

## Supplementary Online Content

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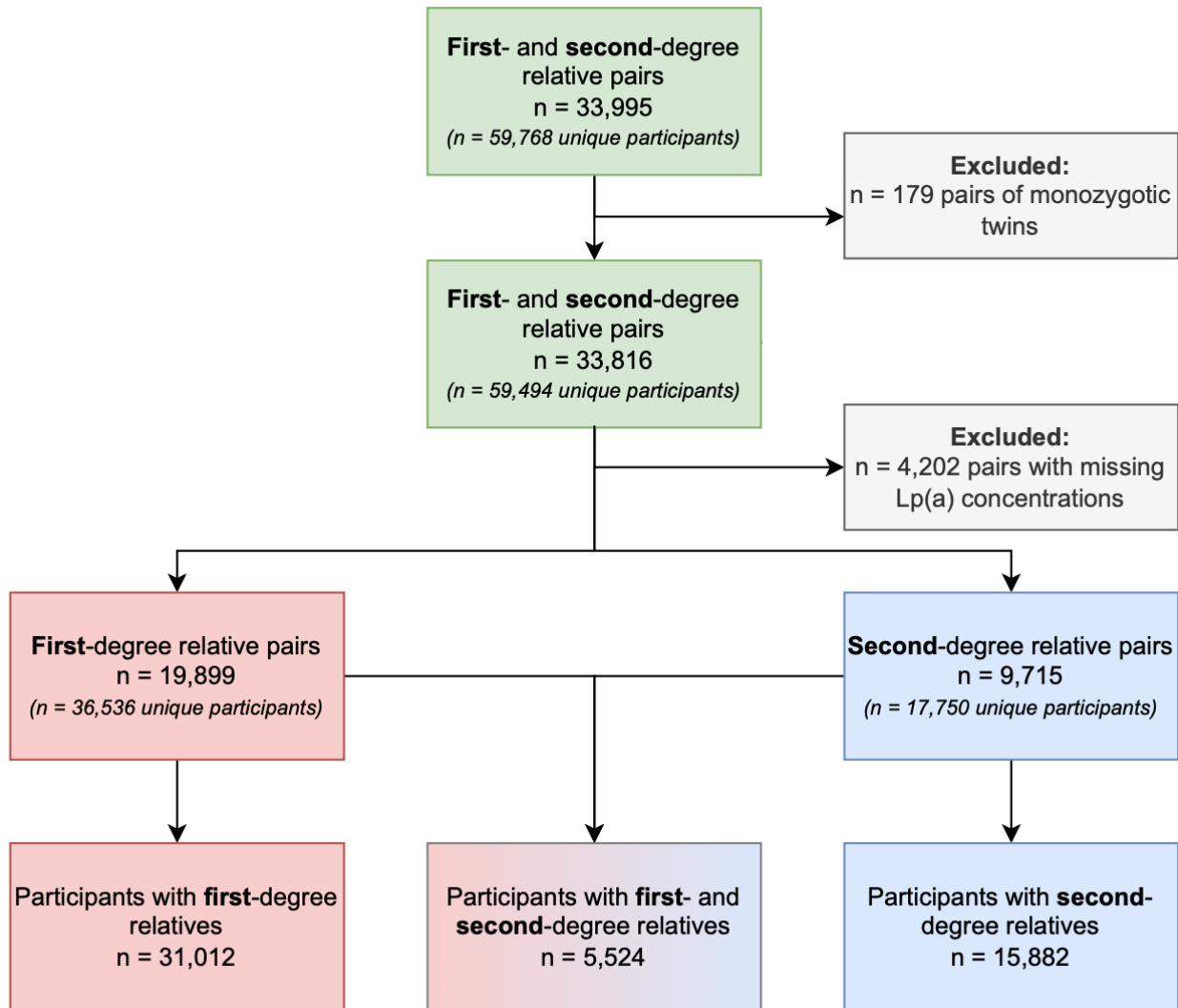
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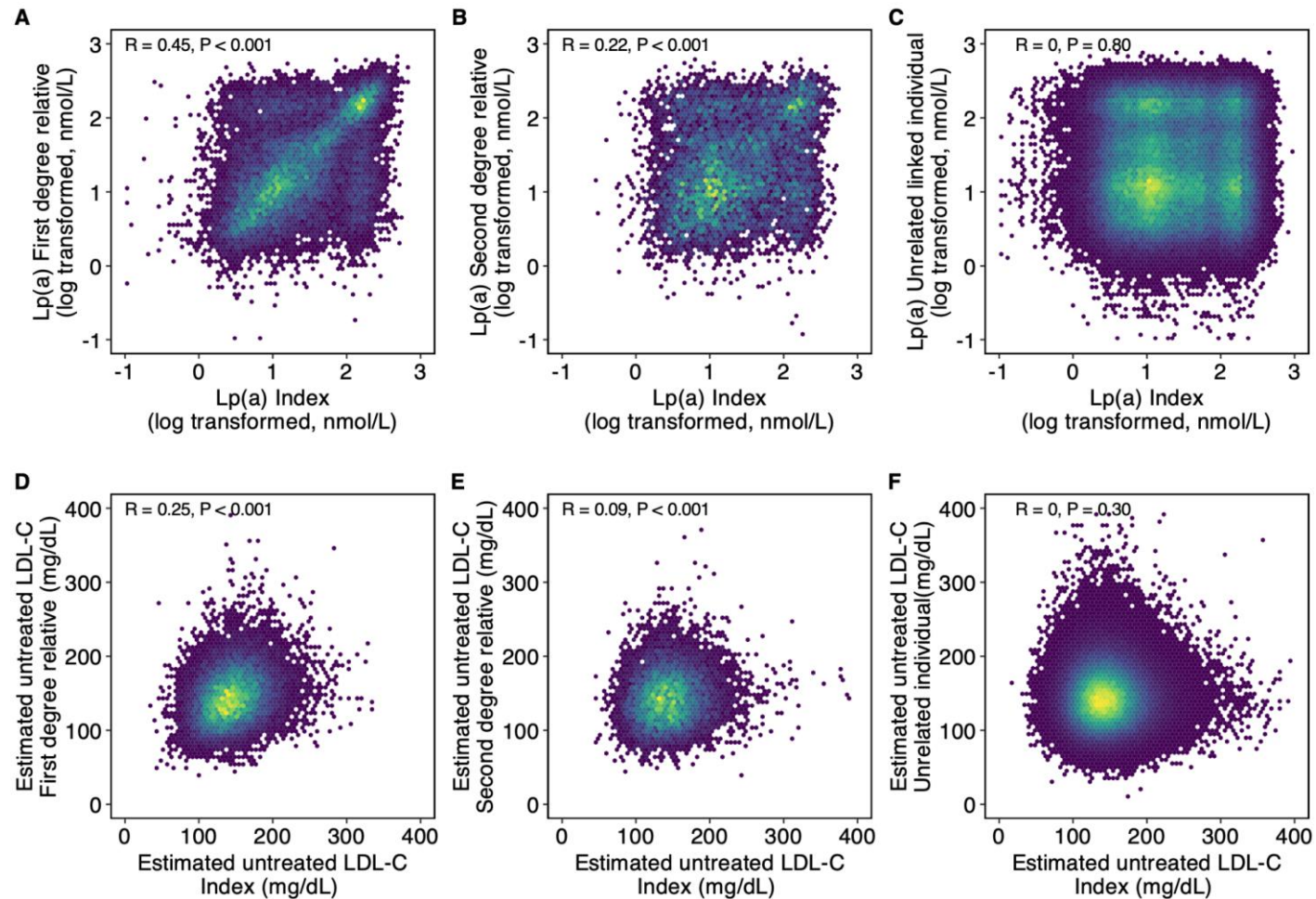
**eReferences**

This supplementary material has been provided by the authors to give readers additional information about their work.

