

Supplementary Table 1

Predicted mean values of biomarkers within 10 years after bilateral oophorectomy or index date, stratified by age at index date (generalized estimating equation [GEE] linear models).

Biomarker	N women (N values) ^a	Predicted mean values (95% CI) from adjusted models ^b					p-values ^c
		Overall	1 year	3 years	5 years	10 years	
Systolic blood pressure (mmHg)^d							
Age <40 years							
Oophorectomy, not on ET	65 (292)	119.0 (116.1-121.9)	118.4 (111.1-125.8)	122.7 (116.2-129.1)	119.5 (113.6-125.4)	123.9 (119.1-128.8)	<0.001
Oophorectomy, on ET	57 (322)	117.9 (115.1-120.8)	116.2 (111.3-121.1)	114.7 (109.8-119.6)	115.1 (110.0-120.2)	126.3 (119.6-133.1)	0.71
Referent	99 (621)	117.6 (115.5-119.7)	114.5 (110.0-119.1)	115.2 (110.8-119.6)	118.3 (114.1-122.6)	124.5 (120.4-128.7)	
Age 40-45 years							
Oophorectomy, not on ET	104 (614)	118.4 (116.6-120.3)	116.1 (111.8-120.4)	119.4 (115.5-123.4)	119.4 (115.6-123.3)	120.5 (116.2-124.7)	0.75
Oophorectomy, on ET	71 (277)	118.0 (115.2-120.7)	117.1 (112.9-121.3)	119.5 (114.2-124.8)	118.3 (111.8-124.8)	116.7 (108.2-125.1)	0.25
Referent	138 (953)	116.1 (114.6-117.6)	116.5 (113.2-119.9)	117.2 (113.8-120.5)	113.7 (110.2-117.3)	114.9 (111.0-118.9)	
Diastolic blood pressure (mmHg)^d							
Age <40 years							
Oophorectomy, not on ET	65 (292)	75.5 (73.4-77.6)	75.2 (69.9-80.6)	79.3 (74.5-84.0)	75.9 (71.6-80.2)	78.7 (75.2-82.2)	0.12
Oophorectomy, on ET	57 (322)	75.3 (73.2-77.4)	73.3 (69.7-76.9)	75.1 (71.5-78.6)	73.7 (70.0-77.4)	76.7 (71.8-81.6)	0.47
Referent	99 (621)	73.3 (71.7-74.8)	73.1 (69.8-76.4)	72.0 (68.8-75.2)	73.9 (70.8-77.0)	75.6 (72.6-78.6)	
Age 40-45 years							
Oophorectomy, not on ET	104 (614)	75.2 (74.0-76.4)	73.8 (70.9-76.7)	74.4 (71.8-77.1)	75.4 (72.8-78.0)	76.6 (73.7-79.4)	0.98
Oophorectomy, on ET	71 (277)	72.8 (71.0-74.6)	73.6 (70.8-76.5)	73.7 (70.1-77.2)	71.8 (67.5-76.2)	71.5 (65.8-77.1)	0.86
Referent	138 (953)	72.6 (71.6-73.6)	71.8 (69.6-74.1)	72.8 (70.5-75.0)	71.9 (69.5-74.2)	71.7 (69.0-74.3)	
Weight (kg)							
Age <40 years							
Oophorectomy, not on ET	62 (294)	81.8 (76.7-86.9)	79.9 (72.2-87.6)	80.9 (73.6-88.2)	82.1 (75.0-89.2)	80.9 (73.7-88.2)	0.047
Oophorectomy, on ET	59 (302)	75.6 (70.4-80.9)	70.6 (63.6-77.7)	73.9 (66.5-81.3)	75.9 (68.6-83.3)	75.4 (67.3-83.5)	0.44
Referent	87 (543)	74.0 (69.7-78.2)	72.1 (65.4-78.9)	73.4 (66.6-80.3)	74.9 (68.3-81.5)	75.4 (68.7-82.0)	
Age 40-45 years							
Oophorectomy, not on ET	142 (828)	85.2 (81.6-88.9)	84.8 (79.4-90.3)	87.1 (81.9-92.4)	87.6 (82.4-92.9)	86.2 (80.9-91.5)	0.009
Oophorectomy, on ET	87 (357)	77.8 (73.2-82.5)	78.9 (72.9-84.8)	78.2 (72.0-84.4)	78.9 (72.3-85.4)	80.1 (72.6-87.6)	0.01
Referent	167 (1,198)	77.2 (73.9-80.4)	75.5 (70.2-80.7)	76.7 (71.5-81.9)	78.6 (73.5-83.8)	78.5 (73.2-83.7)	

