
	Medication costs (£, millions)	1 (1, 1)	6; 424.8% (6, 6)	10; 682.0% (10, 10)	18; 1308.1% (18, 18)	1,593; 113389.8% (1,588, 1,597)
	Acute MI costs (£, millions)	2 (1, 2)	-1; -47.1% (-1, -1)	-1; -57.0% (-1, -1)	-1; -61.0% (-1, -1)	-1; -58.1% (-1, -1)
	Chronic MI costs (£, millions)	11 (8, 15)	-5; -46.9% (-7, -4)	-6; -55.9% (-9, -5)	-7; -59.9% (-9, -5)	-7; -57.2% (-9, -5)
	Total healthcare costs (£, millions)	14 (11, 19)	-0; -0.7% (-2, 1)	2; 16.0% (-0, 4)	11; 73.8% (8, 12)	1,585; 11051.2% (1,580, 1,590)
	ICER (Δ £/ Δ QALY)		-81 (-1,654, 1,150)	1,388 (-87, 3,045)	5,890 (3,687, 9,882)	933,248 (630,417, 1,479,150)
40	N	16,544 (16,513, 16,572)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	3,314 (2,856, 4,123)	-1,132; -34.1% (-1,372, -933)	-1,480; -44.7% (-1,802, -1,240)	-1,634; -49.3% (-1,972, -1,373)	-1,532; -46.2% (-1,872, -1,268)
	Deaths	4,766 (4,180, 5,593)	-382; -8.0% (-671, -153)	-504; -10.6% (-847, -227)	-558; -11.7% (-934, -264)	-520; -10.9% (-889, -237)
	YLL	363,713 (361,695, 365,414)	880; 0.24% (95, 1,681)	1,110; 0.31% (276, 1,954)	1,207; 0.33% (376, 2,050)	1,132; 0.31% (311, 1,988)
	QALYs	300,606 (272,960, 331,465)	1,279; 0.43% (632, 1,942)	1,588; 0.53% (946, 2,311)	1,721; 0.57% (1,072, 2,487)	1,628; 0.54% (980, 2,374)
	Medication costs (£, millions)	2 (2, 2)	5; 242.9% (5, 5)	8; 411.0% (8, 8)	16; 820.3% (16, 16)	1,451; 74070.6% (1,445, 1,457)
	Acute MI costs (£, millions)	2 (1, 3)	-1; -34.7% (-1, -1)	-1; -44.0% (-1, -1)	-1; -48.0% (-1, -1)	-1; -45.2% (-1, -1)
	Chronic MI costs (£, millions)	15 (11, 20)	-5; -34.5% (-7, -4)	-6; -43.0% (-9, -5)	-7; -46.8% (-9, -5)	-6; -44.1% (-9, -5)
	Total healthcare costs (£, millions)	19 (15, 24)	-1; -5.4% (-3, 0)	1; 4.4% (-1, 3)	8; 43.3% (6, 10)	1,444; 7669.1% (1,437, 1,450)
	ICER (Δ £/ Δ QALY)		-808 (-2,760, 350)	511 (-890, 1,973)	4,748 (2,820, 8,195)	887,716 (608,579, 1,476,516)
50	N	16,294 (16,220, 16,353)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	3,176 (2,739, 3,945)	-635; -20.0% (-813, -475)	-924; -29.1% (-1,159, -743)	-1,062; -33.4% (-1,315, -863)	-971; -30.6% (-1,213, -770)
	Deaths	4,569 (4,035, 5,368)	-216; -4.7% (-415, -32)	-316; -6.9% (-565, -112)	-362; -7.9% (-633, -148)	-328; -7.2% (-581, -123)
	YLL	314,105 (311,715, 316,252)	619; 0.20% (-123, 1,331)	842; 0.27% (49, 1,576)	945; 0.30% (146, 1,716)	878; 0.28% (82, 1,624)
	QALYs	251,174 (228,039, 277,209)	857; 0.34% (276, 1,442)	1,153; 0.46% (529, 1,775)	1,290; 0.51% (647, 1,950)	1,201; 0.48% (570, 1,836)
	Medication costs (£, millions)	3 (3, 3)	3; 115.3% (3, 3)	6; 220.8% (6, 6)	13; 477.8% (13, 13)	1,253; 46461.9% (1,244, 1,260)
	Acute MI costs (£, millions)	3 (2, 4)	-1; -20.2% (-1, -0)	-1; -28.5% (-1, -1)	-1; -32.2% (-1, -1)	-1; -29.6% (-1, -1)
	Chronic MI costs (£, millions)	17 (13, 23)	-3; -19.9% (-5, -2)	-5; -27.1% (-6, -3)	-5; -30.3% (-7, -4)	-5; -28.0% (-7, -4)
	Total healthcare costs (£, millions)	23 (18, 28)	-1; -3.9% (-2, 0)	1; 2.2% (-1, 2)	7; 29.7% (5, 8)	1,247; 5471.5% (1,237, 1,255)
	ICER (Δ £/ Δ QALY)		-1,016 (-3,896, 342)	414 (-1,178, 2,014)	5,168 (3,136, 10,694)	1,037,877 (679,485, 2,188,117)
60	N	15,702 (15,584, 15,803)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	2,836 (2,423, 3,547)	-168; -5.9% (-218, -125)	-373; -13.2% (-465, -305)	-471; -16.6% (-587, -385)	-402; -14.2% (-520, -317)
	Deaths	4,125 (3,676, 4,812)	-56; -1.4% (-95, -27)	-128; -3.1% (-218, -71)	-161; -3.9% (-276, -95)	-138; -3.3% (-239, -80)
	YLL	245,862 (243,116, 248,292)	188; 0.08% (92, 299)	361; 0.15% (227, 545)	448; 0.18% (292, 658)	387; 0.16% (244, 592)
	QALYs	189,652 (172,352, 209,453)	257; 0.14% (168, 362)	477; 0.25% (348, 633)	583; 0.31% (432, 761)	508; 0.27% (372, 686)
	Medication costs (£, millions)	3 (3, 3)	1; 34.7% (1, 1)	3; 100.7% (3, 3)	9; 261.5% (9, 9)	979; 29033.8% (968, 988)
	Acute MI costs (£, millions)	3 (2, 4)	-0; -6.2% (-0, -0)	-0; -12.6% (-1, -0)	-0; -15.6% (-1, -0)	-0; -13.5% (-1, -0)
	Chronic MI costs (£, millions)	17 (13, 22)	-1; -6.2% (-1, -1)	-2; -11.7% (-3, -2)	-2; -14.4% (-3, -2)	-2; -12.5% (-3, -2)
	Total healthcare costs (£, millions)	23 (19, 29)	-0; -0.3% (-1, 0)	1; 4.4% (0, 2)	6; 25.3% (5, 7)	976; 4175.8% (965, 986)
	ICER (Δ £/ Δ QALY)		-278 (-1,888, 1,262)	2,144 (650, 4,024)	10,049 (7,142, 14,075)	1,927,322 (1,422,921, 2,632,635)

Supplementary Table 14: PSA results – Summary of all interventions – Males with LDL-C ≥3.0 mmol/L.

Age of intervention	Outcome	Absolute value	Difference to control			
		Control	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	N	147,997 (147,997, 147,997)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	35,536 (32,698, 39,355)	-13,762; -38.7% (-15,046, -12,604)	-16,958; -47.7% (-18,472, -15,552)	-18,370; -51.7% (-20,075, -16,907)	-17,417; -49.0% (-19,214, -15,901)
	Deaths	61,628 (56,710, 67,648)	-3,162; -5.1% (-5,097, -1,753)	-3,908; -6.3% (-6,210, -2,219)	-4,258; -6.9% (-6,736, -2,450)	-4,015; -6.5% (-6,345, -2,289)
	YLL	3,506,145 (3,494,269, 3,516,370)	9,524; 0.27% (6,401, 13,125)	11,482; 0.33% (8,255, 15,675)	12,330; 0.35% (8,981, 16,812)	11,714; 0.33% (8,453, 16,039)
	QALYs	3,070,341 (2,790,990, 3,363,907)	14,358; 0.47% (11,282, 18,179)	17,226; 0.56% (13,817, 21,554)	18,526; 0.60% (14,927, 23,135)	17,571; 0.57% (14,169, 22,232)
	Medication costs (£, millions)	8 (8, 8)	57; 682.6% (56, 57)	88; 1066.3% (88, 89)	166; 2000.1% (165, 166)	14,004; 169152.1% (13,962, 14,042)
	Acute MI costs (£, millions)	17 (12, 23)	-7; -38.5% (-9, -5)	-8; -46.6% (-11, -6)	-9; -50.4% (-12, -6)	-8; -47.9% (-11, -6)
	Chronic MI costs (£, millions)	137 (104, 180)	-51; -37.6% (-68, -39)	-62; -45.3% (-81, -48)	-67; -48.8% (-87, -51)	-63; -46.2% (-84, -48)
	Total healthcare costs (£, millions)	163 (128, 206)	-2; -1.0% (-19, 11)	18; 11.1% (-2, 34)	90; 55.3% (68, 106)	13,933; 8573.6% (13,883, 13,972)
	ICER (Δ £/ Δ QALY)		-113 (-1,282, 780)	1,048 (-119, 2,103)	4,842 (3,412, 6,596)	792,437 (628,240, 981,103)
40	N	146,762 (146,509, 146,968)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	34,842 (32,136, 38,464)	-10,202; -29.3% (-11,234, -9,306)	-12,979; -37.3% (-14,259, -11,851)	-14,260; -40.9% (-15,571, -13,133)	-13,380; -38.4% (-14,792, -12,135)
	Deaths	60,856 (56,077, 66,488)	-2,422; -4.0% (-3,809, -1,312)	-3,106; -5.1% (-4,747, -1,821)	-3,423; -5.6% (-5,197, -2,035)	-3,209; -5.3% (-4,934, -1,872)
	YLL	3,169,356 (3,153,203, 3,183,300)	9,143; 0.29% (6,085, 12,573)	11,370; 0.36% (8,025, 15,260)	12,425; 0.39% (8,907, 16,445)	11,672; 0.37% (8,268, 15,697)
	QALYs	2,697,144 (2,447,556, 2,972,589)	13,237; 0.49% (10,160, 16,669)	16,334; 0.61% (12,785, 20,526)	17,793; 0.66% (14,114, 22,133)	16,834; 0.62% (13,214, 21,155)
	Medication costs (£, millions)	11 (11, 12)	47; 416.2% (47, 47)	76; 669.3% (76, 76)	146; 1285.4% (145, 146)	12,661; 111544.4% (12,601, 12,715)
	Acute MI costs (£, millions)	23 (16, 31)	-7; -28.4% (-9, -5)	-8; -35.7% (-11, -6)	-9; -39.0% (-12, -6)	-8; -36.8% (-12, -6)
	Chronic MI costs (£, millions)	173 (133, 224)	-47; -27.3% (-62, -36)	-59; -33.9% (-76, -45)	-64; -37.1% (-83, -49)	-60; -34.8% (-79, -46)
	Total healthcare costs (£, millions)	207 (166, 260)	-7; -3.2% (-22, 5)	9; 4.2% (-9, 23)	73; 35.1% (54, 88)	12,593; 6075.8% (12,527, 12,649)
	ICER (Δ £/ Δ QALY)		-503 (-1,693, 342)	556 (-525, 1,501)	4,060 (2,758, 5,618)	748,870 (595,278, 952,624)
50	N	143,639 (143,058, 144,130)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	32,958 (30,496, 36,353)	-6,168; -18.7% (-6,885, -5,512)	-8,311; -25.2% (-9,211, -7,525)	-9,334; -28.3% (-10,261, -8,457)	-8,626; -26.2% (-9,616, -7,708)
	Deaths	58,784 (54,328, 63,876)	-1,553; -2.6% (-2,376, -817)	-2,098; -3.6% (-3,119, -1,204)	-2,356; -4.0% (-3,467, -1,407)	-2,162; -3.7% (-3,268, -1,259)
	YLL	2,696,753 (2,676,891, 2,714,261)	6,776; 0.25% (3,569, 9,619)	8,848; 0.33% (5,505, 11,869)	9,821; 0.36% (6,414, 12,925)	9,160; 0.34% (5,805, 12,246)
	QALYs	2,220,877 (2,017,036, 2,448,685)	9,186; 0.41% (6,558, 11,829)	11,913; 0.54% (9,061, 14,955)	13,232; 0.60% (10,226, 16,454)	12,330; 0.56% (9,459, 15,564)
	Medication costs (£, millions)	15 (15, 15)	35; 233.3% (35, 35)	59; 396.8% (59, 60)	119; 794.7% (118, 120)	10,768; 72003.0% (10,688, 10,839)
	Acute MI costs (£, millions)	28 (20, 38)	-5; -17.7% (-7, -4)	-7; -23.5% (-9, -5)	-7; -26.2% (-10, -5)	-7; -24.4% (-9, -5)
	Chronic MI costs (£, millions)	197 (153, 251)	-33; -16.6% (-42, -25)	-42; -21.6% (-54, -33)	-47; -24.1% (-60, -37)	-44; -22.4% (-57, -34)
	Total healthcare costs (£, millions)	241 (197, 296)	-3; -1.1% (-13, 5)	10; 4.2% (-2, 20)	64; 26.6% (51, 75)	10,717; 4452.8% (10,635, 10,791)
	ICER (Δ £/ Δ QALY)		-287 (-1,414, 572)	850 (-214, 1,816)	4,831 (3,484, 6,680)	869,141 (687,402, 1,133,759)
60	N	136,088 (135,202, 136,908)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	28,236 (26,031, 31,380)	-2,652; -9.4% (-2,998, -2,363)	-3,995; -14.1% (-4,483, -3,597)	-4,642; -16.4% (-5,177, -4,211)	-4,198; -14.9% (-4,805, -3,692)
	Deaths	53,534 (49,563, 57,954)	-702; -1.3% (-989, -471)	-1,061; -2.0% (-1,476, -725)	-1,236; -2.3% (-1,724, -847)	-1,111; -2.1% (-1,576, -760)
	YLL	2,051,049 (2,028,353, 2,071,148)	2,897; 0.14% (2,280, 3,619)	4,227; 0.21% (3,426, 5,234)	4,889; 0.24% (3,944, 5,983)	4,421; 0.22% (3,576, 5,583)
	QALYs	1,631,927 (1,484,688, 1,800,069)	3,722; 0.23% (3,022, 4,548)	5,419; 0.33% (4,464, 6,599)	6,243; 0.38% (5,144, 7,594)	5,668; 0.35% (4,604, 7,020)
	Medication costs (£, millions)	17 (17, 17)	21; 121.5% (21, 21)	39; 230.2% (39, 40)	85; 494.6% (84, 85)	8,180; 47820.2% (8,090, 8,260)
	Acute MI costs (£, millions)	30 (22, 40)	-3; -8.7% (-4, -2)	-4; -13.0% (-5, -3)	-4; -15.0% (-6, -3)	-4; -13.6% (-6, -3)
	Chronic MI costs (£, millions)	178 (141, 224)	-14; -7.9% (-18, -11)	-20; -11.5% (-26, -16)	-24; -13.3% (-30, -19)	-21; -12.0% (-28, -17)
	Total healthcare costs (£, millions)	224 (187, 272)	4; 1.9% (0, 7)	15; 6.7% (9, 19)	57; 25.2% (50, 62)	8,154; 3632.7% (8,064, 8,236)
	ICER (Δ £/ Δ QALY)		1,149 (28, 2,134)	2,765 (1,631, 3,971)	9,021 (7,133, 11,310)	1,439,308 (1,160,604, 1,771,271)

