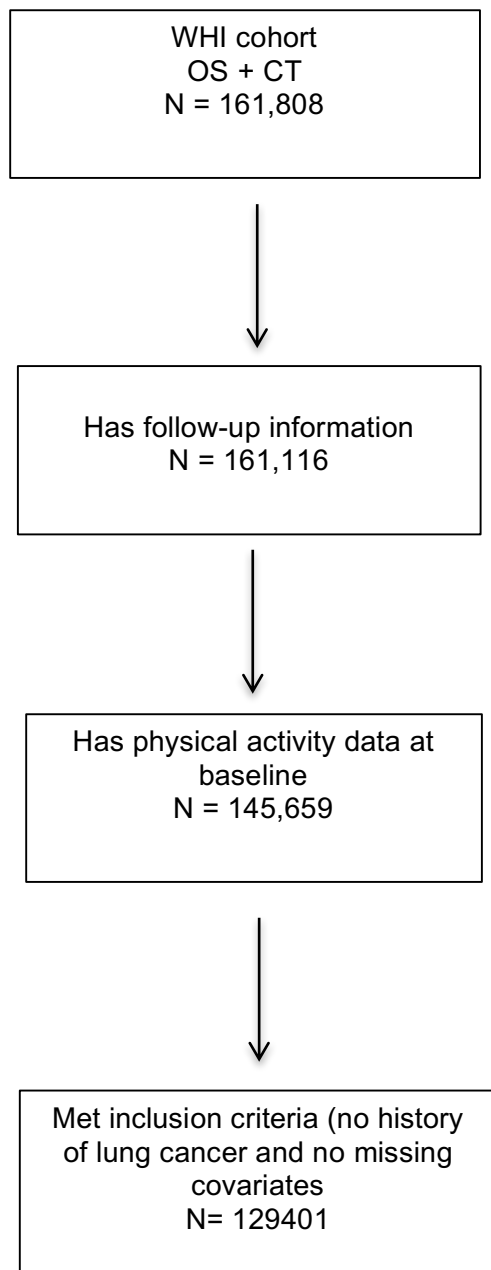


**SUPPLEMENTARY MATERIAL**

**SUPPLEMENTARY FIGURE 1. Analytic Cohort of WHI-OS+CT**

**Legend. Final analytic cohort size of the WHI OS+CT cohort for main analyses after exclusion criteria**



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**Supplementary Table 1: WHI-OS only, physical activity**

**Legend. Baseline characteristics of the WHI-OS only cohort for physical activity analyses**

Variable	Total physical activity in MET hours per week at baseline				p-value
	0-<100	100-<500	500-<1200	1200+	
<i>Total</i>	14632	20679	22868	19272	
<i>Age at baseline</i>					<.0001
<50-59	4890 33.42	6488 31.37	7134 31.20	6389 33.15	
60-69	6235 42.61	9006 43.55	10265 44.89	8715 45.22	
70-79+	3507 23.97	5185 25.07	5469 23.92	4168 21.63	
<i>Age at baseline</i>					<.0001
Age in years	63.39 7.44	63.72 7.41	63.67 7.28	63.19 7.22	
<i>Race/ethnicity</i>					<.0001
American Indian or Alaskan Native	77 0.53	82 0.40	65 0.28	70 0.36	
Asian or Pacific Islander	438 2.99	607 2.94	666 2.91	577 2.99	
Black or African-American	1560 10.66	1658 8.02	1275 5.58	938 4.87	
Hispanic/Latino	633 4.33	763 3.69	569 2.49	496 2.57	
White (not of Hispanic origin)	11755 80.34	17336 83.83	20065 87.74	16997 88.20	
Other	169 1.16	233 1.13	228 1.00	194 1.01	
<i>BMI at baseline</i>					<.0001
<25	4032 27.56	7502 36.28	10291 45.00	10281 53.35	
25-<30	4752 32.48	7254 35.08	7949 34.76	6323 32.81	
30+	5848 39.97	5923 28.64	4628 20.24	2668 13.84	
<i>BMI at baseline</i>					<.0001
BMI	29.53 6.85	27.75 5.89	26.53 5.27	25.54 4.75	
<i>Education</i>					<.0001