Supplementary Table 1 (continued)

Biomarker	N women (N values) ^a	Predicted mean values (95% CI) from adjusted models ^b					p-values ^c
		Overall	1 year	3 years	5 years	10 years	
Body mass index (kg/m²)							
Age <40 years							
Oophorectomy, not on ET	62 (294)	30.1 (28.3-31.9)	29.4 (26.7-32.2)	30.0 (27.4-32.5)	30.5 (28.0-33.0)	30.0 (27.5-32.6)	0.01
Oophorectomy, on ET	59 (302)	28.2 (26.4-30.1)	26.6 (24.1-29.0)	27.8 (25.2-30.4)	28.6 (26.0-31.1)	28.4 (25.6-31.3)	0.45
Referent	87 (543)	26.7 (25.2-28.1)	26.1 (23.8-28.5)	26.6 (24.2-29.0)	27.1 (24.8-29.4)	27.3 (25.0-29.7)	
Age 40-45 years							
Oophorectomy, not on ET	142 (828)	31.2 (29.9-32.5)	31.2 (29.3-33.1)	32.0 (30.2-33.9)	32.1 (30.3-34.0)	31.6 (29.7-33.4)	0.006
Oophorectomy, on ET	87 (357)	28.8 (27.1-30.4)	29.1 (27.0-31.2)	28.7 (26.5-30.9)	29.2 (26.8-31.5)	29.7 (27.0-32.4)	0.02
Referent	167 (1,198)	28.4 (27.3-29.6)	27.7 (25.9-29.6)	28.2 (26.3-30.0)	28.9 (27.0-30.7)	28.8 (26.9-30.6)	
Total cholesterol (mg/dL)^e							
Age <40 years							
Oophorectomy, not on ET	37 (115)	211.4 (199.4-223.4)	204.7 (179.0-230.4)	216.4 (196.0-236.8)	222.1 (204.5-239.7)	231.2 (214.7-247.7)	0.10
Oophorectomy, on ET	25 (62)	214.4 (200.2-228.5)	176.9 (150.4-203.4)	212.9 (188.5-237.3)	226.0 (204.8-247.1)	216.5 (194.5-238.6)	0.04
Referent	62 (153)	199.5 (190.7-208.3)	190.7 (172.8-208.7)	190.3 (173.4-207.3)	189.8 (174.0-205.6)	212.5 (195.8-229.1)	
Age 40-45 years							
Oophorectomy, not on ET	58 (146)	208.9 (199.6-218.3)	205.6 (181.8-229.4)	203.2 (186.5-219.9)	205.4 (188.2-222.6)	224.9 (206.3-243.4)	0.32
Oophorectomy, on ET	37 (91)	213.5 (201.0-225.9)	206.8 (186.6-226.9)	206.8 (188.0-225.5)	218.1 (199.5-236.7)	210.0 (178.8-241.1)	0.41
Referent	94 (290)	200.4 (193.4-207.5)	189.6 (174.7-204.4)	193.9 (180.0-207.7)	198.2 (183.9-212.5)	213.5 (198.8-228.2)	
Triglycerides (mg/dL)^e							
Age <40 years							
Oophorectomy, not on ET	37 (112)	150.2 (123.8-176.6)	113.6 (61.5-165.6)	152.7 (108.7-196.7)	142.1 (104.9-179.4)	196.1 (159.9-232.3)	0.07
Oophorectomy, on ET	24 (61)	131.7 (100.1-163.2)	72.0 (17.0-127.0)	169.7 (119.2-220.2)	133.3 (88.4-178.2)	131.7 (85.3-178.2)	<0.001
Referent	61 (145)	112.5 (92.6-132.4)	136.2 (96.4-176.1)	100.9 (63.7-138.1)	99.6 (66.1-133.1)	121.0 (85.0-157.0)	
Age 40-45 years							
Oophorectomy, not on ET	57 (143)	131.5 (116.2-146.7)	136.7 (93.1-180.4)	130.2 (100.9-159.6)	146.4 (115.9-177.0)	132.8 (100.2-165.4)	0.26
Oophorectomy, on ET	37 (90)	152.1 (131.5-172.7)	127.0 (91.8-162.2)	131.0 (97.4-164.6)	117.6 (85.0-150.3)	232.4 (175.1-289.8)	0.26
Referent	93 (287)	110.4 (99.1-121.6)	103.6 (77.6-129.5)	108.8 (84.6-132.9)	107.3 (82.2-132.4)	113.9 (88.3-139.5)	

