

## **SUPPLEMENTAL MATERIAL**

**SupplementalTable 1.** Baseline characteristics of WHS participants according to concordant or discordant LDL-C and non-HDL-C categories

	LDL-C < median		LDL-C ≥ median	
	NHDL-C < median (Concordant)	NHDL-C ≥ median (Discordant)	NHDL-C < median (Discordant)	NHDL-C ≥ median (Concordant)
	N=12,026	N=1,569	N=1,616	N=12,322
Age, mean (SD), y	53.5 (6.6)	55.1 (7.0)	54.2 (7.1)	55.9 (7.3)
Current smoking, %	9.4	16.1	8.8	13.5
Hypertension, %	20.1	34.9	18.8	29.6
Diabetes, %	1.9	6.1	1.2	3.3
Postmenopausal, %	58.2	75.3	59.4	74.1
Hormone use, %	45.6	56.2	35.2	41.2
Parental history of premature MI, %	11.5	15.7	12.6	13.9
Body mass index, mean (SD), kg/m <sup>2</sup>	25.1 (4.8)	27.8 (5.4)	24.8 (4.4)	26.6 (4.9)
Laboratory measurements, median (25 <sup>th</sup> -75 <sup>th</sup> percentile)				
LDL-C, mg/dL	98 (86-109)	113 (105-118)	126 (123-130)	148 (135-165)
NHDL-C, mg/dL	126 (111-138)	164 (158-175)	148 (144-151)	184 (169-207)
HDL-C, mg/dL	54 (45-65)	41 (35-51)	57 (49-67)	50 (42-60)
Triglycerides, mg/dL	95 (70-134)	249 (186-348)	83 (67-103)	146 (106-201)
ApoB, mg/dL	83 (72-92)	112 (100-122)	96 (91-104)	122 (110-136)
LDL-P, nmol/L	977 (824-1148)	1356 (1169-1552)	1144 (1026-1271)	1484 (1270-1735)
LDL size, nm	21.2 (20.8-21.6)	20.4 (19.8-21.0)	21.4 (21.1-21.7)	21.1 (20.5-21.5)
Cholesterol per LDL particle*	2562 (2206-2947)	2098 (1799-2459)	2864 (2578-3208)	2614 (2279-3026)
hsCRP, mg/L	1.65 (0.62-3.80)	3.72 (1.89-6.69)	1.05 (0.48-2.51)	2.34 (1.06-4.76)

Median values of LDL-C and NHDL-C were 121 mg/dL and 154 mg/dL

SD: standard deviation; Parental history: history of myocardial infarction in parent <60 years old; hsCRP: high-sensitivity C-reactive protein.

\*Estimate of the number of cholesterol molecules per LDL particle, calculated by dividing LDL-C (nmol/L) by LDL-P (nmol/L).

**Supplemental Table 2.** Baseline characteristics of WHS participants according to concordant or discordant LDL-C and apoB categories

	LDL-C < median		LDL-C ≥ median	
	ApoB < median (Concordant)	ApoB ≥ median (Discordant)	ApoB < median (Discordant)	ApoB ≥ median (Concordant)
	N=11,033	N=2,562	N=2,634	N=11,304
Age, mean (SD), y	53.3 (6.5)	55.4 (7.1)	54.1 (7.0)	56.0 (7.3)
Current smoking, %	9.5	12.8	8.9	13.9
Hypertension, %	19.2	32.8	18.9	30.6
Diabetes, %	1.8	5.0	1.1	3.5
Postmenopausal, %	56.7	74.9	60.9	75.0
Hormone use, %	44.2	58.0	35.1	41.7
Parental history of premature MI, %	11.5	14.0	11.9	14.1
Body mass index, mean (SD), kg/m <sup>2</sup>	25.0 (4.7)	27.5 (5.5)	24.9 (4.2)	26.7 (5.0)
Laboratory measurements, median (25 <sup>th</sup> -75 <sup>th</sup> percentile)				
LDL-C, mg/dL	98 (85-108)	111 (101-117)	130 (125-139)	148 (135-166)
NHDL-C, mg/dL	125 (110-137)	152 (142-164)	157 (148-169)	185 (170-207)
HDL-C, mg/dL	55 (46-66)	42 (35-52)	60 (51-71)	49 (42-58)
Triglycerides, mg/dL	93 (68-131)	182 (129-266)	94 (73-125)	149 (107-204)
ApoB, mg/dL	81 (71-89)	112 (106-121)	93 (88-97)	124 (113-138)
LDL-P, nmol/L	955 (806-1109)	1359 (1182-1533)	1121 (993-1243)	1522 (1315-1761)
LDL size, nm	21.3 (20.9-21.6)	20.7 (20.0-21.2)	21.4 (21.1-21.7)	21.1 (20.5-21.5)
Cholesterol per LDL particle*	2607 (2269-2986)	2067 (1769-2396)	3061 (2729-3541)	2559 (2243-2931)
hsCRP, mg/L	1.56 (0.59-3.62)	3.40 (1.58-6.29)	1.24 (0.55-2.84)	2.41 (1.11-4.87)