Supplementary Table 15: PSA results – Summary of all interventions – Males with LDL-C ≥4.0 mmol/L.

Age of intervention	Outcome	Absolute value	Difference to control			
		Control	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	N	56,981 (56,981, 56,981)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	17,510 (16,204, 19,305)	-6,957; -39.7% (-7,622, -6,352)	-8,640; -49.3% (-9,408, -7,935)	-9,372; -53.5% (-10,205, -8,633)	-8,872; -50.7% (-9,816, -8,099)
	Deaths	24,574 (22,520, 27,205)	-1,550; -6.3% (-2,550, -791)	-1,948; -7.9% (-3,199, -1,035)	-2,112; -8.6% (-3,431, -1,159)	-2,006; -8.2% (-3,176, -1,084)
	YLL	1,346,798 (1,341,136, 1,351,103)	5,168; 0.38% (3,327, 7,240)	6,216; 0.46% (4,123, 8,659)	6,657; 0.49% (4,590, 9,136)	6,354; 0.47% (4,310, 8,733)
	QALYs	1,177,651 (1,069,735, 1,289,466)	7,824; 0.66% (6,039, 9,997)	9,401; 0.80% (7,344, 11,738)	10,101; 0.86% (7,923, 12,594)	9,609; 0.82% (7,492, 12,053)
	Medication costs (£, millions)	4 (4, 4)	21; 508.2% (21, 21)	33; 806.5% (33, 33)	63; 1532.6% (63, 63)	5,386; 131468.2% (5,369, 5,401)
	Acute MI costs (£, millions)	9 (6, 12)	-4; -40.2% (-5, -3)	-4; -49.1% (-6, -3)	-5; -52.8% (-6, -3)	-4; -50.2% (-6, -3)
	Chronic MI costs (£, millions)	70 (53, 92)	-28; -39.6% (-37, -21)	-33; -47.9% (-44, -26)	-36; -51.6% (-48, -28)	-34; -48.9% (-45, -26)
	Total healthcare costs (£, millions)	83 (65, 106)	-10; -12.6% (-20, -4)	-5; -5.8% (-16, 3)	22; 26.6% (10, 31)	5,347; 6459.7% (5,326, 5,364)
	ICER (Δ £/ Δ QALY)		-1,325 (-2,613, -467)	-501 (-1,714, 373)	2,182 (974, 3,447)	556,804 (443,243, 713,859)
40	N	56,412 (56,294, 56,526)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	17,146 (15,914, 18,824)	-5,060; -29.5% (-5,550, -4,581)	-6,530; -38.1% (-7,117, -5,982)	-7,218; -42.1% (-7,819, -6,641)	-6,746; -39.3% (-7,456, -6,130)
	Deaths	24,240 (22,241, 26,727)	-1,180; -4.9% (-1,862, -610)	-1,544; -6.4% (-2,387, -858)	-1,702; -7.0% (-2,608, -970)	-1,600; -6.6% (-2,459, -866)
	YLL	1,214,216 (1,206,721, 1,220,203)	4,907; 0.40% (3,132, 6,846)	6,098; 0.50% (4,242, 8,300)	6,662; 0.55% (4,678, 8,972)	6,257; 0.52% (4,348, 8,584)
	QALYs	1,030,526 (935,661, 1,136,234)	7,116; 0.69% (5,385, 8,977)	8,844; 0.86% (6,898, 11,069)	9,658; 0.94% (7,557, 11,963)	9,078; 0.88% (7,030, 11,402)
	Medication costs (£, millions)	6 (6, 6)	17; 300.2% (17, 17)	28; 496.7% (28, 28)	55; 974.8% (54, 55)	4,856; 86508.6% (4,831, 4,880)
	Acute MI costs (£, millions)	12 (8, 16)	-3; -29.3% (-5, -2)	-4; -37.2% (-6, -3)	-5; -40.6% (-6, -3)	-4; -38.4% (-6, -3)
	Chronic MI costs (£, millions)	88 (68, 115)	-25; -28.6% (-33, -19)	-32; -35.7% (-41, -24)	-34; -39.0% (-45, -26)	-32; -36.7% (-43, -25)
	Total healthcare costs (£, millions)	106 (85, 133)	-12; -11.3% (-20, -6)	-8; -7.6% (-18, -0)	16; 14.8% (5, 24)	4,819; 4563.8% (4,791, 4,843)
	ICER (Δ £/ Δ QALY)		-1,674 (-2,940, -783)	-905 (-2,107, -33)	1,604 (498, 2,693)	530,430 (421,881, 686,067)
50	N	54,944 (54,662, 55,199)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	16,160 (15,040, 17,697)	-2,907; -18.0% (-3,289, -2,546)	-4,042; -25.0% (-4,498, -3,627)	-4,574; -28.3% (-5,026, -4,127)	-4,196; -26.0% (-4,740, -3,719)
	Deaths	23,342 (21,498, 25,509)	-712; -3.1% (-1,171, -295)	-997; -4.3% (-1,518, -519)	-1,134; -4.9% (-1,698, -624)	-1,046; -4.5% (-1,593, -548)
	YLL	1,026,872 (1,018,000, 1,034,794)	3,499; 0.34% (1,716, 5,269)	4,613; 0.45% (2,744, 6,529)	5,118; 0.50% (3,234, 7,083)	4,767; 0.46% (2,867, 6,689)
	QALYs	842,417 (765,705, 929,393)	4,718; 0.56% (3,223, 6,355)	6,247; 0.74% (4,539, 8,090)	6,965; 0.83% (5,248, 8,889)	6,466; 0.77% (4,836, 8,352)
	Medication costs (£, millions)	7 (7, 8)	12; 155.2% (11, 12)	21; 280.5% (21, 21)	44; 585.4% (43, 44)	4,104; 55134.1% (4,068, 4,133)
	Acute MI costs (£, millions)	14 (10, 19)	-2; -17.4% (-3, -2)	-3; -23.7% (-5, -2)	-4; -26.6% (-5, -3)	-3; -24.6% (-5, -2)
	Chronic MI costs (£, millions)	100 (77, 129)	-17; -16.6% (-22, -13)	-22; -22.1% (-29, -17)	-25; -24.8% (-32, -19)	-23; -22.9% (-30, -18)
	Total healthcare costs (£, millions)	122 (99, 151)	-8; -6.3% (-13, -3)	-5; -3.7% (-12, 1)	15; 12.4% (8, 21)	4,077; 3352.8% (4,041, 4,107)
	ICER (Δ £/ Δ QALY)		-1,601 (-2,976, -699)	-727 (-1,925, 108)	2,158 (1,011, 3,450)	631,317 (487,580, 847,443)
60	N	51,396 (50,944, 51,798)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	13,668 (12,658, 15,053)	-1,069; -7.8% (-1,218, -936)	-1,776; -13.0% (-1,984, -1,590)	-2,116; -15.5% (-2,345, -1,917)	-1,880; -13.8% (-2,167, -1,644)
	Deaths	20,993 (19,427, 22,731)	-277; -1.3% (-393, -176)	-466; -2.2% (-650, -314)	-554; -2.6% (-773, -380)	-492; -2.3% (-700, -333)
	YLL	770,069 (760,425, 778,810)	1,297; 0.17% (973, 1,647)	2,021; 0.26% (1,622, 2,510)	2,361; 0.31% (1,881, 2,927)	2,118; 0.28% (1,684, 2,740)
	QALYs	610,362 (554,408, 673,532)	1,677; 0.27% (1,317, 2,101)	2,599; 0.43% (2,111, 3,186)	3,034; 0.50% (2,497, 3,712)	2,734; 0.45% (2,194, 3,419)
	Medication costs (£, millions)	9 (8, 9)	6; 66.6% (6, 6)	13; 148.3% (13, 13)	30; 347.2% (29, 30)	3,071; 35934.5% (3,034, 3,105)
	Acute MI costs (£, millions)	15 (11, 20)	-1; -7.5% (-2, -1)	-2; -12.1% (-2, -1)	-2; -14.3% (-3, -2)	-2; -12.7% (-3, -1)
	Chronic MI costs (£, millions)	88 (70, 111)	-6; -7.0% (-8, -5)	-10; -11.0% (-12, -8)	-11; -12.9% (-14, -9)	-10; -11.5% (-13, -8)
	Total healthcare costs (£, millions)	112 (93, 136)	-2; -1.4% (-3, -0)	1; 1.1% (-2, 3)	16; 14.5% (13, 19)	3,059; 2741.4% (3,021, 3,094)
	ICER (Δ £/ Δ QALY)		-937 (-2,119, -74)	469 (-630, 1,401)	5,269 (3,826, 6,955)	1,117,871 (892,194, 1,394,101)

Supplementary Table 16: PSA results – Summary of all interventions – Males with LDL-C ≥5.0 mmol/L.