Supplementary Table 1 (continued)

Biomarker	N women (N values) ^a	Predicted mean values (95% CI) from adjusted models ^b					p-values ^c
		Overall	1 year	3 years	5 years	10 years	
HDL cholesterol (mg/dL)^e							
Age <40 years							
Oophorectomy, not on ET	37 (110)	57.9 (52.4-63.5)	64.8 (53.4-76.2)	55.8 (46.2-65.3)	58.4 (50.4-66.4)	54.6 (46.9-62.2)	0.46
Oophorectomy, on ET	23 (59)	66.6 (59.9-73.2)	69.4 (55.0-83.7)	65.6 (54.6-76.6)	68.9 (59.2-78.6)	68.8 (58.8-78.7)	0.002
Referent	61 (144)	57.2 (53.1-61.4)	45.2 (36.8-53.7)	61.3 (53.3-69.3)	58.9 (51.8-66.1)	62.2 (54.6-69.8)	
Age 40-45 years							
Oophorectomy, not on ET	59 (143)	63.4 (59.5-67.3)	64.3 (53.4-75.3)	61.1 (54.4-67.8)	56.3 (49.4-63.1)	62.9 (55.5-70.4)	0.11
Oophorectomy, on ET	37 (89)	72.5 (67.4-77.5)	66.3 (58.2-74.5)	75.5 (67.9-83.1)	75.2 (67.7-82.7)	70.7 (58.2-83.2)	0.07
Referent	94 (288)	64.0 (61.1-66.9)	61.4 (55.3-67.4)	63.0 (57.5-68.6)	61.8 (56.0-67.6)	67.2 (61.3-73.1)	
LDL cholesterol (mg/dL)^e							
Age <40 years							
Oophorectomy, not on ET	36 (107)	124.5 (112.5-136.6)	119.4 (95.8-143.0)	130.6 (110.3-150.9)	134.2 (117.5-150.8)	137.6 (121.4-153.8)	0.65
Oophorectomy, on ET	23 (57)	122.7 (108.4-137.0)	123.2 (94.2-152.3)	117.6 (95.0-140.2)	129.4 (109.2-149.6)	119.7 (99.1-140.3)	0.58
Referent	57 (131)	118.0 (108.8-127.2)	103.9 (81.8-126.0)	114.7 (97.9-131.6)	113.3 (97.8-128.7)	127.1 (110.4-143.7)	
Age 40-45 years							
Oophorectomy, not on ET	58 (138)	119.6 (110.4-128.8)	109.2 (84.0-134.5)	114.8 (99.0-130.7)	119.0 (103.1-134.8)	132.8 (115.6-150.1)	0.62
Oophorectomy, on ET	37 (85)	111.7 (99.0-124.3)	117.3 (98.6-136.1)	107.9 (90.4-125.4)	122.2 (104.8-139.5)	99.6 (65.6-133.6)	0.46
Referent	92 (278)	114.6 (107.8-121.5)	106.5 (91.7-121.2)	110.1 (97.0-123.2)	115.3 (101.9-128.8)	123.5 (109.8-137.2)	

CI = confidence interval; ET = estrogen therapy; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

^a The numbers represent the number of unique women and the number of total values across all time points for each group separately.