**eFigure 1.** Flowchart of Participants and Relative Pair Selection

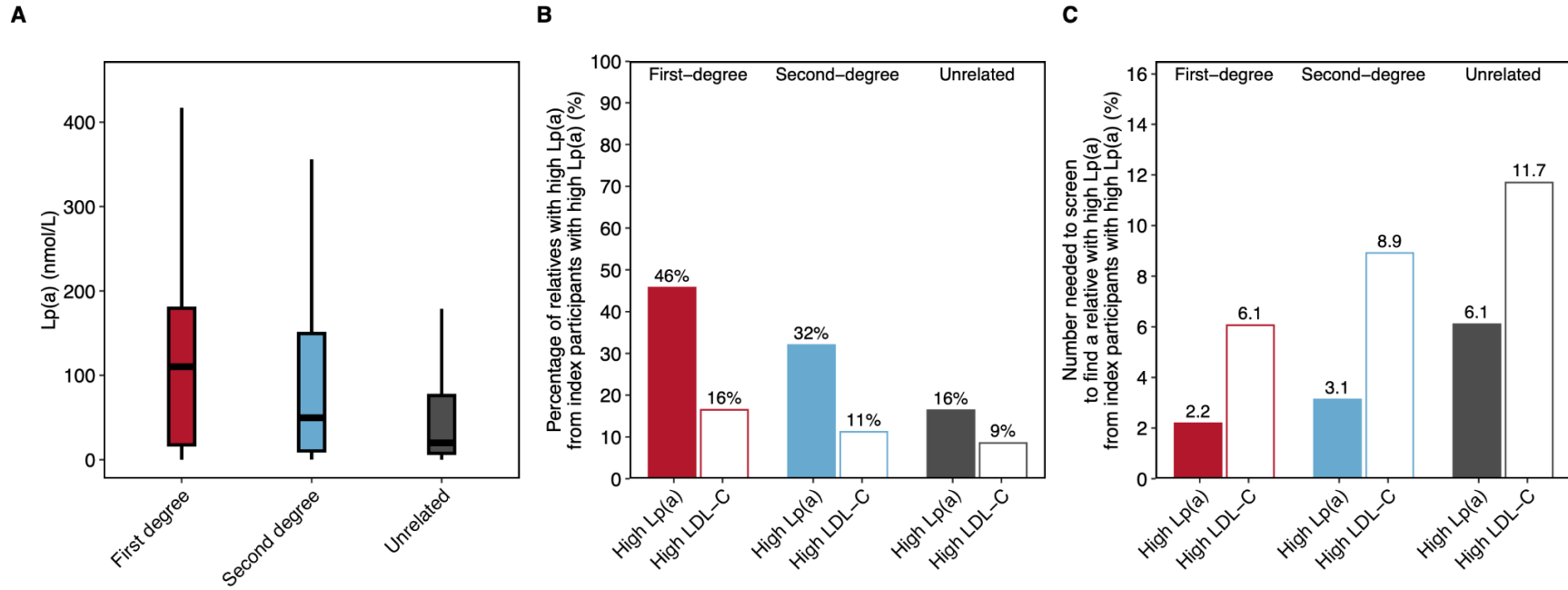


**eFigure 2.** Correlation in Lp(a) and Estimated Untreated LDL Cholesterol Plasma Levels Between First- and Second-Degree Relatives



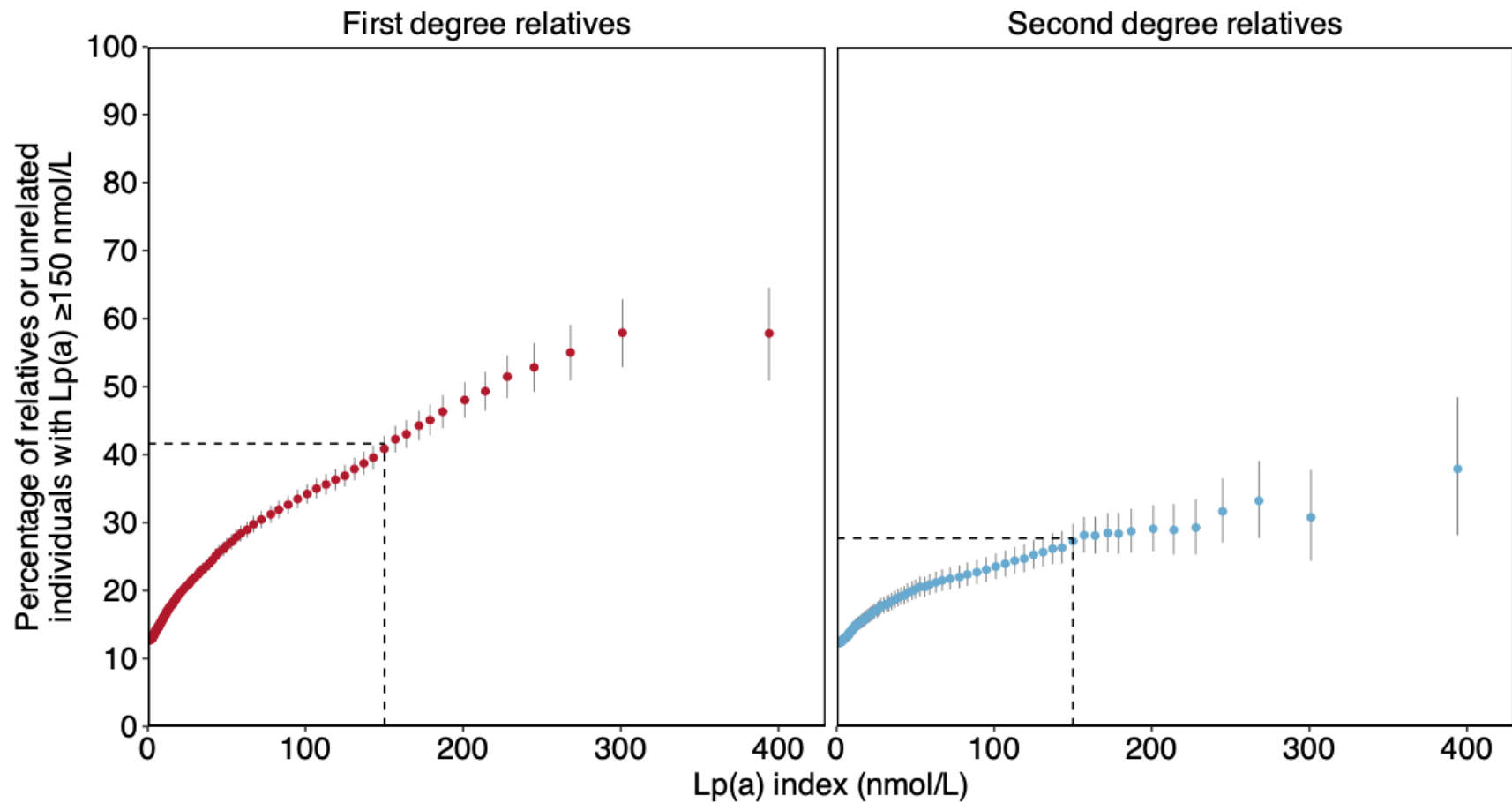
Scatterplot and correlation coefficients of Lp(a) concentrations among first-degree and second-degree relatives (A, B) and unrelated individuals (C). As a comparison, LDL cholesterol concentrations are shown as well (D, E, F). Correlation was determined using the Spearman's Rank correlation coefficient on untransformed concentration values.

**eFigure 3.** Sensitivity Analysis for Lp(a) Levels, Concordance in High Lp(a), and Numbers Needed to Screen Among Relatives of Index Participants With High Lp(a) After Excluding Index Participants Using Therapies to Lower Lipid Levels



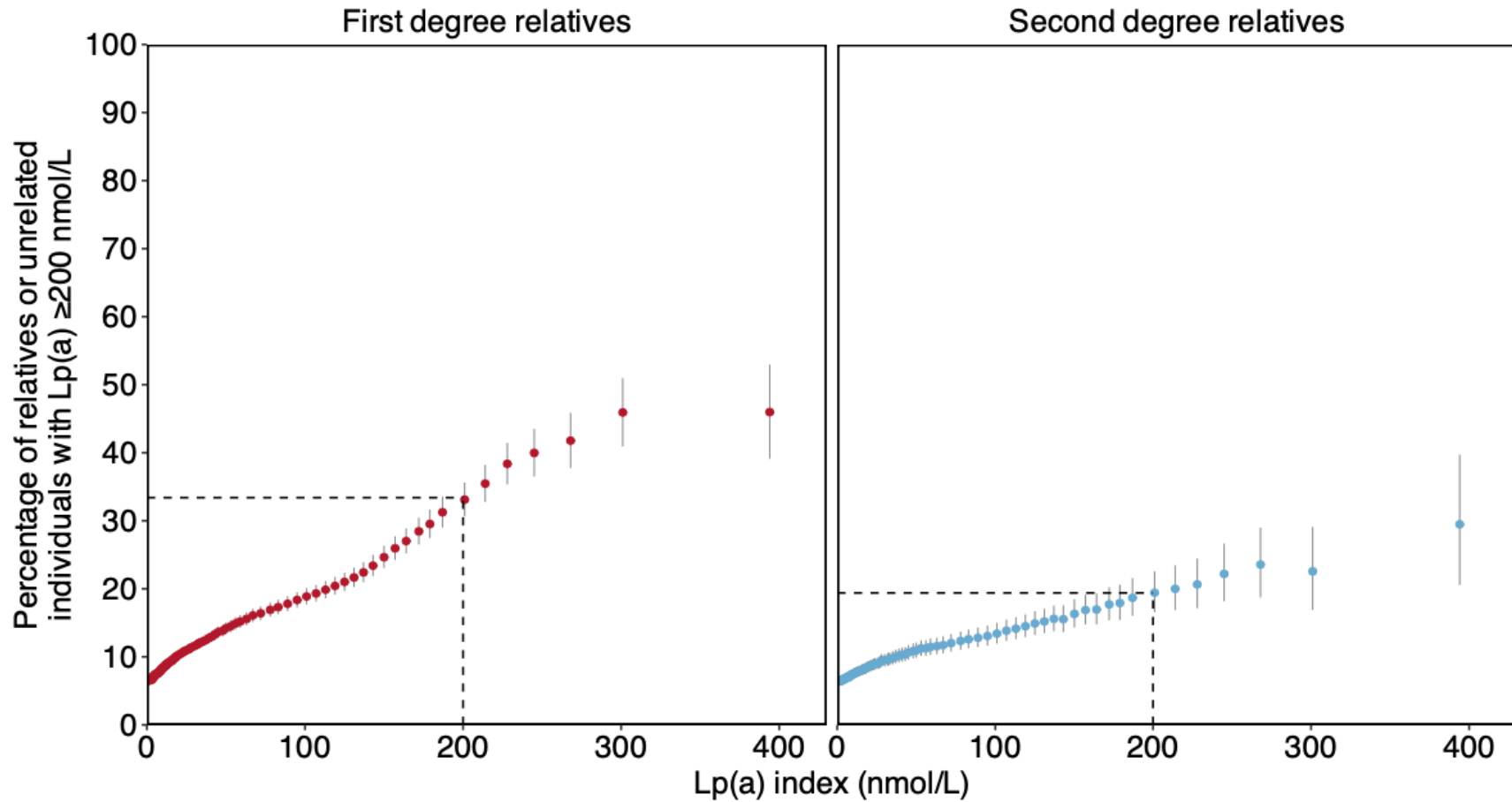
Lp(a) concentrations in relatives of index participants with high Lp(a) ( $\geq 125$  nmol/L) for first- and second-degree relatives (A), resulting in a high percentage of relatives that also have high Lp(a) (B) and a low number needed to screen to identify 1 relative with high Lp(a) (C). As a comparator, Lp(a) concentrations in unrelated randomly matched pairs of individuals with high Lp(a) are included in all panels, and the concordance and number needed to screen among relatives is also shown for high LDL-C ( $\geq 190$  mg/dL). This analysis included 15,976 and 7,747, pairs of first- and second-degree relatives, respectively and 148,337 pairs of unrelated individuals after exclusion of index participants using lipid lowering therapies.