Age of intervention	Outcome	Absolute value	Difference to control			
		Control	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	N	9,188 (9,188, 9,188)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	3,872 (3,594, 4,209)	-1,476; -38.1% (-1,635, -1,319)	-1,896; -49.0% (-2,072, -1,721)	-2,082; -53.8% (-2,270, -1,905)	-1,954; -50.5% (-2,149, -1,750)
	Deaths	4,168 (3,762, 4,724)	-312; -7.5% (-565, -103)	-411; -9.9% (-708, -172)	-454; -10.9% (-765, -197)	-425; -10.2% (-732, -175)
	YLL	216,191 (215,004, 217,101)	1,288; 0.60% (625, 1,971)	1,570; 0.73% (864, 2,281)	1,694; 0.78% (979, 2,457)	1,608; 0.74% (890, 2,322)
	QALYs	188,277 (171,004, 206,193)	1,995; 1.06% (1,352, 2,628)	2,414; 1.28% (1,726, 3,101)	2,595; 1.38% (1,896, 3,322)	2,468; 1.31% (1,781, 3,189)
	Medication costs (£, millions)	1 (1, 1)	3; 329.3% (3, 3)	5; 540.2% (5, 5)	10; 1053.2% (10, 10)	866; 92812.4% (863, 870)
	Acute MI costs (£, millions)	2 (1, 3)	-1; -40.4% (-1, -1)	-1; -50.2% (-1, -1)	-1; -54.5% (-2, -1)	-1; -51.4% (-1, -1)
	Chronic MI costs (£, millions)	17 (13, 22)	-7; -41.4% (-9, -5)	-8; -50.1% (-11, -6)	-9; -54.1% (-12, -7)	-9; -51.4% (-12, -7)
	Total healthcare costs (£, millions)	20 (16, 26)	-5; -23.7% (-7, -3)	-4; -22.4% (-7, -2)	-0; -2.2% (-4, 2)	857; 4313.2% (852, 861)
	ICER (Δ £/ Δ QALY)		-2,390 (-3,998, -1,407)	-1,854 (-3,269, -938)	-164 (-1,407, 755)	347,777 (268,089, 481,998)
40	N	9,062 (9,026, 9,094)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	3,783 (3,518, 4,087)	-1,004; -26.5% (-1,140, -866)	-1,366; -36.1% (-1,517, -1,214)	-1,536; -40.6% (-1,688, -1,379)	-1,420; -37.5% (-1,592, -1,246)
	Deaths	4,101 (3,718, 4,616)	-218; -5.3% (-412, -58)	-308; -7.5% (-529, -123)	-348; -8.5% (-588, -158)	-321; -7.8% (-547, -130)
	YLL	193,771 (192,057, 195,054)	1,165; 0.60% (447, 1,875)	1,479; 0.76% (757, 2,223)	1,624; 0.84% (900, 2,384)	1,525; 0.79% (781, 2,274)
	QALYs	163,522 (148,324, 180,102)	1,731; 1.06% (1,129, 2,324)	2,184; 1.34% (1,558, 2,867)	2,394; 1.46% (1,753, 3,121)	2,248; 1.37% (1,596, 2,965)
	Medication costs (£, millions)	1 (1, 1)	2; 182.0% (2, 2)	4; 320.8% (4, 4)	8; 658.1% (8, 8)	777; 60977.4% (771, 782)
	Acute MI costs (£, millions)	3 (2, 4)	-1; -28.0% (-1, -1)	-1; -36.4% (-1, -1)	-1; -40.5% (-1, -1)	-1; -37.8% (-1, -1)
	Chronic MI costs (£, millions)	21 (16, 28)	-6; -28.5% (-8, -4)	-8; -36.4% (-10, -6)	-8; -40.0% (-11, -6)	-8; -37.5% (-11, -6)
	Total healthcare costs (£, millions)	25 (20, 32)	-4; -17.7% (-7, -3)	-5; -18.2% (-7, -3)	-1; -4.5% (-4, 1)	768; 3046.5% (761, 773)
	ICER (Δ £/ Δ QALY)		-2,568 (-4,604, -1,582)	-2,078 (-3,670, -1,159)	-486 (-1,759, 483)	341,588 (258,456, 479,655)
50	N	8,726 (8,649, 8,792)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	3,520 (3,284, 3,787)	-477; -13.5% (-597, -357)	-752; -21.3% (-878, -627)	-879; -25.0% (-1,008, -749)	-789; -22.4% (-929, -650)
	Deaths	3,915 (3,571, 4,358)	-114; -2.9% (-256, 26)	-182; -4.6% (-336, -39)	-216; -5.5% (-376, -63)	-192; -4.9% (-347, -45)
	YLL	161,545 (159,411, 163,431)	709; 0.44% (52, 1,386)	1,000; 0.62% (316, 1,684)	1,143; 0.71% (465, 1,843)	1,042; 0.64% (355, 1,737)
	QALYs	131,669 (119,367, 145,225)	986; 0.75% (431, 1,537)	1,388; 1.05% (814, 1,948)	1,571; 1.19% (1,006, 2,170)	1,443; 1.10% (862, 2,056)
	Medication costs (£, millions)	2 (2, 2)	1; 79.0% (1, 1)	3; 167.1% (3, 3)	6; 381.3% (6, 6)	646; 38666.8% (638, 653)
	Acute MI costs (£, millions)	3 (2, 4)	-0; -14.2% (-1, -0)	-1; -21.0% (-1, -0)	-1; -24.3% (-1, -1)	-1; -22.0% (-1, -0)
	Chronic MI costs (£, millions)	23 (18, 30)	-3; -14.4% (-5, -2)	-5; -20.5% (-6, -3)	-5; -23.4% (-7, -4)	-5; -21.4% (-7, -4)
	Total healthcare costs (£, millions)	28 (23, 35)	-3; -8.9% (-4, -1)	-3; -9.4% (-4, -1)	0; 0.5% (-2, 2)	641; 2264.1% (632, 648)
	ICER (Δ £/ Δ QALY)		-2,539 (-6,127, -1,204)	-1,948 (-3,886, -865)	86 (-1,155, 1,191)	444,613 (310,148, 744,599)
60	N	7,923 (7,800, 8,038)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
	Incident MIs	2,888 (2,689, 3,126)	-85; -2.9% (-119, -53)	-251; -8.7% (-291, -211)	-331; -11.5% (-377, -288)	-275; -9.5% (-337, -220)
	Deaths	3,432 (3,160, 3,751)	-21; -0.6% (-41, 0)	-64; -1.9% (-98, -35)	-85; -2.5% (-128, -48)	-70; -2.0% (-110, -39)
	YLL	117,405 (115,154, 119,547)	152; 0.13% (47, 266)	333; 0.28% (202, 469)	420; 0.36% (274, 577)	356; 0.30% (228, 518)
	QALYs	92,479 (83,467, 102,183)	199; 0.22% (113, 292)	430; 0.46% (316, 565)	542; 0.59% (407, 692)	465; 0.50% (338, 619)
	Medication costs (£, millions)	2 (2, 2)	0; 21.1% (0, 0)	1; 80.6% (1, 1)	4; 225.5% (4, 4)	468; 26121.2% (459, 476)
	Acute MI costs (£, millions)	3 (2, 4)	-0; -3.3% (-0, -0)	-0; -8.4% (-0, -0)	-0; -10.8% (-0, -0)	-0; -9.1% (-0, -0)
	Chronic MI costs (£, millions)	20 (15, 25)	-1; -3.5% (-1, -0)	-2; -7.9% (-2, -1)	-2; -10.0% (-3, -1)	-2; -8.6% (-2, -1)
	Total healthcare costs (£, millions)	25 (20, 30)	-0; -1.7% (-1, -0)	-0; -1.5% (-1, 0)	2; 7.0% (1, 2)	466; 1895.5% (457, 474)
	ICER (Δ £/ Δ QALY)		-2,073 (-4,344, -659)	-872 (-2,224, 103)	3,138 (1,727, 4,952)	1,004,317 (748,935, 1,381,204)

Supplementary Table 17: Microsimulation results – Summary of all interventions. All results shown are the difference between the intervention and control.

Age of intervention	Outcome	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	Incident MIs	-25,883 (-38.1%)	-31,875 (-46.9%)	-34,586 (-50.9%)	-32,729 (-48.2%)
	QALYs	21,782 (0.23%)	26,939 (0.28%)	29,236 (0.31%)	27,617 (0.29%)
	Total healthcare costs (£)	82,392,888 (28.8%)	161,624,870 (56.4%)	393,715,215 (137.5%)	43,582,356,269 (15216.0%)
	ICER (Δ £/ Δ QALY)	3,783	6,000	13,467	1,578,096
40	Incident MIs	-19,336 (-29.0%)	-24,497 (-36.7%)	-26,885 (-40.3%)	-25,222 (-37.8%)
	QALYs	24,071 (0.29%)	29,312 (0.35%)	31,860 (0.38%)	30,033 (0.36%)
	Total healthcare costs (£)	60,423,157 (16.3%)	129,235,709 (34.9%)	339,000,420 (91.5%)	39,669,178,581 (10711.5%)
	ICER (Δ £/ Δ QALY)	2,510	4,409	10,640	1,320,842
50	Incident MIs	-11,387 (-17.9%)	-15,526 (-24.5%)	-17,500 (-27.6%)	-16,113 (-25.4%)
	QALYs	16,312 (0.23%)	21,172 (0.30%)	23,625 (0.34%)	21,921 (0.31%)
	Total healthcare costs (£)	53,513,442 (12.4%)	111,500,438 (25.8%)	291,367,018 (67.5%)	34,178,901,472 (7912.4%)
	ICER (Δ £/ Δ QALY)	3,281	5,266	12,333	1,559,218
60	Incident MIs	-5,225 (-9.4%)	-7,953 (-14.3%)	-9,242 (-16.7%)	-8,376 (-15.1%)
	QALYs	6,519 (0.12%)	9,769 (0.18%)	11,392 (0.22%)	10,397 (0.20%)
	Total healthcare costs (£)	43,357,929 (10.5%)	90,704,470 (21.9%)	231,710,148 (56.1%)	26,666,171,201 (6452.7%)
	ICER (Δ £/ Δ QALY)	6,651	9,285	20,339	2,564,745

Supplementary Table 18: Microsimulation results – Summary of all interventions. Scenario 1: discounting rate set at 0%. All results shown are the difference between the intervention and control.