^b Predicted mean values, confidence intervals, and p-values for each biomarker were obtained from generalized estimating equation linear models including variables for group status (bilateral oophorectomy not on ET, bilateral oophorectomy on ET, and referent women), years after index date (0-10; as a categorical variable), and the interaction between group and years after index. Each model was adjusted for age at index (as a continuous variable), years of education (≤ 12 , 13-16, > 16), and smoking (current or former vs never). Predicted mean values for each group at each time were calculated as the predicted mean value across all women in the corresponding group.

^c Three p-values are stacked vertically for each model in the following order: 1) the p-value for the overall difference across the three groups of women, 2) the p-value for the years after the index date, and 3) the p-value for the interaction between group and years after index date.

^d Models for blood pressure values excluded 25 women age <40 years (7 bilateral oophorectomy not on ET, 10 bilateral oophorectomy on ET, and 8 referent women) and 70 women age 40-45 years (23 bilateral oophorectomy not on ET, 16 bilateral oophorectomy on ET, and 31 referent women) who had hypertension at index.

^e Models for lipid values excluded 60 women age <40 years (11 bilateral oophorectomy not on ET, 26 bilateral oophorectomy on ET, and 23 referent women) and 149 women age 40-45 years (34 bilateral oophorectomy not on ET, 45 bilateral oophorectomy on ET, and 70 referent women) who had hyperlipidemia at index.

Supplementary Table 2

Predicted mean values of biomarkers within 3 years before and 10 years after bilateral oophorectomy or index date (generalized estimating equation [GEE] linear models).