**eFigure 4.** Percentage of First- and Second-Degree Relatives With Lp(a)  $\geq 150$  nmol/L for Any Index Cutoff Lp(a) Concentration



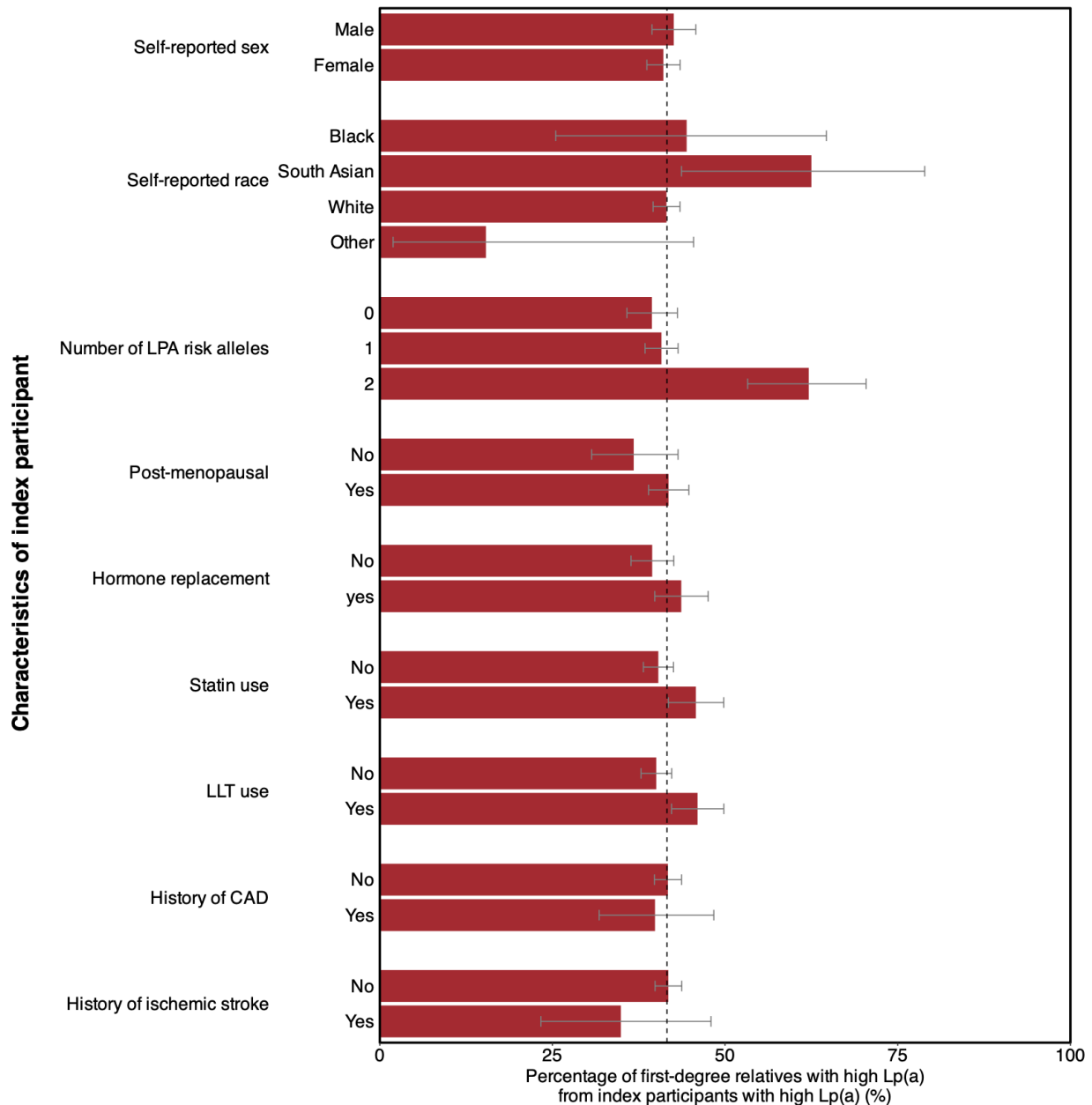
Percentage of relatives with Lp(a)  $\geq 150$  nmol/L for any given Lp(a) cut-off in the index participants patients. Shown with the dotted line is the concordance between Lp(a)  $\geq 150$  nmol/L in index participants and their relatives.

**eFigure 5.** Percentage of First- and Second-Degree Relatives With Lp(a)  $\geq 200$  nmol/L for Any Index Cutoff Lp(a) Concentration



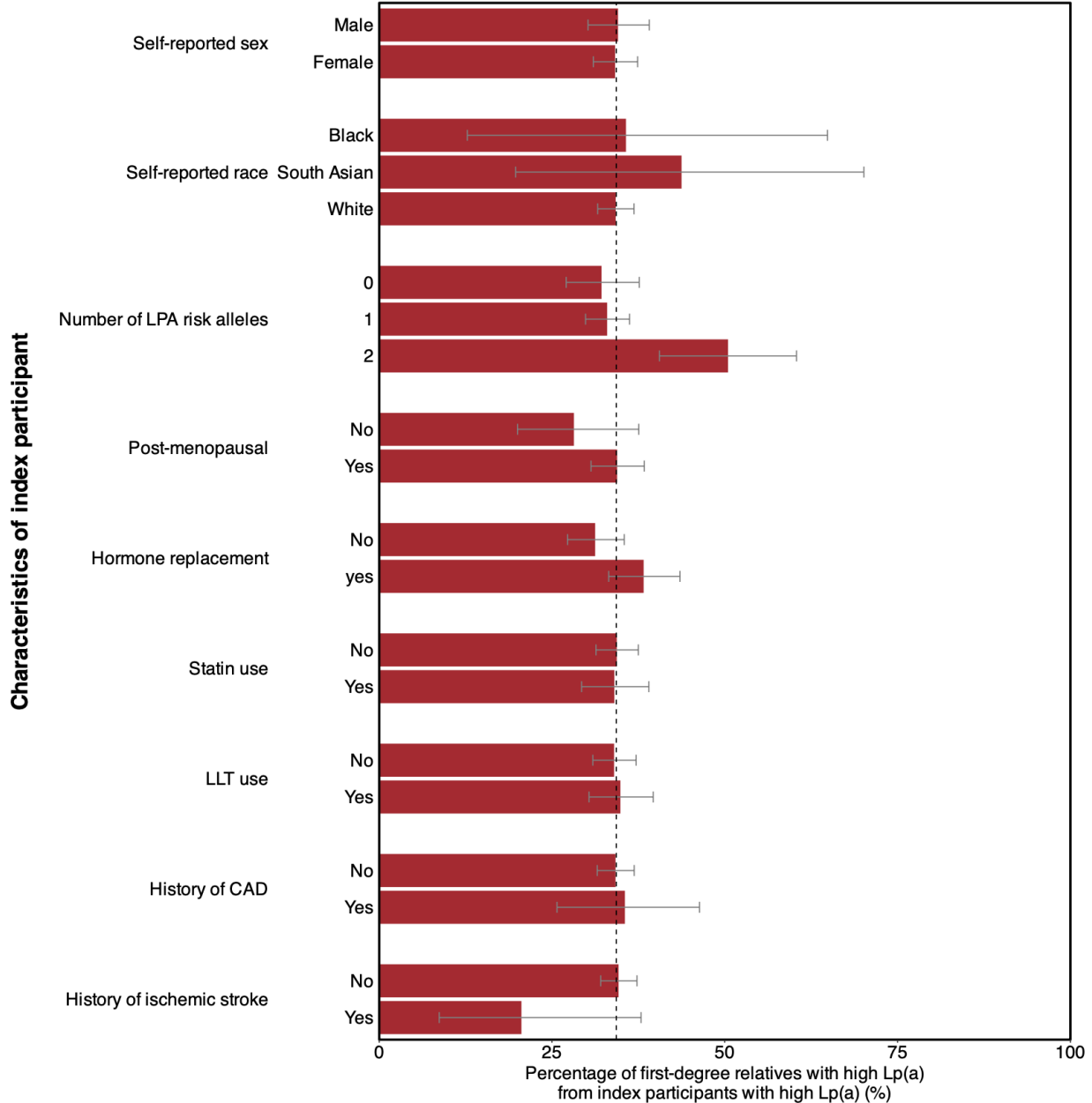
Percentage of relatives with Lp(a)  $\geq 200$  nmol/L for any given Lp(a) cut-off in the index participants patients. Shown with the dotted line is the concordance between Lp(a)  $\geq 200$  nmol/L in index participants and their relatives.