Age of intervention	Outcome	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	Incident MIs	-25,883 (-38.1%)	-31,875 (-46.9%)	-34,586 (-50.9%)	-32,729 (-48.2%)
	QALYs	93,374 (0.47%)	115,674 (0.58%)	125,562 (0.63%)	118,608 (0.60%)
	Total healthcare costs (£)	-36,453,099 (-3.3%)	97,760,617 (8.9%)	582,014,009 (53.2%)	93,797,945,972 (8579.8%)
	ICER (Δ £/ Δ QALY)	-390	845	4,635	790,823
40	Incident MIs	-19,336 (-29.0%)	-24,497 (-36.7%)	-26,885 (-40.3%)	-25,222 (-37.8%)
	QALYs	76,402 (0.49%)	93,385 (0.60%)	101,569 (0.65%)	95,729 (0.61%)
	Total healthcare costs (£)	-8,533,435 (-0.8%)	98,925,224 (9.5%)	488,552,996 (46.9%)	75,529,740,650 (7252.4%)
	ICER (Δ £/ Δ QALY)	-112	1,059	4,810	788,996
50	Incident MIs	-11,387 (-17.9%)	-15,526 (-24.5%)	-17,500 (-27.6%)	-16,113 (-25.4%)
	QALYs	39,602 (0.34%)	51,684 (0.45%)	57,780 (0.50%)	53,529 (0.46%)
	Total healthcare costs (£)	36,020,700 (3.9%)	120,348,459 (13.1%)	415,515,481 (45.2%)	57,151,962,076 (6211.3%)
	ICER (Δ £/ Δ QALY)	910	2,329	7,191	1,067,690
60	Incident MIs	-5,225 (-9.4%)	-7,953 (-14.3%)	-9,242 (-16.7%)	-8,376 (-15.1%)
	QALYs	12,361 (0.16%)	18,586 (0.24%)	21,661 (0.28%)	19,761 (0.26%)
	Total healthcare costs (£)	47,823,117 (6.9%)	112,043,302 (16.2%)	315,526,128 (45.7%)	38,895,130,994 (5631.1%)
	ICER (Δ £/ Δ QALY)	3,869	6,029	14,566	1,968,324

Supplementary Table 19: Microsimulation results – Summary of all interventions. Scenario 2: discounting rate set at 1.5%. All results shown are the difference between the intervention and control.

Age of intervention	Outcome	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	Incident MIs	-25,883 (-38.1%)	-31,875 (-46.9%)	-34,586 (-50.9%)	-32,729 (-48.2%)
	QALYs	48,912 (0.35%)	60,553 (0.43%)	65,721 (0.47%)	62,082 (0.44%)
	Total healthcare costs (£)	45,608,174 (7.6%)	150,959,586 (25.1%)	492,304,095 (82.0%)	65,125,822,589 (10842.4%)
	ICER (Δ £/ Δ QALY)	932	2,493	7,491	1,049,031
40	Incident MIs	-19,336 (-29.0%)	-24,497 (-36.7%)	-26,885 (-40.3%)	-25,222 (-37.8%)
	QALYs	45,782 (0.39%)	55,871 (0.48%)	60,749 (0.52%)	57,260 (0.49%)
	Total healthcare costs (£)	35,885,063 (5.5%)	123,542,460 (18.8%)	415,209,534 (63.4%)	55,884,667,945 (8526.7%)
	ICER (Δ £/ Δ QALY)	784	2,211	6,835	975,975
50	Incident MIs	-11,387 (-17.9%)	-15,526 (-24.5%)	-17,500 (-27.6%)	-16,113 (-25.4%)
	QALYs	26,775 (0.29%)	34,860 (0.38%)	38,940 (0.42%)	36,098 (0.39%)
	Total healthcare costs (£)	47,397,560 (7.2%)	118,522,324 (18.1%)	353,563,081 (53.9%)	45,120,891,316 (6878.4%)
	ICER (Δ £/ Δ QALY)	1,770	3,400	9,080	1,249,939
60	Incident MIs	-5,225 (-9.4%)	-7,953 (-14.3%)	-9,242 (-16.7%)	-8,376 (-15.1%)
	QALYs	9,333 (0.14%)	14,012 (0.22%)	16,335 (0.25%)	14,905 (0.23%)
	Total healthcare costs (£)	46,061,885 (8.4%)	102,038,095 (18.6%)	274,432,424 (49.9%)	32,795,465,117 (5968.1%)
	ICER (Δ £/ Δ QALY)	4,935	7,282	16,800	2,200,348

Supplementary Table 20: Microsimulation results – Summary of all interventions. Scenario 3: Interventions decrease in efficacy at 1% per year. All results shown are the difference between the intervention and control.

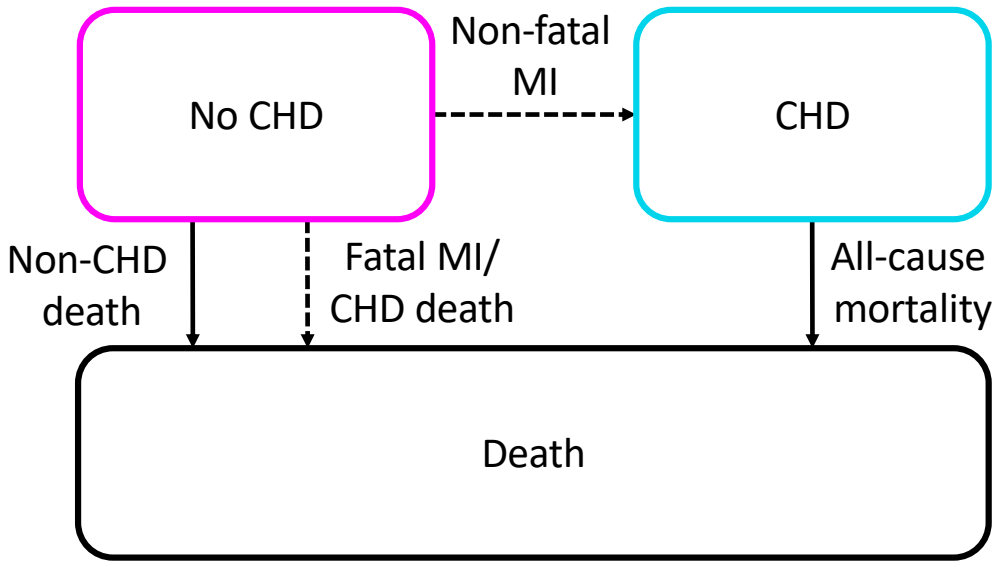
Age of intervention	Outcome	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	Incident MIs	-15,801 (-22.9%)	-20,263 (-29.4%)	-22,262 (-32.3%)	-27,941 (-40.5%)
	QALYs	13,723 (0.14%)	17,401 (0.18%)	19,106 (0.20%)	24,213 (0.25%)
	Total healthcare costs (£)	113,452,108 (39.4%)	197,535,931 (68.6%)	431,581,629 (149.8%)	43,584,306,649 (15126.3%)
	ICER (Δ £/ Δ QALY)	8,267	11,352	22,589	1,800,056
40	Incident MIs	-11,905 (-17.6%)	-15,764 (-23.3%)	-17,517 (-25.8%)	-22,227 (-32.8%)
	QALYs	16,902 (0.20%)	21,072 (0.25%)	22,909 (0.27%)	27,689 (0.33%)
	Total healthcare costs (£)	89,373,665 (24.0%)	163,202,445 (43.8%)	375,115,442 (100.6%)	39,670,251,707 (10642.5%)
	ICER (Δ £/ Δ QALY)	5,288	7,745	16,374	1,432,698
50	Incident MIs	-6,730 (-10.4%)	-9,743 (-15.1%)	-11,191 (-17.3%)	-14,635 (-22.7%)
	QALYs	11,143 (0.16%)	14,773 (0.21%)	16,529 (0.24%)	20,514 (0.29%)
	Total healthcare costs (£)	74,805,651 (17.2%)	137,849,638 (31.7%)	319,735,009 (73.4%)	34,177,605,838 (7850.2%)
	ICER (Δ £/ Δ QALY)	6,713	9,331	19,344	1,666,038
60	Incident MIs	-2,892 (-5.1%)	-4,957 (-8.8%)	-5,955 (-10.5%)	-8,154 (-14.4%)
	QALYs	3,664 (0.07%)	6,180 (0.12%)	7,445 (0.14%)	10,169 (0.19%)
	Total healthcare costs (£)	54,631,235 (13.1%)	104,787,786 (25.1%)	247,353,143 (59.2%)	26,661,683,325 (6380.4%)
	ICER (Δ £/ Δ QALY)	14,909	16,957	33,226	2,621,841

Supplementary Table 21: Microsimulation results – Summary of all interventions. Scenario 4: 40% of people stop taking therapy immediately. All results shown are the difference between the intervention and control.

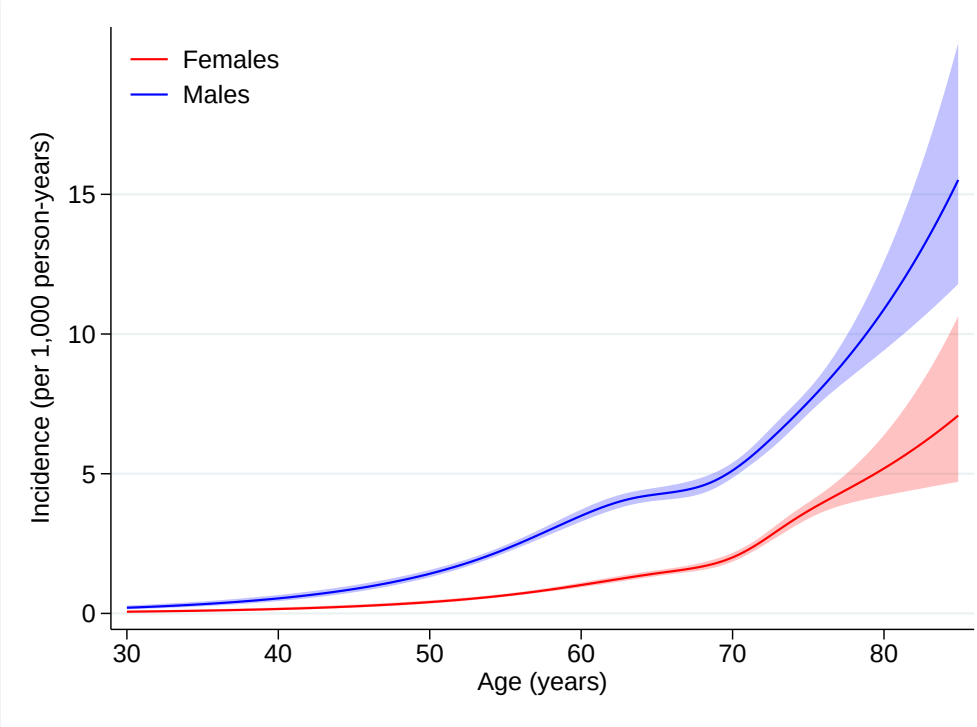
Age of intervention	Outcome	Low/moderate intensity statins	High intensity statins	Low/moderate intensity statins and ezetimibe	Inclisiran
30	Incident MIs	-10,975 (-15.7%)	-14,350 (-20.5%)	-15,876 (-22.7%)	-14,786 (-21.1%)
	QALYs	8,967 (0.09%)	11,695 (0.12%)	13,007 (0.14%)	12,072 (0.13%)
	Total healthcare costs (£)	55,322,129 (19.4%)	103,355,471 (36.3%)	242,568,844 (85.1%)	26,124,530,785 (9163.4%)
	ICER (Δ £/ Δ QALY)	6,169	8,837	18,650	2,163,993
40	Incident MIs	-7,950 (-11.6%)	-10,821 (-15.7%)	-12,120 (-17.6%)	-11,198 (-16.3%)
	QALYs	12,334 (0.15%)	15,454 (0.18%)	16,841 (0.20%)	15,876 (0.19%)
	Total healthcare costs (£)	39,954,918 (10.8%)	81,955,266 (22.2%)	207,556,429 (56.3%)	23,776,594,442 (6452.9%)
	ICER (Δ £/ Δ QALY)	3,239	5,303	12,324	1,497,676
50	Incident MIs	-4,049 (-6.2%)	-6,334 (-9.7%)	-7,435 (-11.3%)	-6,644 (-10.1%)
	QALYs	7,738 (0.11%)	10,544 (0.15%)	11,938 (0.17%)	10,958 (0.16%)
	Total healthcare costs (£)	35,140,731 (8.2%)	70,627,421 (16.5%)	178,563,991 (41.6%)	20,495,961,413 (4773.9%)
	ICER (Δ £/ Δ QALY)	4,541	6,699	14,957	1,870,453
60	Incident MIs	-1,578 (-2.7%)	-3,117 (-5.4%)	-3,860 (-6.7%)	-3,352 (-5.8%)
	QALYs	2,012 (0.04%)	3,909 (0.07%)	4,819 (0.09%)	4,193 (0.08%)
	Total healthcare costs (£)	24,702,586 (6.0%)	53,358,030 (13.0%)	138,093,188 (33.7%)	15,990,249,011 (3897.5%)
	ICER (Δ £/ Δ QALY)	12,276	13,650	28,658	3,813,926