Biomarker	N women (N values) ^a	Predicted mean values (95% CI) from adjusted models ^b					p-values ^c
		Overall	-3 years	1 year	5 years	10 years	
Systolic blood pressure (mmHg) ^d							0.07
Oophorectomy	258 (2,588)	120.9 (119.6-122.2)	120.8 (117.8-123.7)	119.8 (117.2-122.4)	121.6 (118.9-124.3)	124.4 (121.7-127.2)	<0.001
Referent	265 (2,447)	119.4 (118.1-120.6)	118.0 (115.0-121.0)	118.4 (115.8-121.1)	118.7 (115.9-121.5)	123.5 (120.7-126.4)	0.44
Diastolic blood pressure (mmHg) ^d							<0.001
Oophorectomy	258 (2,588)	76.2 (75.3-77.0)	74.7 (72.7-76.6)	75.6 (73.9-77.3)	76.7 (74.9-78.5)	78.6 (76.7-80.5)	0.001
Referent	265 (2,447)	74.3 (73.5-75.1)	74.4 (72.4-76.4)	73.6 (71.8-75.4)	74.3 (72.5-76.2)	76.1 (74.2-78.0)	0.66
Weight (kg)							0.001
Oophorectomy	266 (2,396)	80.9 (78.3-83.4)	79.2 (75.2-83.3)	79.6 (75.7-83.6)	82.9 (78.9-86.9)	81.5 (77.4-85.5)	<0.001
Referent	269 (2,284)	75.4 (73.0-77.9)	73.8 (69.5-78.0)	74.3 (70.2-78.3)	77.2 (73.1-81.3)	77.3 (73.1-81.4)	0.11
Body mass index (kg/m ²)							<0.001
Oophorectomy	266 (2,396)	29.8 (28.9-30.7)	29.3 (27.8-30.7)	29.4 (28.0-30.8)	30.6 (29.2-32.0)	30.1 (28.6-31.5)	<0.001
Referent	269 (2,284)	27.6 (26.8-28.5)	27.0 (25.5-28.5)	27.2 (25.8-28.7)	28.2 (26.8-29.7)	28.3 (26.8-29.7)	0.11
Total cholesterol (mg/dL) ^e							<0.001
Oophorectomy	244 (1,163)	211.6 (207.1-216.0)	200.5 (189.4-211.7)	211.3 (203.0-219.6)	218.9 (211.0-226.9)	226.1 (217.8-234.4)	<0.001
Referent	248 (984)	199.5 (195.2-203.9)	198.6 (187.3-209.8)	192.0 (183.2-200.9)	202.8 (194.1-211.5)	208.2 (199.3-217.1)	0.006
Triglycerides (mg/dL) ^e							<0.001
Oophorectomy	242 (1,147)	146.9 (136.4-157.4)	159.5 (132.6-186.3)	145.5 (125.8-165.1)	152.2 (133.4-171.0)	171.6 (151.9-191.2)	0.03
Referent	244 (959)	114.8 (104.5-125.0)	116.3 (89.5-143.0)	108.2 (87.0-129.4)	118.1 (97.5-138.7)	125.2 (104.2-146.3)	0.53
HDL cholesterol (mg/dL) ^e							0.33
Oophorectomy	239 (1,123)	59.5 (57.6-61.4)	50.5 (45.9-55.1)	60.3 (57.0-63.7)	61.3 (58.1-64.5)	60.9 (57.6-64.3)	<0.001
Referent	243 (951)	58.3 (56.4-60.1)	54.4 (49.9-59.0)	56.0 (52.4-59.6)	59.2 (55.7-62.7)	61.6 (58.0-65.2)	0.19
LDL cholesterol (mg/dL) ^e							0.07
Oophorectomy	234 (1,041)	123.3 (118.8-127.8)	116.8 (104.9-128.7)	123.6 (115.3-131.8)	127.5 (119.9-135.0)	131.5 (123.5-139.5)	0.003
Referent	233 (889)	117.9 (113.5-122.3)	120.6 (109.6-131.6)	113.0 (104.2-121.8)	120.1 (111.8-128.4)	122.0 (113.5-130.5)	0.04

CI = confidence interval; ET = estrogen therapy; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

^a The numbers represent the number of unique women and the number of total values across all time points for each group separately.