**eFigure 6.** Subgroup Analysis for Concordance in High Lp(a) ( $\geq 150$  nmol/L) Among First-Degree Relatives



Subgroup analysis for high Lp(a) ( $\geq 150$  nmol/L) concordance in first-degree relatives according to the presence or absence of certain traits in index participants. The concordance of high Lp(a) among relatives was largely the same among subgroups and ranged from 15.4% (95%-CI: 1.9 - 45.4) in those with no self-reported or other race and ethnicity to 62.5% (95%-CI: 43.7 - 78.9) in South Asian participants. Number of *LPA* risk alleles is defined as the number of variants (rs1045872 and rs3798220) in the *LPA* gene, which were previously associated with Lp(a) concentrations and coronary artery disease (CAD).<sup>1</sup> Genetic subgroup analyses were only performed in White participants. For the subgroup analyses including menopause and hormone replacement therapy, only first-degree relative pairs with female index participants were included. *LPA*, lipoprotein(a) gene; LLT, lipid lowering therapy; CAD, coronary artery disease.

**eFigure 7.** Subgroup Analysis for Concordance in High Lp(a) ( $\geq 200$  nmol/L) Among First-Degree Relatives



Subgroup analysis for high Lp(a) ( $\geq 200$  nmol/L) concordance in first-degree relatives according to the presence or absence of certain traits in index participants. The concordance of high Lp(a) among relatives was largely the same among subgroups and ranged from 20.6% (95%-CI: 8.7 - 37.9) in those with a history of ischemic stroke to 50.5% (95%-CI: 40.5 - 60.4) in those with a strong genetic predisposition in high Lp(a). Number of LPA risk alleles is defined as the number of variants (rs1045872 and rs3798220) in the LPA gene, which were previously associated with Lp(a) concentrations and coronary artery disease (CAD).<sup>1</sup> Genetic subgroup analyses were only performed in White participants. For the subgroup analyses including menopause and hormone replacement therapy, only first-degree relative pairs with female index participants were included. LPA, lipoprotein(a) gene; LLT, lipid lowering therapy; CAD, coronary artery disease.



**eTable 1.** Characteristics of Cohort by Self-Reported Race and Ethnicity

	Black		South Asian		White		Other / Not Reported	
	First- & second-degree relatives	Unrelated control group	First- & second-degree relatives	Unrelated control group	First- & second-degree relatives	Unrelated control group	First- & second-degree relatives	Unrelated control group
<b>n</b>	439	5,876	582	7,454	50,406	347,796	281	8,402
<b>Males</b>	159 (36.2)	2,574 (43.8)	297 (51.0)	4,070 (54.6)	21,714 (43.1)	160,471 (46.1)	100 (35.6)	3,609 (43.0)
<b>Age, years</b>	51.8 ± 7.6	52.5 ± 8.1	54.1 ± 7.6	53.8 ± 8.5	57.1 ± 8.0	57.3 ± 8.0	53.4 ± 8.1	53.5 ± 8.2
<b>BMI, kg/m<sup>2</sup></b>	29.8 ± 5.9	29.5 ± 5.4	27.4 ± 4.5	27.1 ± 4.4	27.4 ± 4.7	27.4 ± 4.8	26.9 ± 4.8	27.2 ± 5.0
<b>Currently smoking</b>	71 (16.2)	721 (12.4)	58 (10.0)	724 (9.8)	5,462 (10.9)	35,917 (10.4)	39 (14.7)	1,104 (14.0)
<b>Hypertension</b>	143 (34.0)	2299 (40.6)	194 (35.1)	2,370 (33.5)	14,027 (29.1)	98,154 (29.5)	73 (26.9)	2,216 (27.4)
<b>Diabetes mellitus</b>	39 (8.9)	702 (11.9)	78 (13.4)	1,319 (17.7)	2,526 (5.0)	17,682 (5.1)	19 (6.8)	722 (8.6)
<b>Total cholesterol, mg/dL</b>	207 ± 42	210 ± 44	217 ± 42	218 ± 43	229 ± 42	229 ± 42	219 ± 40	221 ± 43
<b>Estimated untreated LDL cholesterol, mg/dL</b>	131 ± 35	134 ± 36	141 ± 33	142 ± 34	146 ± 33	146 ± 33	140 ± 33	141 ± 34
<b>LDL cholesterol, mg/dL</b>	125 ± 31	126 ± 33	131 ± 33	129 ± 33	138 ± 34	138 ± 34	132 ± 31	134 ± 33
<b>HDL cholesterol, mg/dL</b>	57 ± 13	55 ± 14	50 ± 12	49 ± 13	56 ± 15	56 ± 15	55 ± 14	54 ± 15
<b>Triglycerides, mg/dL</b>	90 [68, 129]	94 [69, 133]	145 [106, 209]	156 [108, 227]	135 [95, 198]	136 [95, 198]	119 [83, 167]	130 [90, 194]
<b>Lp(a), nmol/L</b>	73 [47, 136]	74 [43, 133]	38 [13, 89]	31 [12, 69]	19 [8, 74]	19 [7, 73]	33 [13, 70]	27 [9, 74]
<b>Statin use,</b>	47 (10.7)	846 (14.4)	130 (22.3)	1,866 (25.0)	8,124 (16.1)	56,485 (16.2)	43 (15.3)	1,243 (14.8)
<b>Ezetimibe use</b>	1 (0.2)	25 (0.4)	6 (1.0)	51 (0.7)	305 (0.6)	1,994 (0.6)	281 (100.0)	41 (0.5)
<b>ASCVD at enrollment*</b>	15 (3.4)	183 (3.1)	34 (5.8)	512 (6.9)	2,495 (4.9)	16,944 (4.9)	3 (1.1)	296 (3.5)

All values are reported as n (%), mean ± SD, or median [IQR]. \*ASCVD was defined as a composite of coronary artery disease (myocardial infarction and its acute complications, coronary artery bypass graft surgery, or percutaneous angioplasty/stent placement) and ischemic stroke (cerebral infarction due to thrombosis or cerebral atherosclerosis or cerebrovascular syndromes).<sup>2</sup> Race and ethnicity were self-reported. The other / not reported category included participants with a mixed racial background, participants who did not know their racial background, participants who did not identify with any of the other provided categories, or participants who chose not to answer. SI conversion factor: to convert cholesterol to mmol/L, multiply by 0.0259; triglycerides to mmol/L, multiply by 0.0113. BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; Lp(a), lipoprotein(a); ASCVD, atherosclerotic cardiovascular disease.

