Case-Control Selection for BAA24:
Metabolomics of CHD in the WHI

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Eligible population:

All HT participants, having at least 250 uL of plasma EDTA at the baseline, were eligible for selection. Eligible OS participants included those selected for the BAA 22 study who met sample availability requirements and did not report history of any of the following conditions at baseline: MI, stroke, TIA, cardiac arrest, cardiac catheterization, CHF, carotid disease, and aortic aneurysm.

Case selection:

Within the HT, 738 of the 781 CHD cases, defined as those experiencing MI or CHD death occurring during the HT intervention period, had baseline samples available. Of these 738 cases, 145 white and African American cases who did not have prior CVD conditions at baseline, including MI, stroke, TIA, PTCA, CABG, cardiac arrest, CHF, carotid disease, and aortic aneurysm, were selected as cases for overlap between the BAA 23, 24 and 25 studies. In addition to the 145 of overlap cases, an additional 536 with biomarker data available were selected for this study. Of the 536, 405 had Year 1 samples available and CHD event after the Year 1 visit.

Within the OS, 400 cases were initially selected from the CHD cases previously selected for BAA 22. CHD cases who experienced a stroke before an MI or CHD death were excluded from selection. The cases included 124 non-white cases meeting the inclusion criteria and having controls available for matching. These 124 cases included 69 African American, 15 Hispanic, 5 American Indian, 15 Asian/Pacific Islander, and 20 Unknown/other race/ethnicity. The remaining 276 cases were randomly selected from the BAA 22 white cases, who met the inclusion criteria for this study.

Because not all of the HT cases had sample availability and biomarker data, an additional 109 cases were selected from the BAA 22 OS sample.

Control selection:

Controls for the 145 (139 white and 6 African American) HT overlapping sample between the three BAA studies were selected by frequency matching on 5 year age intervals, race/ethnicity, 2 year enrollment time intervals, and hysterectomy status. Controls with prior CVD conditions, including MI, stroke, TIA, PTCA, CABG, cardiac arrest, CHF, carotid disease, and aortic aneurysm, were excluded. The overlapping cases and controls were matched on hysterectomy status at baseline, but were not matched on HRT trial arm. Controls previously selected for the HT biomarker studies were given first priority for selection for the overlap sample.

The remaining 536 incident CHD cases from the HT intervention period with available samples and biomarkers measured in the HT CVD biomarker study, core study or W54/58 were

frequency matched to controls on 5 year age intervals, race/ethnicity, 2 year enrollment time intervals, prior CVD conditions, and HRT trial arm.

HT Cases/Controls:

	# with biomarkers	# with Yr 1 samples and biomarkers
All Cases	681	540
E+P	175	134
E+P placebo	140	113
E-alone	184	147
E-alone placebo	182	146
All Controls	681	532
E+P	176	132
E+P placebo	139	112
E-alone	179	139
E-alone placebo	187	149

Controls for the OS cases were selected from the BAA 22 subcohort by frequency matching on 5 year age intervals, race/ethnicity, 2 year enrollment year intervals, and hysterectomy status. Controls who later experienced the CHD outcome were excluded from potential selection, as were CHD cases selected for the BAA 22 subcohort. For the 13 cases that did not have exact matches on the matching factors, either the age interval or enrollment year interval was expanded.

Controls for the additional 109 OS cases were also frequency matched to controls in the BAA 22 subcohort on the same matching factors.

	OS (cases/controls)	HT (cases/controls)
White	385/385	569/569
Black	69/69	78/78
Asian	15/15	4/4
Hispanic	15/15	20/20
American Indian	5/5	2/2
Unknown	20/20	8/8