Median values of LDL-C and apoB were 121 mg/dL and 100 mg/dL, respectively.

SD: standard deviation; Parental history: history of myocardial infarction in parent <60 years old; hsCRP: high-sensitivity C-reactive protein.

\*Estimate of the number of cholesterol molecules per LDL particle, calculated by dividing LDL-C (nmol/L) by LDL-P (nmol/L).

**Supplemental Table 3.** Baseline characteristics of WHS participants according to concordant or discordant LDL-C and LDL-P categories

	LDL-C < median		LDL-C ≥ median	
	LDL-P < median (Concordant)	LDL-P ≥ median (Discordant)	LDL-P < median (Discordant)	LDL-P ≥ median (Concordant)
			N=10,341	N=3,254
Age, mean (SD), y	53.3 (6.6)	54.9 (7.0)	54.6 (7.1)	56.0 (7.3)
Current smoking, %	9.5	12.3	10.3	13.9
Hypertension, %	18.5	32.3	20.2	31.0
Diabetes, %	1.7	4.5	1.1	3.7
Postmenopausal, %	56.9	70.6	63.6	75.3
Hormone use, %	44.3	54.7	36.7	41.7
Parental history of premature MI, %	11.3	14.3	12.7	14.0
Body mass index, mean (SD), kg/m <sup>2</sup>	24.7 (4.6)	27.7 (5.5)	24.9 (4.4)	26.9 (5.0)
Laboratory measurements, median (25 <sup>th</sup> -75 <sup>th</sup> percentile)				
LDL-C, mg/dL	97 (84-108)	109 (99-115)	133 (126-145)	149 (135-167)
NHDL-C, mg/dL	124 (109-137)	147 (135-159)	162 (152-176)	187 (170-209)
HDL-C, mg/dL	56 (47-67)	43 (36-52)	61 (52-71)	48 (41-57)
Triglycerides, mg/dL	92 (67-129)	163 (113-235)	97 (74-129)	152 (110-210)
ApoB, mg/dL	80 (70-89)	104 (94-114)	99 (91-109)	125 (113-139)
LDL-P, nmol/L	931 (794-1057)	1374 (1282-1511)	1093 (997-1158)	1555 (1379-1787)
LDL size, nm	21.3 (21.0-21.6)	20.7 (20.1-21.1)	21.5 (21.2-21.8)	21.0 (20.4-21.4)
Cholesterol per LDL particle*	2688 (2396-3033)	1990 (1746-2189)	3276 (2989-3671)	2483 (2206-2764)
hsCRP, mg/L	1.49 (0.57-3.51)	3.29 (1.51-6.10)	1.28 (0.57-2.90)	2.51 (1.17-4.97)

Median values of LDL-C and LDL-P were 121 mg/dL and 1216 nmol/L, respectively.

SD: standard deviation; Parental history: history of myocardial infarction in parent <60 years old; hsCRP: high-sensitivity C-reactive protein.

\*Estimate of the number of cholesterol molecules per LDL particle, calculated by dividing LDL-C (nmol/L) by LDL-P (nmol/L).