**eTable 2.** Concordance and Number Needed to Screen (NNS) for High Lp(a) in First-Degree Relatives

Percentile index	Mean Lp(a) concentration, nmol/L	Proportion of first-degree relatives with Lp(a) $\geq 125$ nmol/L, % (95%-CI)	NNS for Lp(a) $\geq 125$ nmol/L	Proportion of first-degree relatives with Lp(a) $\geq 150$ nmol/L, % (95%-CI)	NNS for Lp(a) $\geq 150$ nmol/L	Proportion of first-degree relatives with Lp(a) $\geq 200$ nmol/L, % (95%-CI)	NNS for Lp(a) $\geq 200$ nmol/L
0	1	16.9 (16.4 - 17.4)	5.9	12.7 (12.2 - 13.1)	7.9	6.5 (6.2 - 6.9)	15.4
1	2	17.0 (16.5 - 17.6)	5.9	12.7 (12.3 - 13.2)	7.9	6.5 (6.2 - 6.9)	15.3
2	2	17.1 (16.6 - 17.6)	5.8	12.8 (12.4 - 13.3)	7.8	6.6 (6.2 - 6.9)	15.2
3	2	17.2 (16.7 - 17.7)	5.8	12.9 (12.4 - 13.4)	7.8	6.6 (6.3 - 7.0)	15.1
4	3	17.3 (16.7 - 17.8)	5.8	12.9 (12.5 - 13.4)	7.7	6.7 (6.3 - 7.0)	15
5	3	17.4 (16.8 - 17.9)	5.8	13.0 (12.5 - 13.5)	7.7	6.7 (6.3 - 7.0)	15
6	3	17.4 (16.9 - 18.0)	5.7	13.1 (12.6 - 13.6)	7.6	6.7 (6.4 - 7.1)	14.9
7	3	17.6 (17.0 - 18.1)	5.7	13.2 (12.7 - 13.7)	7.6	6.8 (6.4 - 7.2)	14.7
8	3	17.7 (17.1 - 18.2)	5.7	13.3 (12.8 - 13.8)	7.5	6.8 (6.5 - 7.2)	14.6
9	4	17.8 (17.3 - 18.4)	5.6	13.4 (12.9 - 13.9)	7.5	6.9 (6.5 - 7.3)	14.5
10	4	17.9 (17.4 - 18.5)	5.6	13.5 (13.0 - 14.0)	7.4	7.0 (6.6 - 7.4)	14.3
11	4	18.0 (17.5 - 18.6)	5.5	13.6 (13.1 - 14.1)	7.4	7.0 (6.7 - 7.4)	14.2
12	4	18.2 (17.6 - 18.7)	5.5	13.7 (13.2 - 14.2)	7.3	7.1 (6.7 - 7.5)	14.1
13	4	18.3 (17.7 - 18.9)	5.5	13.8 (13.3 - 14.3)	7.3	7.1 (6.8 - 7.5)	14
14	5	18.4 (17.9 - 19.0)	5.4	13.9 (13.4 - 14.4)	7.2	7.2 (6.8 - 7.6)	13.9
15	5	18.6 (18.0 - 19.2)	5.4	14.0 (13.5 - 14.5)	7.2	7.3 (6.9 - 7.7)	13.8
16	5	18.7 (18.1 - 19.3)	5.3	14.1 (13.6 - 14.7)	7.1	7.3 (6.9 - 7.7)	13.7
17	5	18.9 (18.3 - 19.5)	5.3	14.2 (13.7 - 14.8)	7	7.4 (7.0 - 7.8)	13.5
18	6	19.0 (18.4 - 19.6)	5.3	14.3 (13.8 - 14.9)	7	7.4 (7.0 - 7.8)	13.5
19	6	19.1 (18.5 - 19.8)	5.2	14.4 (13.9 - 15.0)	6.9	7.5 (7.1 - 7.9)	13.4
20	6	19.3 (18.6 - 19.9)	5.2	14.5 (14.0 - 15.1)	6.9	7.5 (7.1 - 7.9)	13.3
21	7	19.3 (18.7 - 20.0)	5.2	14.6 (14.0 - 15.1)	6.9	7.6 (7.2 - 8.0)	13.2
22	7	19.5 (18.9 - 20.1)	5.1	14.7 (14.1 - 15.2)	6.8	7.6 (7.2 - 8.0)	13.1
23	7	19.7 (19.0 - 20.3)	5.1	14.8 (14.2 - 15.4)	6.8	7.7 (7.3 - 8.1)	13
24	7	19.8 (19.2 - 20.4)	5.1	14.9 (14.3 - 15.5)	6.7	7.7 (7.3 - 8.1)	13

25	8	19.9 (19.3 - 20.6)	5	15.0 (14.5 - 15.6)	6.7	7.8 (7.4 - 8.2)	12.8
26	8	20.1 (19.5 - 20.8)	5	15.2 (14.6 - 15.8)	6.6	7.9 (7.4 - 8.3)	12.7
27	8	20.3 (19.7 - 21.0)	4.9	15.3 (14.7 - 15.9)	6.5	7.9 (7.5 - 8.4)	12.6
28	9	20.5 (19.9 - 21.2)	4.9	15.5 (14.9 - 16.1)	6.5	8.0 (7.6 - 8.5)	12.5
29	9	20.7 (20.0 - 21.4)	4.8	15.6 (15.0 - 16.2)	6.4	8.1 (7.7 - 8.6)	12.3
30	9	20.9 (20.2 - 21.6)	4.8	15.8 (15.2 - 16.4)	6.3	8.2 (7.8 - 8.7)	12.2
31	10	21.0 (20.4 - 21.7)	4.8	15.9 (15.3 - 16.5)	6.3	8.3 (7.8 - 8.8)	12.1
32	10	21.2 (20.6 - 21.9)	4.7	16.0 (15.4 - 16.6)	6.2	8.4 (7.9 - 8.8)	12
33	10	21.4 (20.7 - 22.1)	4.7	16.1 (15.5 - 16.8)	6.2	8.4 (7.9 - 8.9)	11.9
34	11	21.6 (20.9 - 22.3)	4.6	16.3 (15.7 - 17.0)	6.1	8.5 (8.0 - 9.0)	11.7
35	11	21.8 (21.1 - 22.5)	4.6	16.5 (15.8 - 17.1)	6.1	8.6 (8.1 - 9.1)	11.6
36	12	22.0 (21.3 - 22.7)	4.5	16.7 (16.0 - 17.3)	6	8.7 (8.2 - 9.2)	11.5
37	12	22.2 (21.5 - 23.0)	4.5	16.8 (16.2 - 17.5)	5.9	8.8 (8.3 - 9.3)	11.4
38	12	22.4 (21.7 - 23.2)	4.5	17.0 (16.3 - 17.6)	5.9	8.9 (8.4 - 9.4)	11.3
39	13	22.6 (21.9 - 23.4)	4.4	17.1 (16.4 - 17.8)	5.8	9.0 (8.5 - 9.5)	11.2
40	13	22.9 (22.1 - 23.6)	4.4	17.3 (16.6 - 18.0)	5.8	9.1 (8.5 - 9.6)	11
41	14	23.1 (22.4 - 23.9)	4.3	17.5 (16.8 - 18.2)	5.7	9.2 (8.6 - 9.7)	10.9
42	14	23.4 (22.6 - 24.2)	4.3	17.7 (17.0 - 18.4)	5.7	9.2 (8.7 - 9.8)	10.8
43	15	23.6 (22.8 - 24.4)	4.2	17.8 (17.1 - 18.5)	5.6	9.3 (8.8 - 9.9)	10.7
44	16	23.8 (23.0 - 24.6)	4.2	18.0 (17.3 - 18.7)	5.6	9.4 (8.9 - 10)	10.6
45	16	24.1 (23.3 - 24.9)	4.2	18.2 (17.5 - 19.0)	5.5	9.6 (9.0 - 10.1)	10.5
46	17	24.4 (23.6 - 25.3)	4.1	18.5 (17.8 - 19.2)	5.4	9.7 (9.2 - 10.3)	10.3
47	18	24.7 (23.9 - 25.6)	4	18.7 (18.0 - 19.5)	5.3	9.9 (9.3 - 10.4)	10.2
48	18	25.0 (24.1 - 25.8)	4	19.0 (18.2 - 19.7)	5.3	10.0 (9.4 - 10.6)	10
49	19	25.3 (24.5 - 26.2)	3.9	19.3 (18.5 - 20.0)	5.2	10.1 (9.6 - 10.7)	9.9
50	20	25.6 (24.8 - 26.5)	3.9	19.5 (18.7 - 20.3)	5.1	10.3 (9.7 - 10.9)	9.7
51	21	25.9 (25.1 - 26.8)	3.9	19.7 (18.9 - 20.5)	5.1	10.4 (9.8 - 11.0)	9.6
52	22	26.3 (25.4 - 27.2)	3.8	20.0 (19.2 - 20.8)	5	10.6 (10.0 - 11.2)	9.5
53	23	26.6 (25.7 - 27.5)	3.8	20.3 (19.5 - 21.1)	4.9	10.7 (10.1 - 11.3)	9.3
54	24	27.0 (26.1 - 27.9)	3.7	20.6 (19.8 - 21.4)	4.9	10.9 (10.2 - 11.5)	9.2
55	26	27.4 (26.5 - 28.3)	3.7	20.9 (20.1 - 21.8)	4.8	11.1 (10.4 - 11.7)	9
56	27	27.8 (26.9 - 28.7)	3.6	21.2 (20.4 - 22.1)	4.7	11.2 (10.5 - 11.9)	8.9