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Primary	328	309	192	139
	2.24	1.49	0.84	0.72
Some HS	764	768	488	376
	5.22	3.71	2.13	1.95
HS	3280	3723	3294	2229
	22.42	18.00	14.40	11.57
Some college	5691	7833	8103	6547
	38.89	37.88	35.43	33.97
College	1343	2228	2897	2588
	9.18	10.77	12.67	13.43
Graduate	3226	5818	7894	7393
	22.05	28.13	34.52	38.36
<i>History of cancer</i>				0.0004
No history of cancer	12687	17991	20049	16967
	86.71	87.00	87.67	88.04
History of cancer	1945	2688	2819	2305
	13.29	13.00	12.33	11.96
<i>History of asthma</i>				<.0001
No history of asthma	13242	19100	21143	17880
	90.50	92.36	92.46	92.78
History of asthma	1390	1579	1725	1392
	9.50	7.64	7.54	7.22
<i>History of emphysema or chronic bronchitis</i>				<.0001
No history of emphysema or chronic bronchitis	13793	19864	22136	18739
	94.27	96.06	96.80	97.23
History of emphysema or chronic bronchitis	839	815	732	533
	5.73	3.94	3.20	2.77
<i>Vitamin D from diet and supplements at baseline</i>				<.0001
<400 IU	8720	11425	11375	9184
	59.60	55.25	49.74	47.65
>=400 IU	5912	9254	11493	10088
	40.40	44.75	50.26	52.35
<i>Main occupation (Missing N=2591)</i>				<.0001

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Managerial / Professional	4998 35.57	8294 41.51	10440 47.14	9345 50.03	
Technical / Sales / Admin	4610 32.81	6198 31.02	6118 27.62	4631 24.80	
Service / Labor	2890 20.57	3456 17.30	3366 15.20	2815 15.07	
Homemaker only	1554 11.06	2034 10.18	2225 10.05	1886 10.10	
<i>Alcohol consumption at baseline</i>					<.0001
Non drinker	2176 14.87	2589 12.52	2306 10.08	1480 7.68	
Past drinker	3523 24.08	4092 19.79	3651 15.97	2923 15.17	
<1 drink per month	2188 14.95	2565 12.40	2611 11.42	1797 9.32	
<1 drink per week	2806 19.18	4264 20.62	4710 20.60	3896 20.22	
1 to <7 drinks per week	2578 17.62	4969 24.03	6447 28.19	6094 31.62	
7+ drinks per week	1361 9.30	2200 10.64	3143 13.74	3082 15.99	
<i>Smoking status</i>					<.0001
Never smoker	7619 52.07	11150 53.92	11863 51.88	9629 49.96	
Former smoker, ≤3 cigarettes/day	2846 19.45	4430 21.42	5525 24.16	5000 25.94	
Former smoker, 4-7 cigarettes/day	2716 18.56	3588 17.35	4354 19.04	3889 20.18	
Current smoker	1451 9.92	1511 7.31	1126 4.92	754 3.91	
<i>Red meat consumption at baseline</i>					<.0001
Servings/day	0.74 0.68	0.64 0.56	0.56 0.51	0.49 0.47	
<i>Fruit consumption at baseline</i>					<.0001
Servings/day	1.61 1.19	1.91 1.24	2.14 1.25	2.37 1.34	
<i>Vegetable consumption at baseline</i>					<.0001
Servings/day	1.85 1.17	2.14 1.26	2.36 1.32	2.65 1.45	

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<i>Hormone therapy use at baseline</i>					<i>&lt;.0001</i>
Never used	6402 43.75	8653 41.84	8706 38.07	7091 36.79	
Past user	2219 15.17	3105 15.02	3380 14.78	2760 14.32	
Current user	6011 41.08	8921 43.14	10782 47.15	9421 48.88	
<i>Oral contraceptive use ever at baseline</i>					<i>&lt;.0001</i>
No	8815 60.24	12509 60.49	13449 58.81	10989 57.02	
Yes	5817 39.76	8170 39.51	9419 41.19	8283 42.98	
<i>Incident lung cancer during main trial</i>					<i>&lt;.0001</i>
No	14322 97.88	20348 98.40	22517 98.47	18962 98.39	
Yes	310 2.12	331 1.60	351 1.53	310 1.61	
<i>Death during main trial</i>					<i>&lt;.0001</i>
No	12411 84.82	18047 87.27	20403 89.22	17470 90.65	
Yes	2221 15.18	2632 12.73	2466 10.78	1802 9.35	
<i>Death due to lung cancer after lung cancer diagnosis during main trial</i>					<i>&lt;.0001</i>
No	14414 98.51	20474 99.01	22673 99.15	19095 99.08	
Yes	218 1.49	205 0.99	195 0.85	177 0.92	
<i>HT Trial Arm</i>					
Not randomized to HRT	14632	20679	22868	19272	
<i>CaD Trial Arm</i>					
Not randomized to CaD	14632	20679	22868	19272	
<i>DM Trial Arm</i>					
Not randomized to DM	14632	20679	22868	19272	