**Supplemental Table 4.** Underestimation or overestimation of coronary risk among women with LDL-C discordant with all three alternative LDL-related measures (NHDL-C, apoB, and LDL-P)

	LDL-C < median	LDL-C < median	P value
	NHDL-C & ApoB & LDL-P < median (Concordant)	NHDL-C & ApoB & LDL-P ≥ median (Discordant)	
LDL-C, median (25 <sup>th</sup> -75 <sup>th</sup> percentile), mg/dL	96 (83-107)	114 (107-118)	
NHDL-C, median (25 <sup>th</sup> -75 <sup>th</sup> percentile), mg/dL	122 (107-133)	167 (160-178)	
ApoB, median (25 <sup>th</sup> -75 <sup>th</sup> percentile), mg/dL	79 (69-87)	117 (111-126)	
LDL-P, median (25 <sup>th</sup> -75 <sup>th</sup> percentile), nmol/L	915 (783-1042)	1508 (1376-1663)	
No. events/N	150/9,355	63/908	
Incidence rate, per 1000 p-y (95% CI)	0.99 (0.84-1.16)	4.57 (3.57-5.85)	
Age-adjusted HR (95% CI)	1.00	3.90 (2.90-5.25)	<0.001
Minimally-adjusted HR (95% CI) *	1.00	2.91 (2.14-3.96)	<0.001
Fully-adjusted HR (95% CI) †	1.00	1.69 (1.08-2.65)	0.02
	LDL-C ≥ median	LDL-C ≥ median	P value
	NHDL-C & ApoB & LDL-P ≥ median (Concordant)	NHDL-C & ApoB & LDL-P < median (Discordant)	
LDL-C, median (25 <sup>th</sup> -75 <sup>th</sup> percentile), mg/dL	151 (138-169)	126 (123-129)	
NHDL-C, median (25 <sup>th</sup> -75 <sup>th</sup> percentile), mg/dL	190 (174-212)	147 (142-150)	
ApoB, median (25 <sup>th</sup> -75 <sup>th</sup> percentile), mg/dL	127 (117-141)	92 (87-95)	
LDL-P, median (25 <sup>th</sup> -75 <sup>th</sup> percentile), nmol/L	1587 (1409-1814)	1056 (956-1131)	
No. events/N	591/9435	8/856	
Incidence rate, per 1000 p-y (95% CI)	4.05 (3.73-4.39)	0.58 (0.29-1.15)	
Age-adjusted HR (95% CI)	1.00	0.16 (0.08-0.32)	<0.001
Minimally-adjusted HR (95% CI) *	1.00	0.20 (0.10-0.39)	<0.001
Fully-adjusted HR (95% CI) †	1.00	0.41 (0.20-0.84)	0.02

\* Minimally-adjusted model included age, treatment assignment, hormone use, postmenopausal status, smoking, blood pressure

† Minimally-adjusted model variables plus diabetes, body mass index, HDL cholesterol, triglycerides, high-sensitivity C-reactive protein, parental history of premature myocardial infarction