57	28	28.3 (27.3 - 29.2)	3.5	21.6 (20.7 - 22.4)	4.6	11.4 (10.7 - 12.1)	8.8
58	30	28.8 (27.8 - 29.7)	3.5	21.9 (21.1 - 22.8)	4.6	11.6 (10.9 - 12.3)	8.6
59	32	29.3 (28.3 - 30.3)	3.4	22.4 (21.5 - 23.3)	4.5	11.8 (11.1 - 12.5)	8.5
60	33	29.8 (28.8 - 30.8)	3.4	22.8 (21.8 - 23.7)	4.4	12.0 (11.3 - 12.8)	8.3
61	35	30.3 (29.2 - 31.3)	3.3	23.1 (22.2 - 24.1)	4.3	12.2 (11.5 - 13.0)	8.2
62	37	30.8 (29.7 - 31.8)	3.2	23.5 (22.6 - 24.5)	4.3	12.4 (11.7 - 13.2)	8
63	39	31.4 (30.3 - 32.4)	3.2	24.0 (23.0 - 25.0)	4.2	12.7 (12.0 - 13.5)	7.9
64	41	32.0 (30.9 - 33.1)	3.1	24.5 (23.5 - 25.5)	4.1	13 (12.2 - 13.8)	7.7
65	43	32.7 (31.6 - 33.8)	3.1	25.1 (24.0 - 26.1)	4	13.3 (12.5 - 14.1)	7.5
66	45	33.4 (32.3 - 34.5)	3	25.6 (24.6 - 26.7)	3.9	13.6 (12.8 - 14.5)	7.3
67	48	34.0 (32.8 - 35.2)	2.9	26.1 (25.0 - 27.2)	3.8	13.8 (13.0 - 14.7)	7.2
68	50	34.7 (33.5 - 35.9)	2.9	26.6 (25.5 - 27.7)	3.8	14.2 (13.3 - 15.1)	7
69	53	35.4 (34.2 - 36.6)	2.8	27.1 (26.0 - 28.3)	3.7	14.5 (13.6 - 15.4)	6.9
70	56	36.3 (35.1 - 37.5)	2.8	27.8 (26.7 - 29.0)	3.6	14.9 (14.0 - 15.8)	6.7
71	59	37.0 (35.8 - 38.3)	2.7	28.4 (27.2 - 29.6)	3.5	15.2 (14.3 - 16.1)	6.6
72	63	37.8 (36.5 - 39.0)	2.6	28.9 (27.7 - 30.1)	3.5	15.6 (14.6 - 16.5)	6.4
73	67	38.8 (37.5 - 40.1)	2.6	29.7 (28.5 - 31.0)	3.4	16.1 (15.1 - 17.1)	6.2
74	72	39.7 (38.4 - 41.1)	2.5	30.4 (29.2 - 31.7)	3.3	16.4 (15.4 - 17.4)	6.1
75	78	40.6 (39.2 - 42.0)	2.5	31.2 (29.9 - 32.5)	3.2	16.9 (15.9 - 18.0)	5.9
76	83	41.5 (40.1 - 42.9)	2.4	31.9 (30.6 - 33.2)	3.1	17.3 (16.3 - 18.4)	5.8
77	89	42.2 (40.8 - 43.7)	2.4	32.6 (31.3 - 34.0)	3.1	17.8 (16.7 - 18.9)	5.6
78	95	43.2 (41.7 - 44.6)	2.3	33.5 (32.1 - 34.9)	3	18.4 (17.2 - 19.5)	5.4
79	101	44.0 (42.5 - 45.5)	2.3	34.2 (32.8 - 35.6)	2.9	18.9 (17.7 - 20.1)	5.3
80	107	44.9 (43.4 - 46.4)	2.2	35.0 (33.5 - 36.5)	2.9	19.3 (18.1 - 20.6)	5.2
81	113	45.3 (43.7 - 46.9)	2.2	35.6 (34.1 - 37.1)	2.8	19.9 (18.6 - 21.1)	5
82	119	46.0 (44.4 - 47.7)	2.2	36.3 (34.8 - 37.9)	2.8	20.4 (19.1 - 21.7)	4.9
83	125	46.6 (45.0 - 48.3)	2.1	36.9 (35.3 - 38.5)	2.7	21.0 (19.7 - 22.4)	4.8
84	131	47.5 (45.7 - 49.2)	2.1	37.9 (36.2 - 39.5)	2.6	21.7 (20.3 - 23.1)	4.6
85	137	48.3 (46.5 - 50.0)	2.1	38.7 (37.0 - 40.4)	2.6	22.4 (21.0 - 23.9)	4.5
86	143	48.8 (46.9 - 50.6)	2.1	39.5 (37.8 - 41.3)	2.5	23.4 (21.9 - 25.0)	4.3
87	150	49.7 (47.8 - 51.5)	2	40.9 (39.0 - 42.7)	2.4	24.6 (23.0 - 26.3)	4.1
88	157	50.5 (48.6 - 52.5)	2	42.3 (40.3 - 44.2)	2.4	25.9 (24.2 - 27.7)	3.9

89	164	51.0 (49.0 - 53.1)	2	43.0 (41.0 - 45.1)	2.3	27.0 (25.2 - 28.9)	3.7
90	172	51.9 (49.7 - 54.1)	1.9	44.3 (42.1 - 46.4)	2.3	28.4 (26.5 - 30.4)	3.5
91	179	52.2 (50.0 - 54.5)	1.9	45.1 (42.8 - 47.4)	2.2	29.5 (27.5 - 31.6)	3.4
92	187	53.3 (50.8 - 55.7)	1.9	46.3 (43.9 - 48.7)	2.2	31.2 (29.0 - 33.6)	3.2
93	201	54.7 (52.1 - 57.3)	1.8	48.0 (45.4 - 50.6)	2.1	33.1 (30.7 - 35.6)	3
94	214	55.3 (52.4 - 58.1)	1.8	49.3 (46.5 - 52.1)	2	35.5 (32.8 - 38.2)	2.8
95	228	57.3 (54.2 - 60.4)	1.7	51.4 (48.3 - 54.6)	1.9	38.4 (35.3 - 41.5)	2.6
96	245	58.2 (54.7 - 61.7)	1.7	52.8 (49.3 - 56.4)	1.9	40.0 (36.5 - 43.5)	2.5
97	268	60.1 (56.0 - 64.1)	1.7	55.0 (50.9 - 59.1)	1.8	41.8 (37.7 - 45.9)	2.4
98	301	61.7 (56.7 - 66.6)	1.6	57.9 (52.8 - 62.8)	1.7	45.9 (40.9 - 51.0)	2.2
99	394	62.1 (55.2 - 68.7)	1.6	57.8 (50.8 - 64.6)	1.7	46.0 (39.1 - 52.9)	2.2

**eTable 3.** Concordance and Number Needed to Screen (NNS) for High Lp(a) in Second-Degree Relatives

Percentile index	Mean Lp(a) concentration, nmol/L	Proportion of second-degree relatives with Lp(a) ≥125 nmol/L, % (95%-CI)	NNS for Lp(a) ≥125 nmol/L	Proportion of second-degree relatives with Lp(a) ≥150 nmol/L, % (95%-CI)	NNS for Lp(a) ≥150 nmol/L	Proportion of second-degree relatives with Lp(a) ≥200 nmol/L, % (95%-CI)	NNS for Lp(a) ≥200 nmol/L
0	1	16.4 (15.7 - 17.2)	6.1	12.4 (11.7 - 13.0)	8.1	6.5 (6.0 - 7.0)	15.5
1	2	16.4 (15.7 - 17.2)	6.1	12.4 (11.7 - 13.1)	8.1	6.5 (6.0 - 7.0)	15.4
2	2	16.4 (15.7 - 17.2)	6.1	12.3 (11.7 - 13.0)	8.1	6.5 (6.0 - 7.0)	15.4
3	2	16.4 (15.7 - 17.2)	6.1	12.4 (11.7 - 13.1)	8.1	6.5 (6.0 - 7.0)	15.4
4	3	16.5 (15.8 - 17.3)	6.1	12.4 (11.8 - 13.1)	8	6.5 (6.0 - 7.0)	15.3
5	3	16.5 (15.8 - 17.3)	6.1	12.4 (11.8 - 13.1)	8.1	6.5 (6.0 - 7.0)	15.3
6	3	16.6 (15.8 - 17.4)	6	12.5 (11.8 - 13.2)	8	6.6 (6.1 - 7.1)	15.2
7	3	16.7 (15.9 - 17.5)	6	12.6 (11.9 - 13.3)	8	6.6 (6.1 - 7.1)	15.1
8	3	16.7 (15.9 - 17.5)	6	12.6 (11.9 - 13.3)	7.9	6.6 (6.1 - 7.1)	15.1
9	4	16.8 (16.0 - 17.6)	6	12.7 (12.0 - 13.4)	7.9	6.7 (6.1 - 7.2)	15
10	4	16.8 (16.1 - 17.6)	5.9	12.7 (12.0 - 13.4)	7.9	6.7 (6.2 - 7.2)	14.9
11	4	16.9 (16.1 - 17.7)	5.9	12.7 (12.0 - 13.5)	7.9	6.7 (6.2 - 7.2)	14.9
12	4	16.9 (16.1 - 17.7)	5.9	12.8 (12.1 - 13.5)	7.8	6.7 (6.2 - 7.3)	14.9
13	4	17.0 (16.2 - 17.8)	5.9	12.8 (12.1 - 13.5)	7.8	6.7 (6.2 - 7.3)	14.8
14	5	17.1 (16.3 - 17.9)	5.8	12.9 (12.2 - 13.6)	7.8	6.8 (6.3 - 7.4)	14.7
15	5	17.2 (16.3 - 18.0)	5.8	12.9 (12.2 - 13.6)	7.8	6.8 (6.3 - 7.4)	14.6
16	5	17.2 (16.4 - 18.1)	5.8	12.9 (12.2 - 13.7)	7.7	6.9 (6.3 - 7.4)	14.5
17	5	17.3 (16.5 - 18.1)	5.8	13.0 (12.3 - 13.7)	7.7	6.9 (6.3 - 7.4)	14.6
18	6	17.4 (16.6 - 18.2)	5.8	13.1 (12.3 - 13.8)	7.6	6.9 (6.4 - 7.5)	14.5
19	6	17.5 (16.6 - 18.3)	5.7	13.1 (12.4 - 13.9)	7.6	6.9 (6.4 - 7.5)	14.4
20	6	17.5 (16.6 - 18.3)	5.7	13.2 (12.4 - 13.9)	7.6	6.9 (6.4 - 7.5)	14.4
21	7	17.6 (16.7 - 18.5)	5.7	13.2 (12.5 - 14.0)	7.6	7.0 (6.4 - 7.6)	14.3
22	7	17.6 (16.8 - 18.5)	5.7	13.3 (12.5 - 14.1)	7.5	7.0 (6.4 - 7.6)	14.3
23	7	17.7 (16.9 - 18.6)	5.6	13.4 (12.6 - 14.2)	7.5	7.0 (6.5 - 7.6)	14.2
24	7	17.8 (16.9 - 18.7)	5.6	13.4 (12.6 - 14.2)	7.5	7.1 (6.5 - 7.7)	14.2