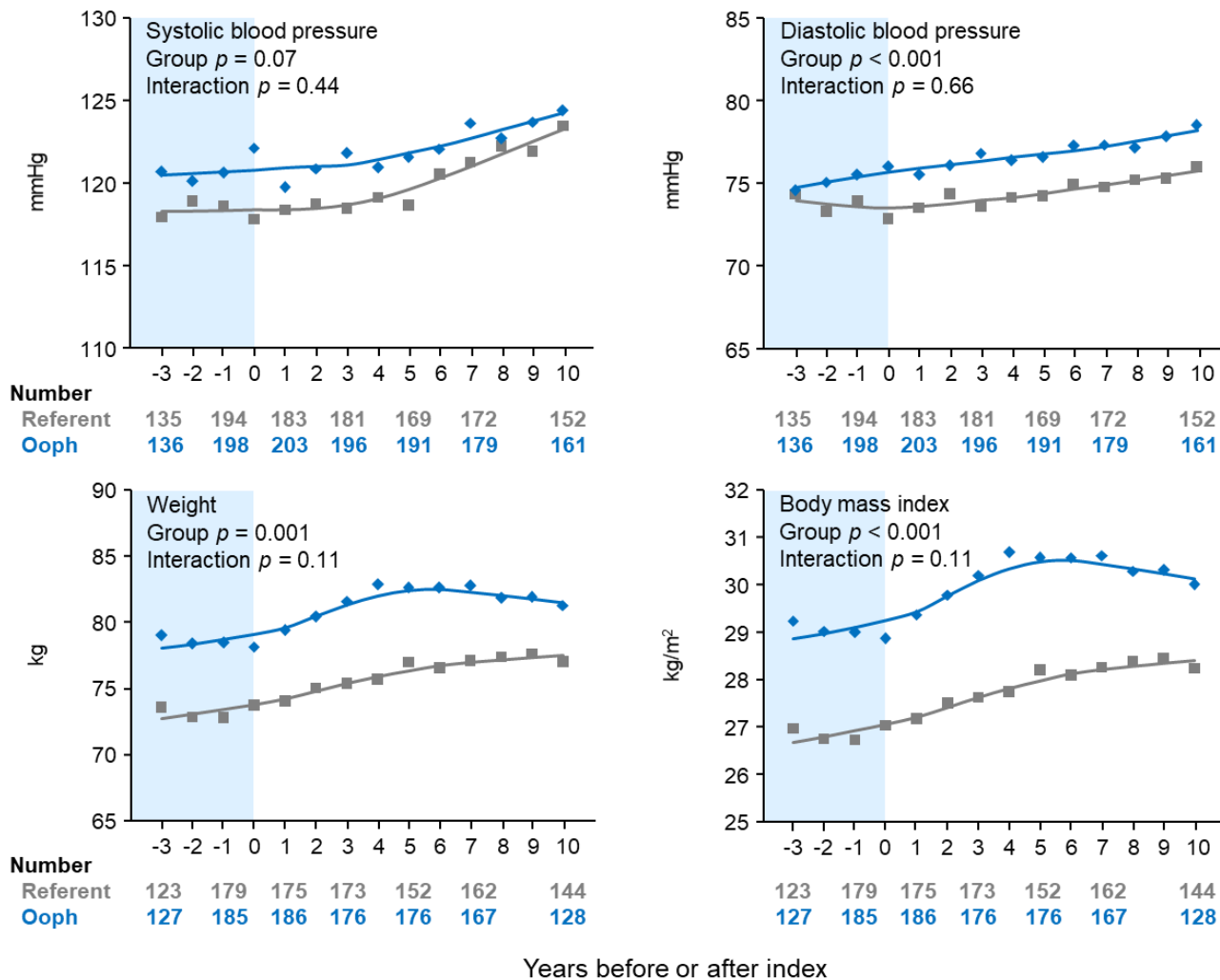
Supplementary Table 2 (*continued*)

^b Predicted mean values, confidence intervals, and p-values for each biomarker were obtained from generalized estimating equation linear models including variables for group status (bilateral oophorectomy not on ET, bilateral oophorectomy on ET, and referent women), years after index date (-3 through 10; as a categorical variable), and the interaction between group and years after index. Each model was adjusted for age at index (as a continuous variable), years of education (≤ 12 , 13-16, >16), and smoking (current or former vs never). Predicted mean values for each group at each time were calculated as the predicted mean value across all women in the corresponding group.