Supplementary Table 22: Maximum annual cost of Inclisiran (£; 284mg dose twice yearly) at which the ICER is under the UK willingness-to-pay (WTP) threshold, by discounting rate, WTP threshold, sex, and LDL-C.

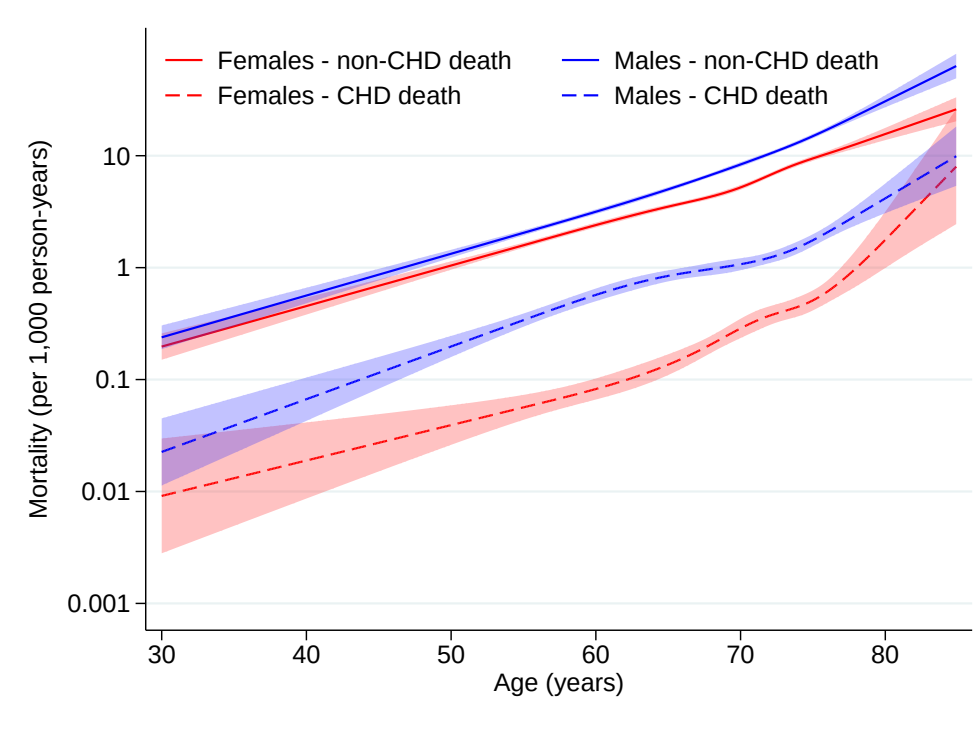
Discounting rate	WTP threshold (£)	Sex	Age of intervention	LDL-C			
				Overall	≥3.0 mmol/L	≥4.0 mmol/L	≥5.0 mmol/L
3.5%	20,000	Female	30	34	46	62	120
			40	43	54	77	124
			50	37	42	62	76
			60	31	36	50	67
		Male	30	98	123	183	273
			40	113	136	197	318
			50	102	122	162	225
			60	63	74	101	100
	30,000	Female	30	48	64	87	168
			40	60	75	108	174
			50	50	57	85	102
			60	41	48	66	88
		Male	30	137	173	259	387
			40	159	192	279	451
			50	143	172	228	316
			60	85	102	138	135
0.0%	20,000	Female	30	70	91	125	229
			40	74	91	131	201
			50	54	62	93	109
			60	39	46	63	83
		Male	30	190	238	348	513
			40	184	221	317	502
			50	144	174	226	303
			60	79	94	126	123
	30,000	Female	30	98	128	175	324
			40	103	128	184	282
			50	74	86	128	146
			60	53	61	84	111
		Male	30	268	338	495	730
			40	260	313	451	715
			50	203	246	319	428
			60	108	130	174	169



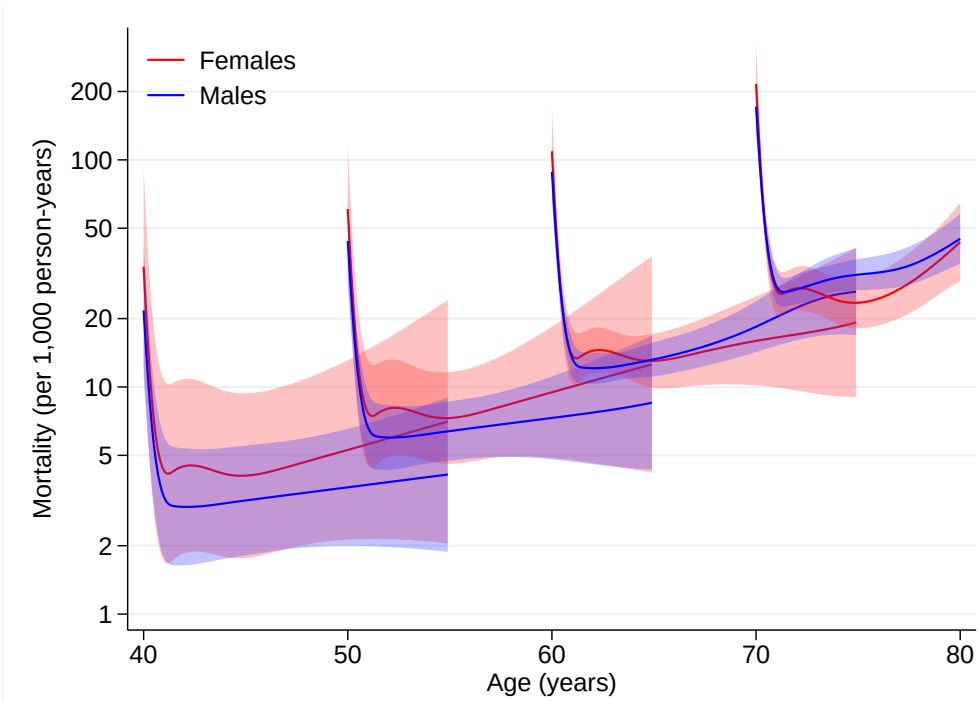
Supplementary Figure 1: Model structure. Dashed lines are transition probabilities influenced by mean cumulative LDL-C; solid lines are transition probabilities not influenced by LDL-C.



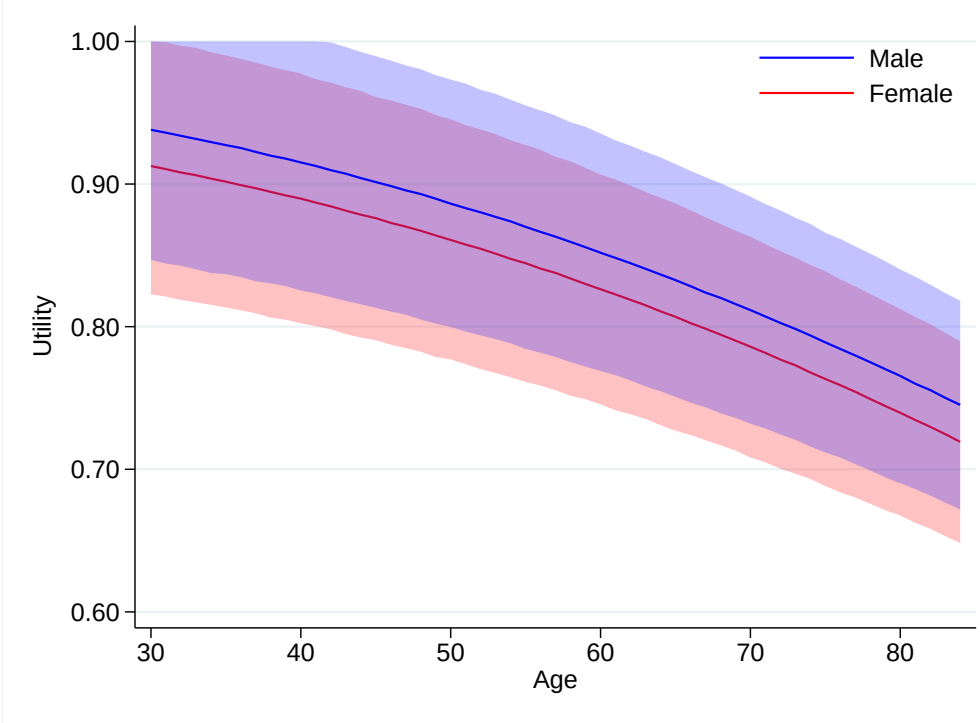
Supplementary Figure 2: Age- and sex-specific incidence of non-fatal MI among UK Biobank participants