25	8	17.9 (17.0 - 18.8)	5.6	13.5 (12.8 - 14.3)	7.4	7.1 (6.5 - 7.7)	14
26	8	18.1 (17.2 - 19.0)	5.5	13.7 (12.9 - 14.5)	7.3	7.2 (6.6 - 7.8)	13.8
27	8	18.2 (17.3 - 19.1)	5.5	13.8 (13.0 - 14.6)	7.2	7.3 (6.7 - 7.9)	13.7
28	9	18.2 (17.3 - 19.2)	5.5	13.8 (13.0 - 14.7)	7.2	7.3 (6.7 - 7.9)	13.7
29	9	18.4 (17.5 - 19.3)	5.4	13.9 (13.1 - 14.8)	7.2	7.3 (6.7 - 7.9)	13.7
30	9	18.4 (17.5 - 19.4)	5.4	14.0 (13.2 - 14.8)	7.1	7.4 (6.8 - 8.0)	13.6
31	10	18.6 (17.6 - 19.5)	5.4	14.1 (13.3 - 15.0)	7.1	7.4 (6.8 - 8.1)	13.5
32	10	18.7 (17.8 - 19.7)	5.3	14.2 (13.4 - 15.1)	7	7.5 (6.9 - 8.2)	13.3
33	10	18.9 (17.9 - 19.8)	5.3	14.4 (13.5 - 15.2)	7	7.5 (6.9 - 8.2)	13.3
34	11	19.0 (18.0 - 20.0)	5.3	14.5 (13.6 - 15.4)	6.9	7.6 (7.0 - 8.3)	13.2
35	11	19.1 (18.1 - 20.1)	5.2	14.6 (13.7 - 15.5)	6.9	7.6 (7.0 - 8.3)	13.1
36	12	19.2 (18.2 - 20.2)	5.2	14.7 (13.8 - 15.6)	6.8	7.7 (7.0 - 8.4)	13
37	12	19.4 (18.4 - 20.4)	5.2	14.8 (13.9 - 15.7)	6.8	7.7 (7.1 - 8.4)	13
38	12	19.6 (18.6 - 20.6)	5.1	14.9 (14 - 15.9)	6.7	7.8 (7.1 - 8.5)	12.9
39	13	19.7 (18.7 - 20.7)	5.1	15.0 (14.1 - 15.9)	6.7	7.8 (7.1 - 8.5)	12.8
40	13	19.7 (18.7 - 20.8)	5.1	15.0 (14.1 - 16.0)	6.7	7.8 (7.1 - 8.6)	12.8
41	14	19.9 (18.8 - 20.9)	5	15.1 (14.2 - 16.1)	6.6	7.9 (7.2 - 8.6)	12.7
42	14	20.0 (18.9 - 21.1)	5	15.2 (14.3 - 16.2)	6.6	7.9 (7.2 - 8.7)	12.6
43	15	20.1 (19.1 - 21.2)	5	15.3 (14.4 - 16.3)	6.5	8.0 (7.3 - 8.8)	12.5
44	16	20.3 (19.2 - 21.4)	4.9	15.4 (14.5 - 16.4)	6.5	8.1 (7.4 - 8.8)	12.4
45	16	20.4 (19.4 - 21.6)	4.9	15.6 (14.6 - 16.6)	6.4	8.2 (7.4 - 8.9)	12.2
46	17	20.6 (19.5 - 21.7)	4.9	15.6 (14.7 - 16.7)	6.4	8.2 (7.5 - 9.0)	12.2
47	18	20.6 (19.5 - 21.8)	4.8	15.7 (14.7 - 16.8)	6.4	8.3 (7.5 - 9.1)	12.1
48	18	20.9 (19.8 - 22.0)	4.8	15.9 (14.9 - 17.0)	6.3	8.4 (7.6 - 9.2)	11.9
49	19	21.1 (19.9 - 22.2)	4.7	16.1 (15.1 - 17.2)	6.2	8.5 (7.7 - 9.3)	11.8
50	20	21.2 (20.0 - 22.4)	4.7	16.2 (15.2 - 17.3)	6.2	8.6 (7.8 - 9.4)	11.7
51	21	21.3 (20.2 - 22.5)	4.7	16.4 (15.3 - 17.5)	6.1	8.7 (7.9 - 9.5)	11.5
52	22	21.6 (20.4 - 22.8)	4.6	16.6 (15.5 - 17.7)	6	8.8 (8.0 - 9.6)	11.4
53	23	21.9 (20.7 - 23.2)	4.6	16.7 (15.7 - 17.9)	6	8.8 (8.0 - 9.7)	11.3
54	24	22.2 (21.0 - 23.4)	4.5	16.9 (15.8 - 18.1)	5.9	9.0 (8.1 - 9.8)	11.2
55	26	22.4 (21.2 - 23.7)	4.5	17.1 (16.0 - 18.3)	5.8	9.1 (8.2 - 10.0)	11
56	27	22.7 (21.4 - 24.0)	4.4	17.4 (16.3 - 18.6)	5.7	9.2 (8.4 - 10.1)	10.8

57	28	23.0 (21.7 - 24.3)	4.3	17.7 (16.6 - 19.0)	5.6	9.4 (8.6 - 10.4)	10.6
58	30	23.2 (21.9 - 24.5)	4.3	17.8 (16.6 - 19.0)	5.6	9.5 (8.6 - 10.4)	10.6
59	32	23.4 (22.1 - 24.7)	4.3	18.0 (16.8 - 19.3)	5.6	9.6 (8.7 - 10.6)	10.4
60	33	23.5 (22.2 - 24.9)	4.2	18.1 (16.9 - 19.4)	5.5	9.7 (8.8 - 10.7)	10.3
61	35	23.8 (22.5 - 25.2)	4.2	18.4 (17.1 - 19.7)	5.4	9.8 (8.9 - 10.8)	10.2
62	37	24.2 (22.8 - 25.6)	4.1	18.7 (17.4 - 20.0)	5.4	10.0 (9.1 - 11.0)	10
63	39	24.5 (23.1 - 25.9)	4.1	18.9 (17.6 - 20.2)	5.3	10.2 (9.2 - 11.2)	9.8
64	41	24.8 (23.3 - 26.2)	4	19.1 (17.8 - 20.5)	5.2	10.3 (9.3 - 11.4)	9.7
65	43	25.0 (23.6 - 26.5)	4	19.3 (17.9 - 20.6)	5.2	10.4 (9.3 - 11.4)	9.7
66	45	25.4 (23.9 - 27.0)	3.9	19.6 (18.3 - 21.0)	5.1	10.6 (9.6 - 11.7)	9.4
67	48	25.8 (24.3 - 27.4)	3.9	20.0 (18.6 - 21.4)	5	10.8 (9.8 - 12.0)	9.2
68	50	26.0 (24.5 - 27.6)	3.8	20.2 (18.8 - 21.6)	5	10.9 (9.9 - 12.1)	9.1
69	53	26.5 (25.0 - 28.2)	3.8	20.6 (19.1 - 22.1)	4.9	11.2 (10.1 - 12.4)	8.9
70	56	26.5 (24.9 - 28.2)	3.8	20.5 (19.0 - 22.0)	4.9	11.2 (10.1 - 12.5)	8.9
71	59	27.0 (25.4 - 28.7)	3.7	20.9 (19.4 - 22.4)	4.8	11.5 (10.3 - 12.7)	8.7
72	63	27.4 (25.8 - 29.2)	3.6	21.2 (19.6 - 22.8)	4.7	11.6 (10.4 - 12.8)	8.7
73	67	27.8 (26.1 - 29.6)	3.6	21.5 (19.9 - 23.1)	4.7	11.7 (10.5 - 13.0)	8.5
74	72	28.1 (26.4 - 29.9)	3.6	21.7 (20.1 - 23.4)	4.6	12.0 (10.8 - 13.4)	8.3
75	78	28.4 (26.6 - 30.3)	3.5	22.0 (20.3 - 23.7)	4.5	12.3 (11.0 - 13.7)	8.1
76	83	28.9 (27.1 - 30.8)	3.5	22.4 (20.7 - 24.1)	4.5	12.6 (11.3 - 14.0)	7.9
77	89	29.4 (27.5 - 31.4)	3.4	22.7 (20.9 - 24.5)	4.4	12.8 (11.4 - 14.3)	7.8
78	95	29.8 (27.9 - 31.8)	3.4	23.1 (21.3 - 24.9)	4.3	13.1 (11.6 - 14.6)	7.7
79	101	30.4 (28.4 - 32.4)	3.3	23.5 (21.7 - 25.4)	4.3	13.4 (11.9 - 15.0)	7.5
80	107	30.9 (28.8 - 33.0)	3.2	23.9 (22.0 - 25.9)	4.2	13.8 (12.3 - 15.5)	7.2
81	113	31.1 (29.0 - 33.3)	3.2	24.4 (22.4 - 26.4)	4.1	14.1 (12.6 - 15.8)	7.1
82	119	31.2 (29.0 - 33.4)	3.2	24.7 (22.7 - 26.8)	4.1	14.5 (12.9 - 16.2)	6.9
83	125	31.6 (29.4 - 33.9)	3.2	25.3 (23.2 - 27.4)	4	14.9 (13.2 - 16.7)	6.7
84	131	31.7 (29.4 - 34.1)	3.2	25.6 (23.5 - 27.9)	3.9	15.2 (13.5 - 17.1)	6.6
85	137	32.0 (29.6 - 34.4)	3.1	26.1 (23.9 - 28.5)	3.8	15.6 (13.8 - 17.5)	6.4
86	143	31.9 (29.5 - 34.5)	3.1	26.3 (24.0 - 28.7)	3.8	15.5 (13.6 - 17.6)	6.4
87	150	32.7 (30.1 - 35.4)	3.1	27.3 (24.8 - 29.8)	3.7	16.3 (14.3 - 18.5)	6.1
88	157	33.0 (30.3 - 35.8)	3	28.1 (25.6 - 30.8)	3.6	16.9 (14.8 - 19.1)	5.9