Note: WHI Cohort N=161808 → OS only N=93676 → Has follow-up data N=93205 → Has physical activity data at baseline N=87407 → meet inclusion criteria (no history of lung cancer and no missing covariates) N=77451

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**Supplementary Table 2: WHI-OS only, sedentary behavior**

**Legend: Baseline characteristics of the WHI-OS only cohort for sedentary behavior analyses**

Variable	Sedentary behavior in sitting hours per day at baseline			p-value
	0-5	6-<10	>=10	
<i>Total</i>	27738	33044	19799	
<i>Age at baseline</i>				<.0001
<50-59	7672 27.66	9340 28.27	8724 44.06	
60-69	12846 46.31	14982 45.34	7738 39.08	
70-79+	7220 26.03	8722 26.40	3337 16.85	
<i>Age at baseline</i>				<.0001
Age in years	64.24 7.17	64.20 7.26	61.53 7.36	
<i>Race/ethnicity</i>				<.0001
American Indian or Alaskan Native	142 0.51	115 0.35	67 0.34	
Asian or Pacific Islander	766 2.76	974 2.95	655 3.31	
Black or African-American	2434 8.77	2107 6.38	1524 7.70	
Hispanic/Latino	1406 5.07	862 2.61	502 2.54	
White (not of Hispanic origin)	22656 81.68	28632 86.65	16871 85.21	
Other	334 1.20	354 1.07	180 0.91	
<i>BMI at baseline</i>				<.0001
<25	12278 44.26	13639 41.28	7294 36.84	
25-<30	9620 34.68	11340 34.32	6409 32.37	
30+	5840 21.05	8065 24.41	6096 30.79	
<i>BMI at baseline</i>				<.0001
BMI	26.60 5.32	27.16 5.71	28.14 6.52	
<i>Education</i>				<.0001

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Primary	662 2.39	327 0.99	132 0.67	
Some HS	1296 4.67	978 2.96	391 1.97	
HS	4926 17.76	5451 16.50	2763 13.96	
Some college	10439 37.63	11931 36.11	7079 35.75	
College	3067 11.06	3876 11.73	2399 12.12	
Graduate	7348 26.49	10481 31.72	7035 35.53	
<i>History of cancer</i>				0.301
No history of cancer	24307 87.63	28820 87.22	17318 87.47	
History of cancer	3431 12.37	4224 12.78	2481 12.53	
<i>History of asthma</i>				<.0001
No history of asthma	25769 92.90	30472 92.22	18015 90.99	
History of asthma	1969 7.10	2572 7.78	1784 9.01	
<i>History of emphysema or chronic bronchitis</i>				0.002
No history of emphysema or chronic bronchitis	26758 96.47	31805 96.25	18975 95.84	
History of emphysema or chronic bronchitis	980 3.53	1239 3.75	824 4.16	
<i>Vitamin D from diet and supplements at baseline</i>				<.0001
<400 IU	15019 54.15	17005 51.46	10610 53.59	
>=400 IU	12719 45.85	16039 48.54	9189 46.41	
<i>Main occupation (Missing N=2837)</i>				<.0001