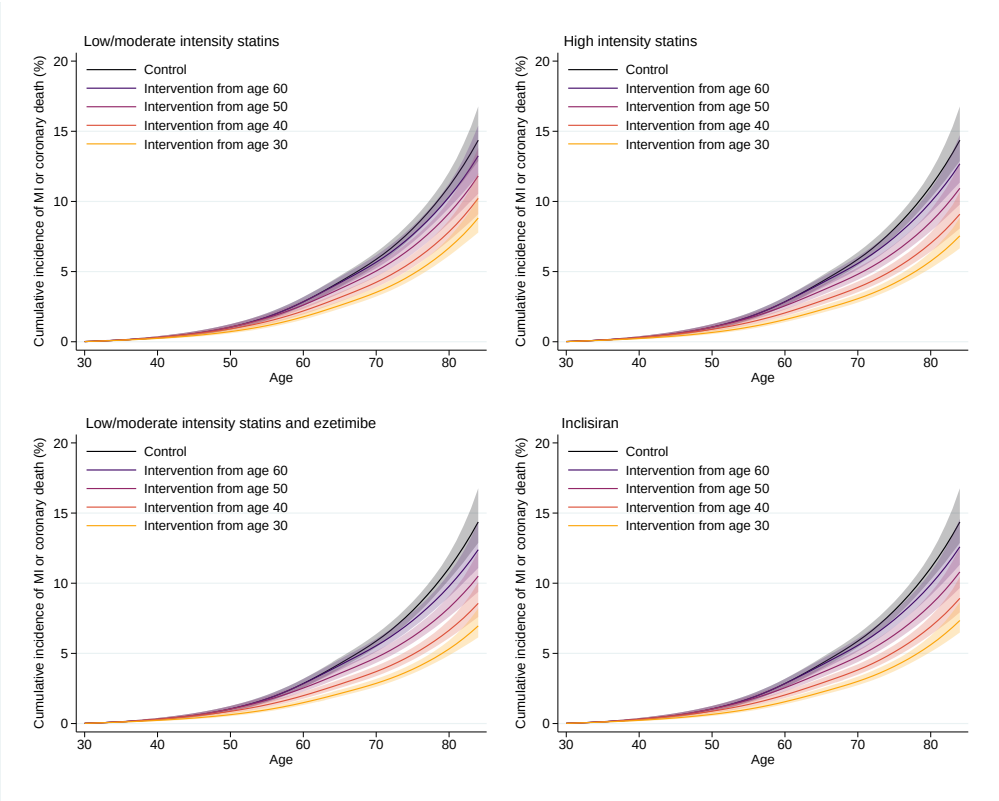
Supplementary Figure 3: Age-, sex-, and cause-specific mortality among UK Biobank participants without CVD



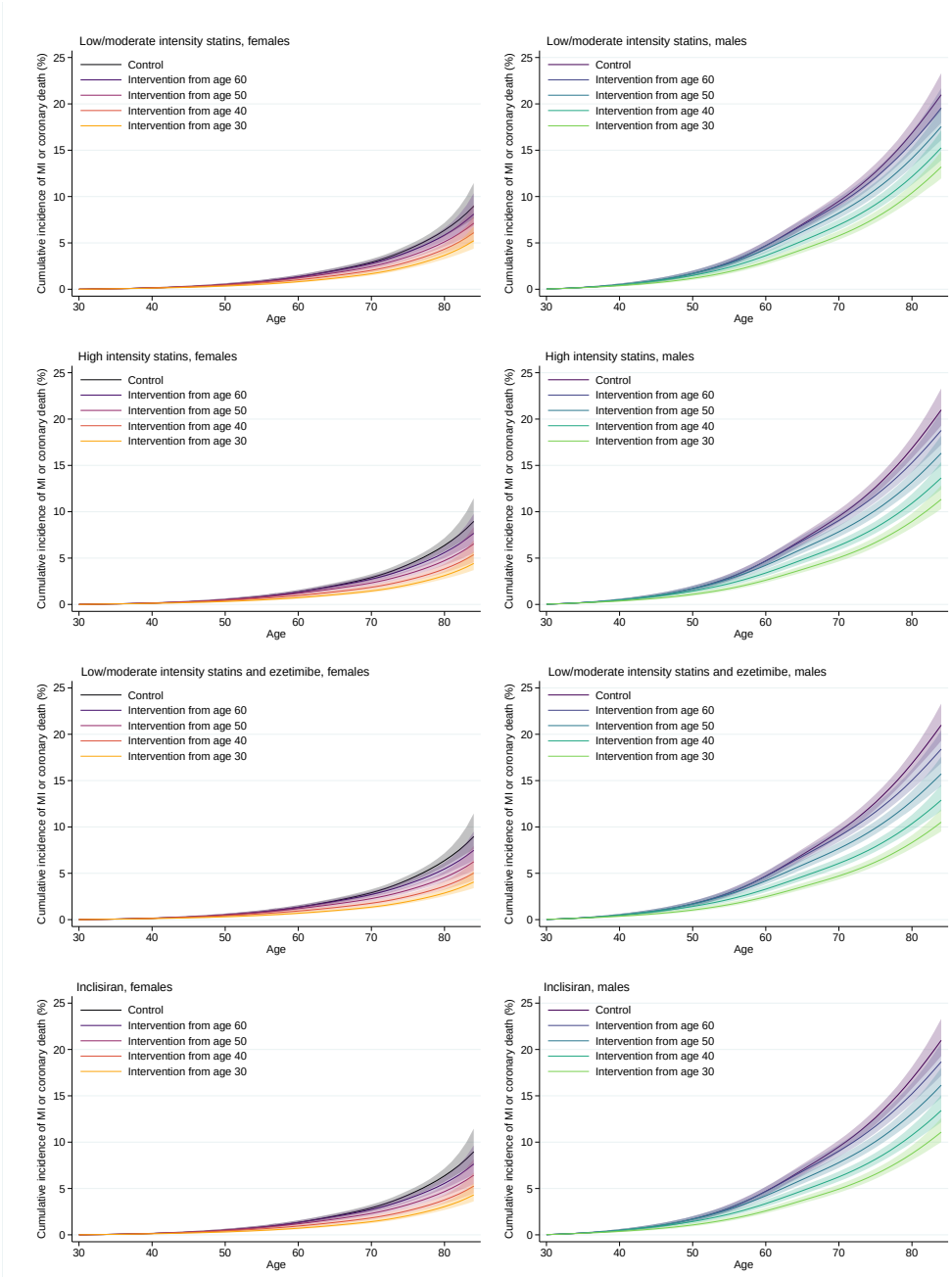
Supplementary Figure 4: Age-, sex-, and time-since-MI-specific mortality among UK Biobank participants with MI



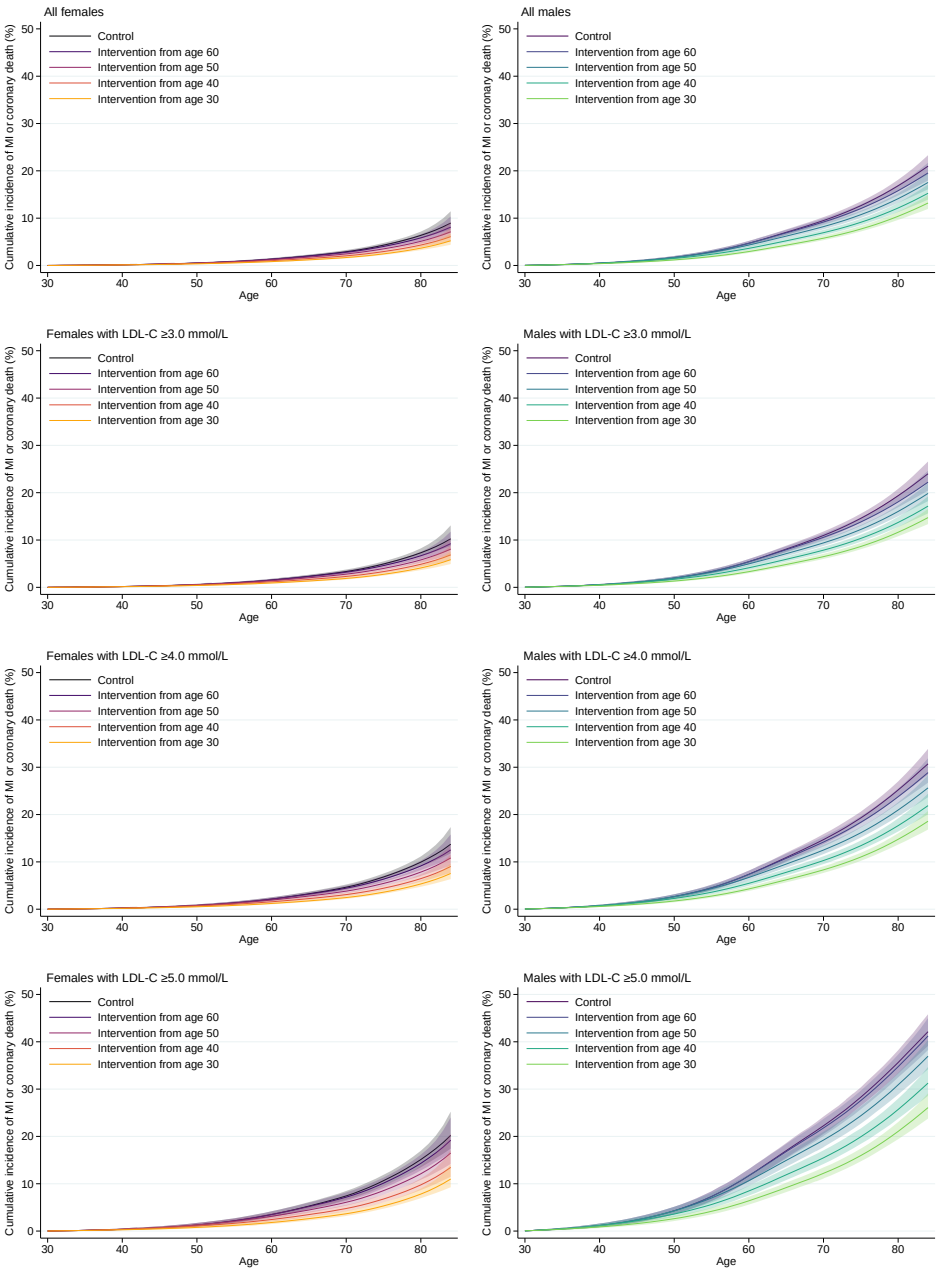
Supplementary Figure 5: Distribution of utility values for people without MI in PSA



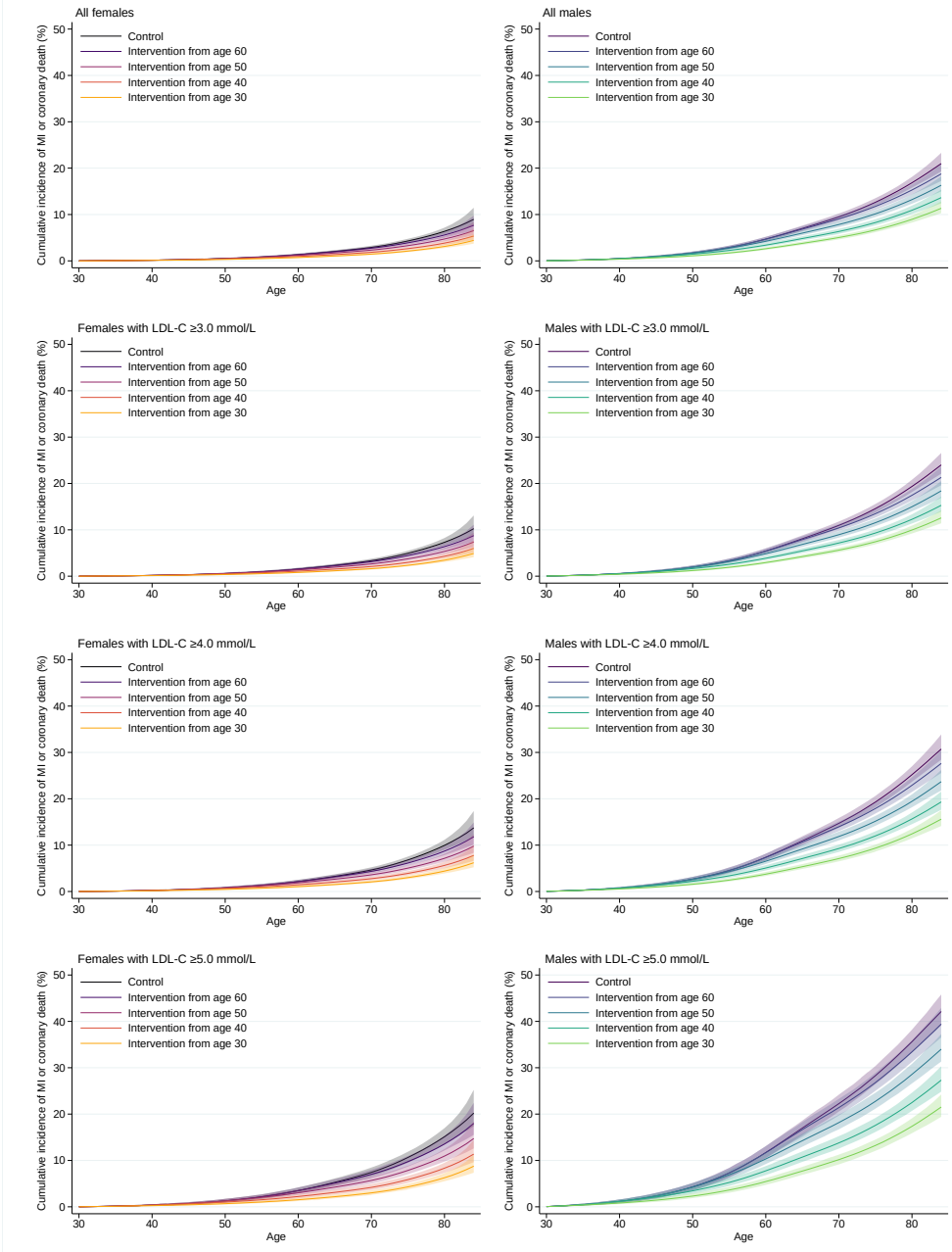
Supplementary Figure 6: Cumulative incidence of MI or coronary death, by intervention