89	164	33.2 (30.4 - 36.1)	3	28.1 (25.4 - 30.9)	3.6	17.0 (14.8 - 19.3)	5.9
90	172	33.8 (30.8 - 36.8)	3	28.5 (25.6 - 31.4)	3.5	17.7 (15.4 - 20.2)	5.6
91	179	33.7 (30.6 - 36.9)	3	28.3 (25.4 - 31.4)	3.5	17.9 (15.4 - 20.6)	5.6
92	187	33.9 (30.6 - 37.4)	2.9	28.7 (25.6 - 32.0)	3.5	18.7 (16.0 - 21.6)	5.4
93	201	34.2 (30.7 - 37.8)	2.9	29.1 (25.7 - 32.6)	3.4	19.4 (16.6 - 22.5)	5.1
94	214	34.1 (30.3 - 38.1)	2.9	28.9 (25.3 - 32.7)	3.5	20.0 (16.9 - 23.4)	5
95	228	34.9 (30.7 - 39.2)	2.9	29.3 (25.3 - 33.5)	3.4	20.6 (17.2 - 24.5)	4.8
96	245	37.5 (32.7 - 42.5)	2.7	31.6 (27.1 - 36.5)	3.2	22.2 (18.2 - 26.6)	4.5
97	268	40.0 (34.2 - 46.0)	2.5	33.2 (27.7 - 39.1)	3	23.6 (18.7 - 29.0)	4.2
98	301	37.9 (31.1 - 45.2)	2.6	30.8 (24.4 - 37.8)	3.2	22.6 (16.9 - 29.1)	4.4
99	394	44.2 (34.0 - 54.8)	2.3	37.9 (28.1 - 48.4)	2.6	29.5 (20.6 - 39.7)	3.4

**eTable 4.** Concordance in High Lp(a) in Index Participants With *LPA* Variants (rs1045872 or rs3798220)

	Number of risk alleles at rs1045872 or rs3798220 in index participants with high Lp(a)			P-value (trend for concordance)	P-value with Lp(a) concentration adjustment
	0	1	≥2		
<b>First-degree relatives, high Lp(a) ≥125 nmol/L</b>					
Number (%) of index participants	1029 (6.3)	2248 (65.2)	143 (91.7)	<0.001	-
Median [IQR] Lp(a) concentration in index participant, nmol/L	177 [151 - 225]	181 [150 - 228]	284 [198 - 362]	<0.001	-
Concordance in high Lp(a)	43.8 (40.6 - 47.0)	46.7 (44.6 - 48.8)	68.8 (60.5 - 76.3)	<0.001	0.007
<b>First-degree relatives, high Lp(a) ≥150 nmol/L</b>					
Number (%) of index participants	783 (4.8)	1692 (49.1)	134 (85.9)	<0.001	-
Median [IQR] Lp(a) concentration in index participant, nmol/L	189 [168 - 243]	203 [173 - 244]	291 [216 - 367]	<0.001	-
Concordance in high Lp(a)	39.4 (35.8 - 43.1)	40.8 (38.4 - 43.2)	62.1 (53.3 - 70.4)	0.001	0.08
<b>First-degree relatives, high Lp(a) ≥200 nmol/L</b>					
Number (%) of index participants	349 (2.1)	878 (25.5)	106 (67.9)	<0.001	-
Median [IQR] Lp(a) concentration in index participant, nmol/L	189 [168 - 243]	203 [173 - 244]	291 [216 - 367]	<0.001	-
Concordance in high Lp(a)	32.2 (27.1 - 37.6)	33.0 (29.9 - 36.2)	50.5 (40.5 - 60.4)	0.01	0.13
<b>Second-degree relatives, high Lp(a) ≥125 nmol/L</b>					
Number (%) of index participants	486 (6.1)	1031 (65.1)	97 (93.3)	<0.001	-
Median [IQR] Lp(a) concentration in index participant, nmol/L	172 [144 - 220]	182 [151 - 230]	275 [217 - 331]	<0.001	-
Concordance in high Lp(a)	28.0 (23.8 - 32.5)	32.2 (29.4 - 35.2)	42.7 (32.7 - 53.2)	0.007	0.05
<b>Second-degree relatives, high Lp(a) ≥150 nmol/L</b>					
Number (%) of index participants	329 (4.1)	781 (49.3)	92 (88.5)	<0.001	-
Median [IQR] Lp(a) concentration in index participant, nmol/L	195 [170 - 246]	206 [174 - 244]	284 [223 - 349]	<0.001	-
Concordance in high Lp(a)	26.5 (21.5 - 32.0)	27.2 (24.1 - 30.5)	36.3 (26.4 - 47.0)	0.17	0.40
<b>Second-degree relatives, high Lp(a) ≥200 nmol/L</b>					
Number (%) of index participants	151 (1.9)	421 (26.6)	81 (77.9)	<0.001	-

Median [IQR] Lp(a) concentration in index participant, nmol/L	251 [224 - 295]	240 [220 - 276]	297 [239 - 368]	<0.001	-
Concordance in high Lp(a)	20.2 (13.6 - 28.1)	18.9 (15.2 - 23.0)	18.8 (10.9 - 29.0)	0.77	0.45

Shown are the number (%) and median Lp(a) concentrations of index participants with high Lp(a) from first- and second-degree relative pairs according to genotype and Lp(a) cutoff (i.e.  $\geq 125$ ,  $\geq 150$ ,  $\geq 200$  nmol/L). The reported concordance in high Lp(a) is the percentage of first- or second-degree relatives that also have high Lp(a) according to genotype and Lp(a) cutoff.

**eTable 5.** Number of Index Participants With High Lp(a) According to Different Definitions of High Lp(a) and Self-Reported Race and Ethnicity

		Self-reported race and Ethnicity				
		All	Black	South Asian	White	Other / not reported
<b>Number (%) off index participants with high Lp(a) among first-degree relatives</b>	Lp(a) ≥125 nmol/L	3,420 (17.2)	34 (24.3)	38 (15.1)	3,303 (17.3)	14 (11)
	Lp(a) ≥150 nmol/L	2,609 (13.1)	27 (19.3)	32 (12.7)	2,512 (13.1)	14 (11)
	Lp(a) ≥200 nmol/L	1,333 (6.7)	14 (10)	16 (6.4)	1,289 (6.7)	6 (4.7)
<b>Number (%) off index participants with high Lp(a) among second-degree relatives</b>	Lp(a) ≥125 nmol/L	1,614 (16.6)	30 (28.6)	10 (11.4)	1,539 (16.5)	6 (20)
	Lp(a) ≥150 nmol/L	1,202 (12.4)	24 (22.9)	9 (10.2)	1,147 (12.3)	3 (10)
	Lp(a) ≥200 nmol/L	653 (6.7)	17 (16.2)	1 (1.1)	622 (6.7)	-
<b>Number (%) off index participants with high Lp(a) among unrelated individuals</b>	Lp(a) ≥125 nmol/L	30,258 (16.4)	809 (27.5)	418 (11.2)	28,442 (16.4)	589 (14)
	Lp(a) ≥150 nmol/L	22,976 (12.4)	622 (21.2)	297 (8)	21,607 (12.4)	450 (10.7)
	Lp(a) ≥200 nmol/L	12,079 (6.5)	314 (10.7)	147 (3.9)	11,395 (6.6)	223 (5.3)

Race and ethnicity were self-reported. The other / not reported category included participants with a mixed racial background, participants who did not know their racial background, participants who did not identify with any of the other provided categories, or participants who chose not to answer.

## eReferences

1. Clarke R, Peden JF, Hopewell JC, et al. Genetic Variants Associated with Lp(a) Lipoprotein Level and Coronary Disease. *N Engl J Med*. 2009;361(26):2518-2528. doi:10.1056/NEJMoa0902604
2. Patel AP, Wang M, Pirruccello JP, et al. Lp(a) (Lipoprotein[a]) Concentrations and Incident Atherosclerotic Cardiovascular Disease. *Arterioscler Thromb Vasc Biol*. 2021;41(1):465-474. doi:10.1161/ATVBAHA.120.315291