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Managerial / Professional	10438 39.25	14141 44.29	9358 48.68
Technical / Sales / Admin	6719 25.26	9164 28.70	6484 33.73
Service / Labor	5793 21.78	5142 16.11	2308 12.01
Homemaker only	3646 13.71	3478 10.89	1073 5.58
<i>Alcohol consumption at baseline</i>			<.0001
Non drinker	3895 14.04	3458 10.46	1710 8.64
Past drinker	5309 19.14	5925 17.93	3745 18.92
<1 drink per month	2970 10.71	3871 11.71	2634 13.30
<1 drink per week	5354 19.30	6695 20.26	4169 21.06
1 to <7 drinks per week	6879 24.80	8790 26.60	5092 25.72
7+ drinks per week	3331 12.01	4305 13.03	2449 12.37
<i>Smoking status</i>			<.0001
Never smoker	15268 55.04	17239 52.17	9478 47.87
Former smoker, ≤3 cigarettes/day	6652 23.98	7673 23.22	4235 21.39
Former smoker, 4-7 cigarettes/day	4253 15.33	6132 18.56	4611 23.29
Current smoker	1565 5.64	2000 6.05	1475 7.45
<i>Red meat consumption at baseline</i>			<.0001
Servings/day	0.56 0.56	0.60 0.53	0.64 0.61
<i>Fruit consumption at baseline</i>			<.0001
Servings/day	2.06 1.33	2.05 1.27	1.95 1.27
<i>Vegetable consumption at baseline</i>			<.0001
Servings/day	2.30 1.40	2.30 1.32	2.17 1.30



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<i>Hormone therapy use at baseline</i>			<.0001
Never used	11278 40.66	13376 40.48	7647 38.62
Past user	4177 15.06	5027 15.21	2758 13.93
Current user	12283 44.28	14641 44.31	9394 47.45
<i>Oral contraceptive use ever at baseline</i>			<.0001
No	17339 62.51	20055 60.69	10504 53.05
Yes	10399 37.49	12989 39.31	9295 46.95
<i>Incident lung cancer during main trial</i>			0.002
No	27339 98.56	32473 98.27	19440 98.19
Yes	399 1.44	571 1.73	359 1.81
<i>Death during main trial</i>			0.0001
No	24650 88.87	29008 87.79	17431 88.04
Yes	3088 11.13	4036 12.21	2368 11.96
<i>Death due to lung cancer after lung cancer diagnosis during main trial</i>			0.003
No	27504 99.16	32687 98.92	19576 98.87
Yes	234 0.84	357 1.08	223 1.13
<i>HT Trial Arm</i>			
Not randomized to HRT	27738	33044	19799
<i>CaD Trial Arm</i>			
Not randomized to CaD	27738	33044	19799
<i>DM Trial Arm</i>			
Not randomized to DM	27738	33044	19799

Note: WHI Cohort N=161808 → OS only N=93676 → Has follow-up data N=93205 → Has siting time data at baseline N=92361 → meet inclusion criteria (no history of lung cancer and no missing covariates) N=80581

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**Supplementary Table 3. Sensitivity Analysis with Smoking Status and Pack Years smoked - Cox Proportional Hazards Model of Time to Lung Cancer Incidence According to Amount of Current (Study Entry Physical Activity and Sedentary Behavior)**

Incident lung cancer, current (study entry) total physical activity (MET-min/wk)

MET minutes per week	No. of cases	Unadjusted model		Adjusted model*	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
0 - <100	581	Ref.	<0.0001	Ref.	0.072
100 - <500	588	0.76 (0.68 – 0.85)		0.89 (0.79 – 0.99)	
500 - <1200	535	0.68 (0.60 – 0.76)		0.87 (0.77 – 0.98)	
1200+	444	0.72 (0.63 – 0.81)		0.95 (0.83 – 1.09)	

Incident lung cancer, current (study entry) strenuous physical activity (MET-min/wk)

MET minutes per week	No. of cases	Unadjusted model		Adjusted model*	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
0 - <100	1675	Ref.	0.049	Ref.	0.162
100 - <500	155	0.83 (0.70 – 0.98)		1.01 (0.85 – 1.19)	
500 - <1200	187	0.87 (0.75 – 1.02)		1.06 (0.91 – 1.24)	
1200+	131	1.02 (0.86 – 1.22)		1.23 (1.02 – 1.47)	

Incident lung cancer, current (study entry) moderate physical activity (MET-min/wk)

MET minutes per week	No. of cases	Unadjusted model		Adjusted model*	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
0 - <100	1388	Ref.	<0.0001	Ref.	0.040
100 - <500	519	0.85 (0.77 – 0.94)		1.01 (0.91 – 1.12)	
500 - <1200	185	0.76 (0.65 – 0.89)		0.85 (0.73 – 1.00)	
1200+	56	1.18 (0.90 – 1.54)		1.30 (0.99 – 1.70)	

Incident lung cancer, current (study entry) mild physical activity (MET-min/wk)