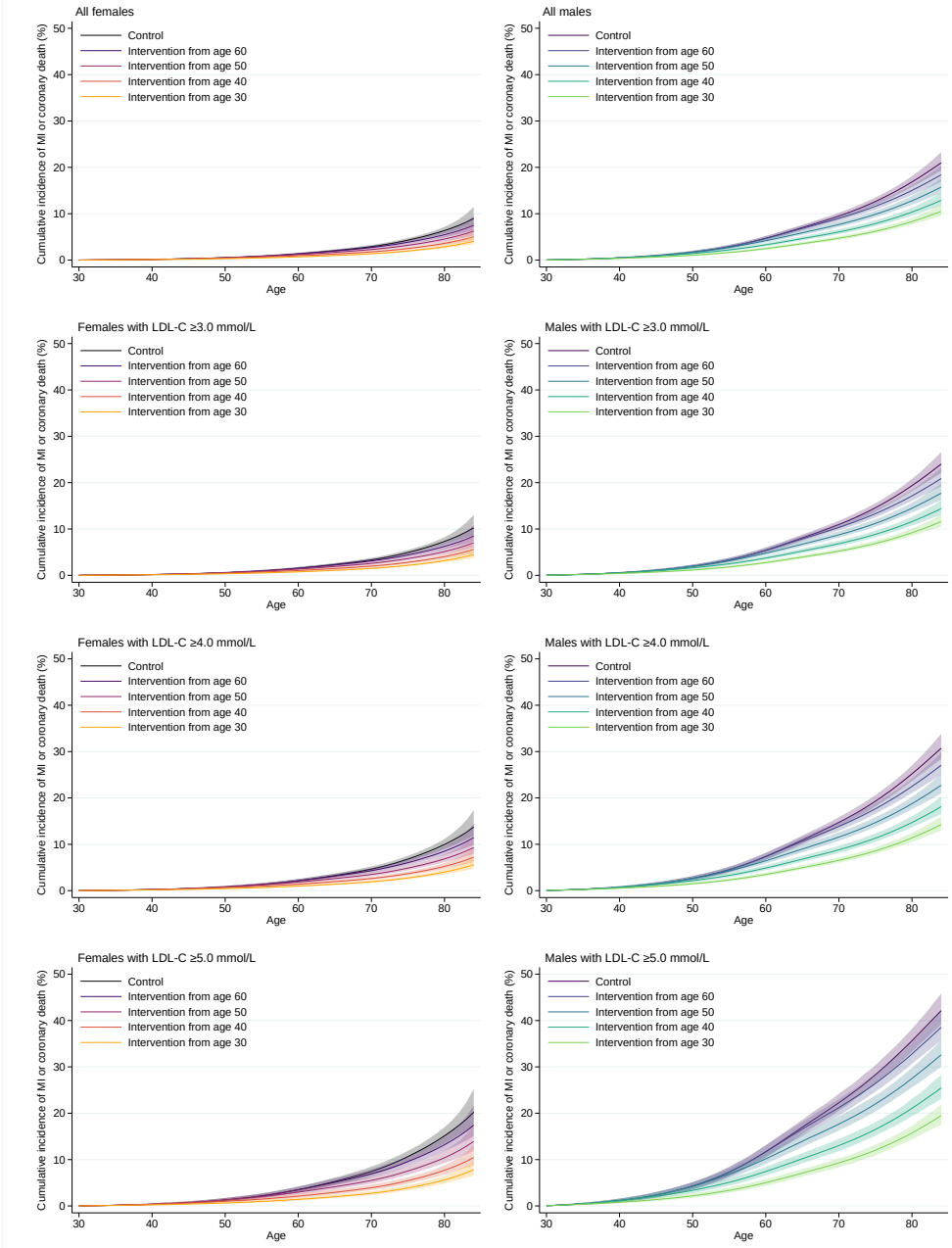
Supplementary Figure 7: Cumulative incidence of MI or coronary death, by intervention and sex



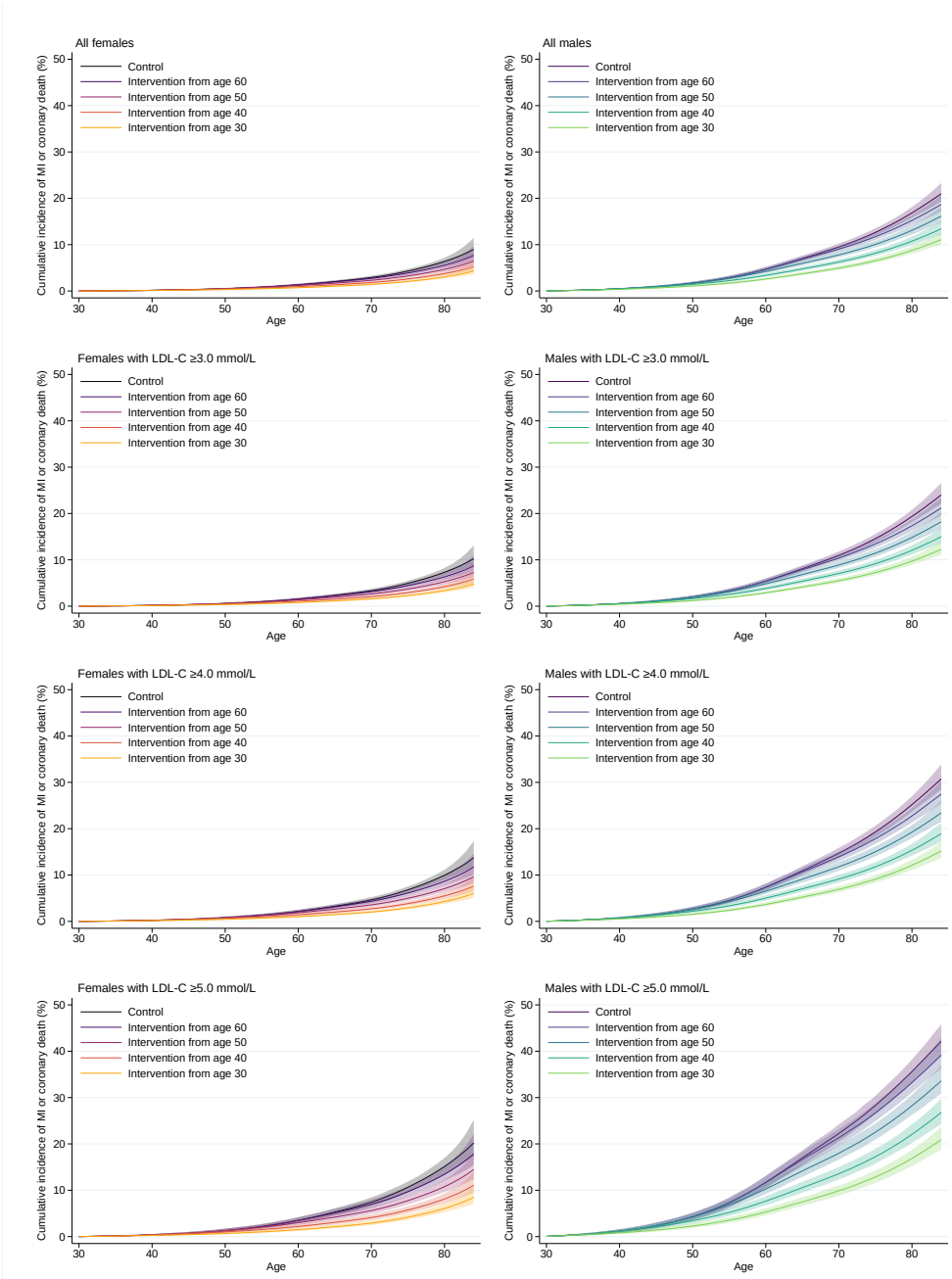
Supplementary Figure 8: Cumulative incidence of MI or coronary death, by sex, LDL-C, and age of intervention – Low/moderate intensity statins



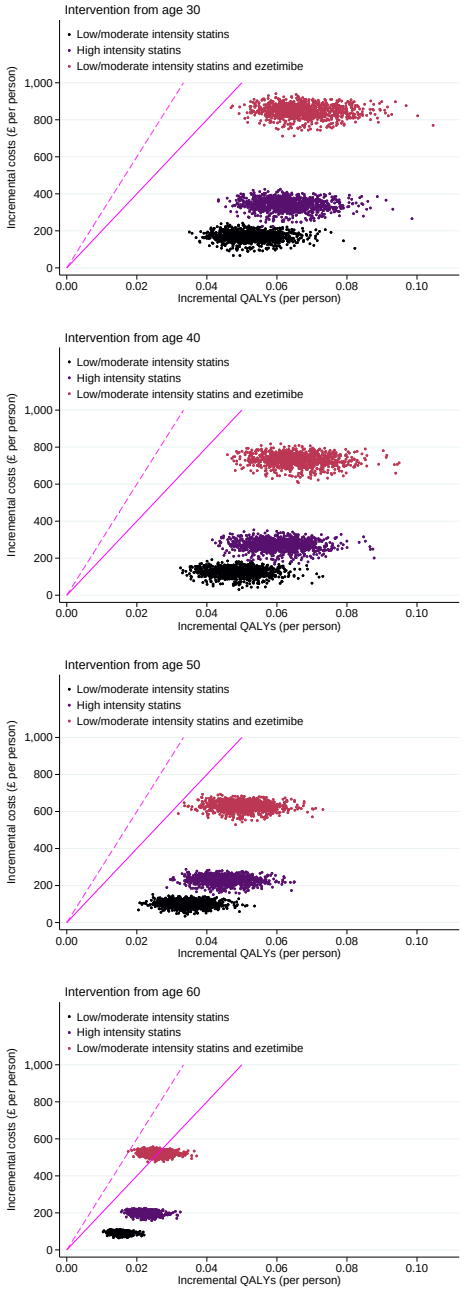
Supplementary Figure 9: Cumulative incidence of MI or coronary death, by sex, LDL-C, and age of intervention – High intensity statins