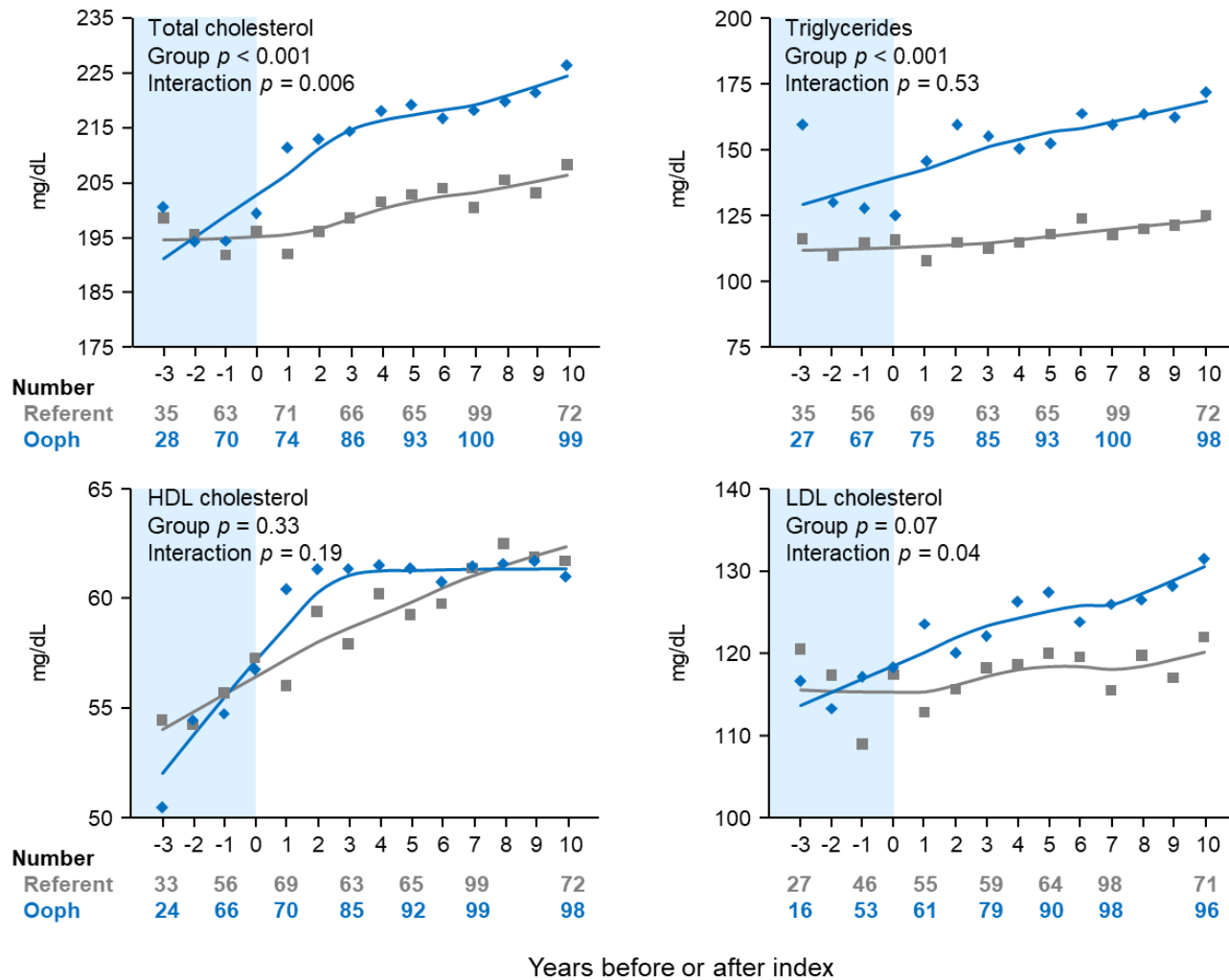
^c Three p-values are stacked vertically for each model in the following order: 1) the p-value for the overall difference across the three groups of women, 2) the p-value for the years after the index date, and 3) the p-value for the interaction between group and years after index date.

^d Models for blood pressure values excluded 14 women (9 bilateral oophorectomy and 5 referent women) who had hypertension more than 3 years before index.

^e Models for lipid values excluded 6 women (5 bilateral oophorectomy and 1 referent woman) who had hyperlipidemia more than 3 years before index.



Supplementary Figure 1. Smoothed curves of mean values predicted by generalized estimating equation (GEE) linear models for outpatient systolic and diastolic blood pressure, weight, and body mass index within three years before and ten years after bilateral oophorectomy or index date. The predicted mean values for the three years before the index date are shown in the shaded segment of each panel. The predicted values were adjusted by age at index, years of education, and cigarette smoking. Women with hypertension more than three years before the index date were excluded from the analyses for systolic and diastolic blood pressure.



Supplementary Figure 2. Smoothed curves of mean values predicted by generalized estimating equation (GEE) linear models for fasting lipid values within three years before and ten years after bilateral oophorectomy or index date. The predicted mean values for the three years before the index date are shown in the shaded segment of each panel. The predicted values were adjusted by age at index, years of education, and cigarette smoking. Women with hyperlipidemia more than three years before the index date were excluded from the analyses for the fasting lipids.