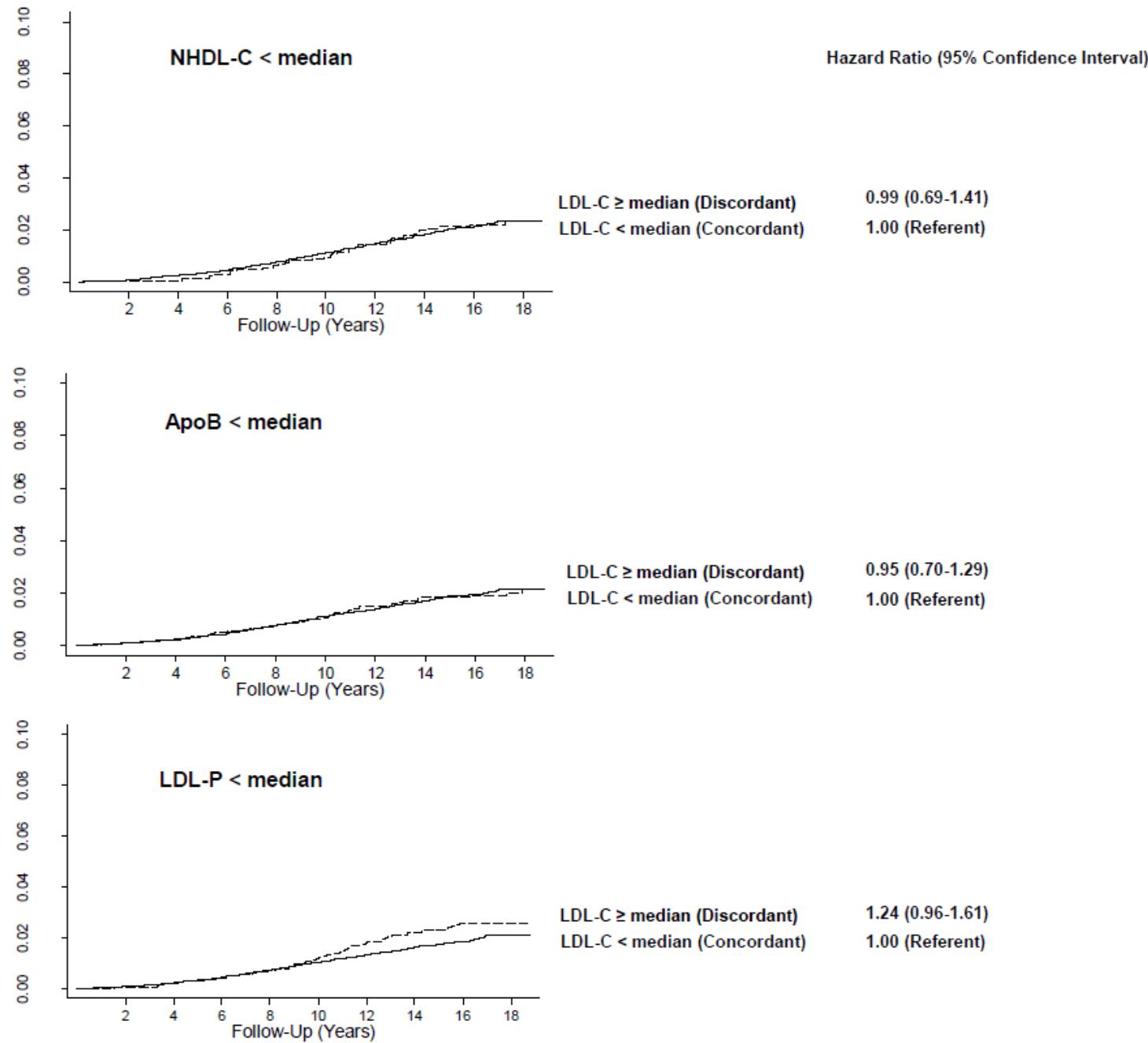
Median values of LDL-C, NHDL-C, apoB, and LDL-P were 121 mg/dL, 154 mg/dL, 100 mg/dL, and 1216 nmol/L, respectively.

## **Supplemental Figure Legends**

**Supplemental Figure 1.** Cumulative probability of incident CHD events by concordant and discordant LDL-C among women with <median NHDL-C, apoB, or LDL-P. Median values of LDL-C, NHDL-C, apoB, and LDL-P were 121 mg/dL, 154 mg/dL, 100 mg/dL, and 1216 nmol/L, respectively. Hazard ratios and 95% confidence intervals obtained from Cox regression models. P for trend obtained from log-rank test.

**Supplemental Figure 2.** Cumulative probability of incident CHD events by concordant and discordant LDL-C among women with  $\geq$  median NHDL-C, apoB, or LDL-P. Median values of LDL-C, NHDL-C, apoB, and LDL-P were 121 mg/dL, 154 mg/dL, 100 mg/dL, and 1216 nmol/L, respectively. Hazard ratios and 95% confidence intervals obtained from Cox regression models. P for trend obtained from log-rank test.

Supplemental Figure 1.



Supplemental Figure 2.