MET minutes per week	No. of cases	Unadjusted model		Adjusted model*	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
0 - <100	1702	Ref.	0.742	Ref.	0.751
100 - <500	348	0.96 (0.86 – 1.08)		0.97 (0.86 – 1.08)	
500 - <1200	84	1.08 (0.86 – 1.34)		0.95 (0.76 – 1.19)	
1200+	14	0.86 (0.51 – 1.45)		0.79 (0.47 – 1.34)	

Incident lung cancer, current (study entry) sedentary behavior (sitting hrs/day)

Sitting Time (hours/day)	No. of cases	Unadjusted model		Adjusted model**	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
<=5	399	Ref.	0.017	Ref.	0.610
6 - <10	571	1.17 (1.03 – 1.33)		1.07 (0.94 – 1.22)	
>=10	359	1.21 (1.05 – 1.39)		1.04 (0.90 – 1.20)	

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\*\*All sedentary behavior adjusted models are adjusted for age, race/ethnicity, BMI, family history of cancer, personal history of cancer, history of asthma, history of emphysema or chronic bronchitis, smoking status, pack years smoked, education, alcohol intake, vitamin D use, hormone therapy, oral contraceptive use, hysterectomy status, NSAID use, servings of fruit, vegetables and red meat

Note: Please note that the women in the cohorts used for the sensitivity analyses are different from the cohorts used in the main analyses. The reason is due to the use of two different variables in the sensitivity analyses—smoking status and pack years smoked instead of the collapsed smoking categories that were used originally. Because the sensitivity analyses were also based on complete cases, any women with missing data on smoking status or pack years were excluded. The N for the combined CT + OS cohort is 129,401, and the N for the OS cohort is 80,581.

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**Supplementary Table 4. Sensitivity Analysis with Smoking Status and Pack Years smoked - Cox Proportional Hazards Model of Time to Lung Cancer Mortality According to Amount of Current (Study Entry) Physical Activity and Sedentary Behavior**

MET minutes per week	No. of cases	Unadjusted model		Adjusted model*	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
0 - <100	412	Ref.	<0.0001	Ref.	0.0008
100 - <500	382	0.70 (0.61 – 0.80)		0.83 (0.72 – 0.95)	
500 - <1200	308	0.55 (0.47 – 0.64)		0.73 (0.62 – 0.85)	
1200+	263	0.60 (0.51 – 0.70)		0.83 (0.70 – 0.98)	

Lung cancer mortality, current (study entry) strenuous physical activity (MET-min/wk)

MET minutes per week	No. of cases	Unadjusted model		Adjusted model*	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
0 - <100	1102	Ref.	<0.0001	Ref.	0.093
100 - <500	87	0.70 (0.57 – 0.88)		0.88 (0.71 – 1.10)	
500 - <1200	95	0.67 (0.55 – 0.83)		0.86 (0.69 – 1.06)	
1200+	81	0.96 (0.77 – 1.20)		1.21 (0.96 – 1.52)	

Lung cancer mortality, current (study entry) moderate physical activity (MET-min/wk)

MET minutes per week	No. of cases	Unadjusted model		Adjusted model*	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
0 - <100	922	Ref.	<0.0001	Ref.	0.006
100 - <500	301	0.74 (0.65 – 0.85)		0.91 (0.80 – 1.04)	
500 - <1200	105	0.65 (0.53 – 0.80)		0.75 (0.61 – 0.92)	
1200+	37	1.17 (0.84 – 1.62)		1.33 (0.95 – 1.85)	

Lung cancer mortality, current (study entry) mild physical activity (MET-min/wk)

MET minutes per week	No. of cases	Unadjusted model		Adjusted model*	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
0 - <100	1081	Ref.	0.955	Ref.	0.907
100 - <500	222	0.97 (0.84 – 1.12)		0.98 (0.85 – 1.13)	
500 - <1200	51	1.03 (0.77 – 1.36)		0.90 (0.68 – 1.20)	
1200+	11	1.06 (0.59 – 1.92)		0.99 (0.55 – 1.80)	

Lung cancer mortality, current (study entry) sedentary behavior (sitting hrs/day)

Sitting Time (hours/day)	No. of cases	Unadjusted model		Adjusted model**	
		HR (95% CI)	Global p-value	HR (95% CI)	Global p-value
<=5	234	Ref.	0.013	Ref.	0.413
6 - <10	357	1.25 (1.06 – 1.47)		1.12 (0.95 – 1.32)	
>=10	223	1.27 (1.06 – 1.53)		1.08 (0.89 – 1.30)	