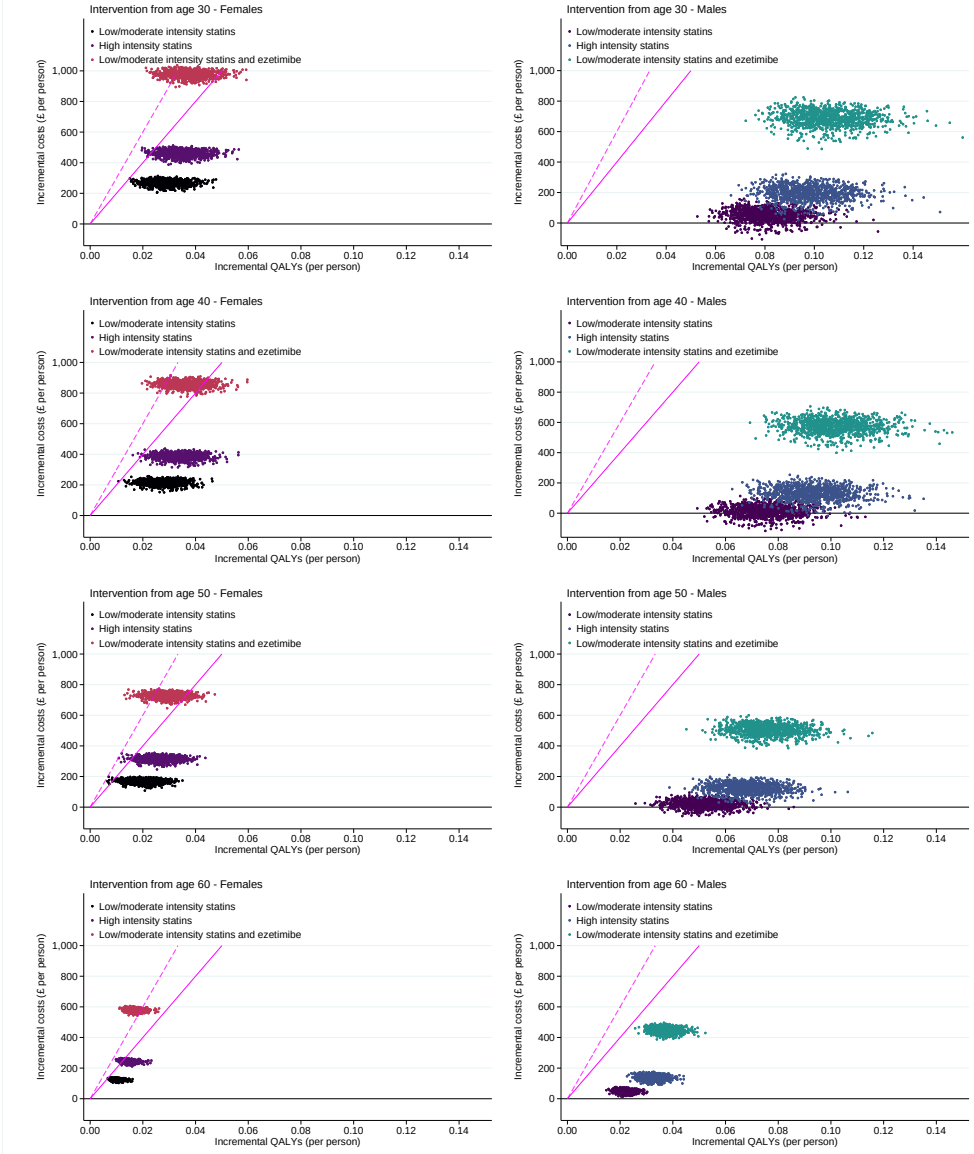
Supplementary Figure 10: Cumulative incidence of MI or coronary death, by sex, LDL-C, and age of intervention – Low/moderate intensity statins and ezetimibe



Supplementary Figure 11: Cumulative incidence of MI or coronary death, by sex, LDL-C, and age of intervention – Inclisiran

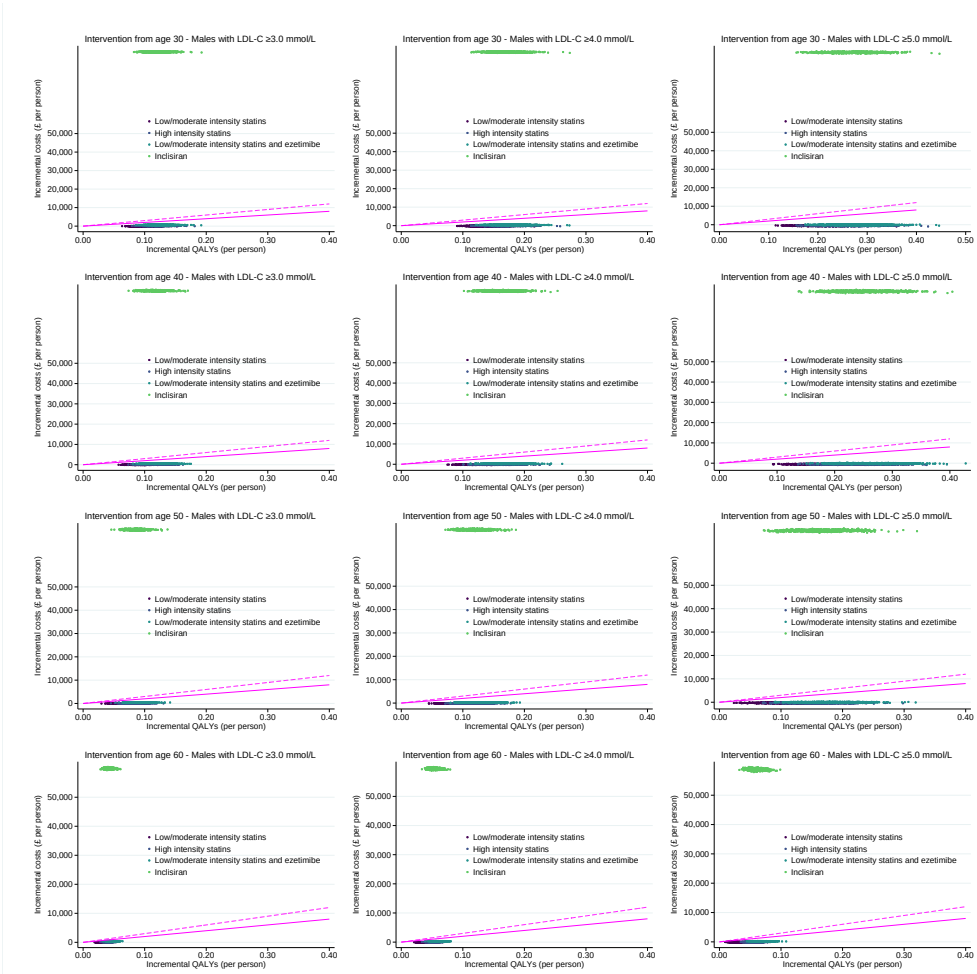


Supplementary Figure 12: PSA simulations presented in a common cost-effectiveness plane, by age of intervention, excluding Inclisiran. Solid line: £20,000 per QALY willingness-to-pay threshold; dashed line: £30,000 per QALY willingness-to-pay threshold



Supplementary Figure 13: PSA simulations presented in a common cost-effectiveness plane, by age of intervention and sex, excluding Inclisiran. Solid line: £20,000 per QALY willingness-to-pay threshold; dashed line: £30,000 per QALY willingness-to-pay threshold

Supplementary Figure 14: PSA simulations presented in a common cost-effectiveness plane, by age of intervention and LDL-C. Females.



Supplementary Figure 15: PSA simulations presented in a common cost-effectiveness plane, by age of intervention and LDL-C. Males.

Supplementary Figure 16: Tornado diagrams for each intervention strategy - Overall
The results of the OSA for the overall population are shown here. For results stratified by sex and LDL-C, see the protocol, pp.174-178.

References

[1] Stephen P Adams, Michael Tsang, and James M Wright. Atorvastatin for lowering lipids. *Cochrane Database of Systematic Reviews*, (3), 2015.

[2] Baishali M Ambegaonkar, Diane Tipping, Adam B Polis, Joanne E Tomassini, and Andrew M Tershakovec. Achieving goal lipid levels with ezetimibe plus statin add-on or switch therapy compared with doubling the statin dose. a pooled analysis. *Atherosclerosis*, 237(2):829–837, 2014.

[3] Kausik K. Ray, R. Scott Wright, David Kallend, Wolfgang Koenig, Lawrence A. Leiter, Frederick J. Raal, Jenna A. Bisch, Tara Richardson, Mark Jaros, Peter L.J. Wijngaard, and John J.P. Kastelein. Two phase 3 trials of inclisiran in patients with elevated ldl cholesterol. *New England Journal of Medicine*, 382(16):1507–1519, 2020. PMID: 32187462.

[4] Brian A. Ference, Deepak L. Bhatt, Alberico L. Catapano, Chris J. Packard, Ian Graham, Stephen Kaptoge, Thatcher B. Ference, Qi Guo, Ulrich Laufs, Christian T. Ruff, Arjen Cupido, G. Kees Hovingh, John Danesh, Michael V. Holmes, George Davey Smith, Kausik K. Ray, Stephen J. Nicholls, and Marc S. Sabatine. Association of Genetic Variants Related to Combined Exposure to Lower Low-Density Lipoproteins and Lower Systolic Blood Pressure With Lifetime Risk of Cardiovascular Disease. *JAMA*, 322(14):1381–1391, 10 2019.

[5] Roberta Ara and John E. Brazier. Populating an economic model with health state utility values: Moving toward better practice. *Value in Health*, 13(5):509–518, 2010.

[6] Marissa Blieden Betts, Pratik Rane, Evelien Bergrath, Madhura Chitnis, Mohit Kumar Bhutani, Claudia Gulea, Yi Qian, and Guillermo Villa. Utility value estimates in cardiovascular disease and the effect of changing elicitation methods: a systematic literature review. *Health and Quality of Life Outcomes*, 18(1):251, 2020.

[7] Eldrin F Lewis, Yanhong Li, Marc A Pfeffer, Scott D Solomon, Kevin P Weinfurt, Eric J Velazquez, Robert M Califf, Jean-Lucien Rouleau, Lars Kober, Harvey D White, et al. Impact of cardiovascular events on change in quality of life and utilities in patients after myocardial infarction: a valiant study (valsartan in acute myocardial infarction). *JACC: Heart Failure*, 2(2):159–165, 2014.

[8] Mark D Danese, Michelle Gleeson, Lucie Kutikova, Robert I Griffiths, Ali Azough, Kamlesh Khunti, Sreenivasa Rao Kondapally Seshasai, and Kausik K Ray. Estimating the economic burden of cardiovascular events in patients receiving lipid-modifying therapy in the uk. *BMJ Open*, 6(8), 2016.

[9] National health service. prescription services. nhs electronic drug tariff june 2021. available at: https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/drug-tariff/back-copies-drug-tariff accessed 25 november 2022.

[10] National health service. english prescribing dataset june 2021. available at: https://opendata.nhsbsa.net/dataset/english-prescribing-data-epd accessed 25 november 2022.

[11] National health service dictionary of medicines and devices. actual medicinal product pack (ampp). leqvio 284mg/1.5ml solution for injection pre-filled syringes (novartis pharmaceuticals uk ltd) 1 pre-filled disposable injection. available at: https://services.nhsbsa.nhs.uk/dmd-browser/ampp/view/184240 [accessed 2 decemeber 2022].