

Supplement 1

(Major Supplementary Tables)

Genetic Risk, Health-Associated Lifestyle, and Risk of Early-onset Total Cancer and Breast Cancer

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eTable 1

List of published cancer site-specific PRSs included in the lasso regression in females, and list of cancer site-specific PRSs selected from the lasso regression for the development of the female-specific composite total cancer PRS

eTable 2

List of published cancer site-specific PRSs included in the lasso regression in males, and list of cancer site-specific PRSs selected from the lasso regression for the development of the male-specific composite total cancer PRS

eTable 3

Summary of early-onset cancer spectrum in females and males, showcasing cancers with published site-specific PRSs qualified for inclusion in the lasso regression.

eTable 4

Components of female-specific HLS and male-specific HLS

eTable 5

Characteristics of female participants (N=34383) at baseline according to breast cancer PRS

eTable 6

Characteristics of female participants (N=34383) at baseline according to female-specific HLS

eTable 7

Characteristics of male participants (N=31925) at baseline according to male-specific HLS

eTable 1. List of published cancer site-specific PRSs included in the lasso regression in females, and list of cancer site-specific PRSs selected from the lasso regression for the development of the female-specific composite total cancer PRS

Cancer Types	Polygenic Score ID & Name (PGS catalog) included in the lasso regression ^a	Number of SNPs	Publication	PMID	Selected from the lasso regression
Breast	<u>PGS000004 (PRS313_BC)</u> ^b	313	<u>Mavaddat N et al. Am J Hum Genet (2018)</u>	30554720	Yes
Melanoma	<u>PGS000790 (CC_Melanoma_IV)</u>	24	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Colorectum *	<u>PGS002252 (PRS_CRC)</u>	141	<u>Archambault AN et al. J Natl Cancer Inst (2022)</u> <u>Huyghe JR et al. Nat Genet (2019)</u>	35026030 30510241	No
Non-Hodgkin lymphoma	<u>PGS000791 (CC_NHL_IV)</u>	19	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Ovary	<u>PGS003394 (PRS_Stepwise)</u>	36	<u>Dareng EO et al. Eur J Hum Genet (2022)</u>	35027648	No
Brain *	<u>PGS000624 (PRSWEB_PHECODE191.11_GWAS-Catalog-r2019-05-03-X191.11_PT_UKB_20200608)</u>	5	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	No
Head and neck	<u>PGS000792 (CC_Oral_IV)</u>	14	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Lung	<u>PGS000740 (PRS128_LC)</u>	128	<u>Hung RJ et al. Cancer Res (2021)</u>	33472890	Yes
Endometrium	<u>PGS000786 (CC_Endo_IV)</u>	9	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Thyroid	<u>PGS000797 (CC_Thyroid_IV)</u>	12	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Kidney	<u>PGS000787 (CC_Kidney_IV)</u>	19	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Multiple myeloma *	<u>PGS000653 (PRSWEB_PHECODE204.4_GWAS-Catalog-r2019-05-03-X204.4_P_5e-08_UKB_20200608)</u>	22	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	Yes
Cervix	<u>PGS000784 (CC_Cervix_IV)</u>	10	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No

Pancreas	<u>PGS000794 (CC_Pancreas_IV)</u>	22	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Stomach	<u>PGS002299 (PRS3_gastric)</u>	3	<u>Choi J et al. Int J Cancer (2020)</u> <u>Helgason et al. Nat Genet (2015)</u>	32588423 26098866	Yes
Lymphoid leukemia	<u>PGS000788 (CC_LL_IV)</u>	75	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Esophagus	<u>PGS000364 (PRSWEB_PHECODE150_C15_LASSOSUM_MGI_20200608)</u>	2001	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	No
Hodgkin's lymphoma	<u>PGS000639 (PRSWEB_PHECODE201_GWAS-Catalog-r2019-05-03-X201_PT_MGI_20200608)</u>	20	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	No
Trachea *	<u>PGS000392 (PRSWEB_PHECODE165.1_GWAS-Catalog-r2019-05-03-X165.1_PT_UKB_20200608)</u>	19	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	No

Abbreviations: PRS, polygenic risk score; GRCh37, Genome Reference Consortium Human Build 37.

^a Published cancer site-specific PRSs included in the lasso regression were selected based on their training sample size, developing methods, test-set performance, possibility of overfit (i.e. training sample should not include UK Biobank), and the availability of SNPs and weights.

^b PGS000004 (PRS313_BC) was used specifically in analyses of breast cancer PRS and early-onset breast cancer among females.

* UK Biobank was included in the training set.

eTable 2. List of published cancer site-specific PRSs included in the lasso regression in males, and list of cancer site-specific PRSs selected from the lasso regression for the development of the male-specific composite total cancer PRS

Cancer Types	Polygenic Score ID & Name (PGS catalog) included in the lasso regression ^a	Number of SNPs	Publication	PMID	Selected from the lasso regression
Breast	<u>PGS000004 (PRS313_BC)</u> ^b	313	<u>Mavaddat N et al. Am J Hum Genet (2018)</u>	30554720	No
Melanoma	<u>PGS000790 (CC_Melanoma_IV)</u>	24	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	Yes
Colorectum *	<u>PGS002252 (PRS_CRC)</u>	141	<u>Archambault AN et al. J Natl Cancer Inst (2022)</u> <u>Huyghe JR et al. Nat Genet (2019)</u>	35026030 30510241	No
Non-Hodgkin lymphoma	<u>PGS000791 (CC_NHL_IV)</u>	19	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Prostate	<u>PGS000662 (GRS.PCa.269)</u>	269	<u>Conti DV et al. Nat Genet (2021)</u>	33398198	No
Brain *	<u>PGS000624 (PRSWEB_PHECODE191.11_GWAS-Catalog-r2019-05-03-X191.11_PT_UKB_20200608)</u>	5	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	No
Head and neck	<u>PGS000792 (CC_Oral_IV)</u>	14	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Lung	<u>PGS000740 (PRS128_LC)</u>	128	<u>Hung RJ et al. Cancer Res (2021)</u>	33472890	Yes
Testis	<u>PGS000796 (CC_Testis_IV)</u>	52	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Thyroid	<u>PGS000797 (CC_Thyroid_IV)</u>	12	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Kidney	<u>PGS000787 (CC_Kidney_IV)</u>	19	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	Yes
Multiple myeloma *	<u>PGS000653 (PRSWEB_PHECODE204.4_GWAS-Catalog-r2019-05-03-X204.4_P_5e-08_UKB_20200608)</u>	22	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	No
Pancreas	<u>PGS000794 (CC_Pancreas_IV)</u>	22	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	Yes
Stomach	<u>PGS002299 (PRS3_gastric)</u>	3	<u>Choi J et al. Int J Cancer (2020)</u>	32588423 26098866	No

			<u>Helgason et al. Nat Genet (2015)</u>		
Lymphoid leukemia	<u>PGS000788 (CC LL IV)</u>	75	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Bladder	<u>PGS000782 (CC Bladder IV)</u>	15	<u>Kachuri L et al. Nat Commun (2020)</u>	33247094	No
Esophagus	<u>PGS000364 (PRSWEB_PHECODE150_C15_LASSOSUM_MGI_20200608)</u>	2001	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	No
Hodgkin's lymphoma	<u>PGS000639 (PRSWEB_PHECODE201_GWAS-Catalog-r2019-05-03-X201_PT_MGI_20200608)</u>	20	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	No
Larynx	<u>PGS000362 (PRSWEB_PHECODE149.4_UKBB-SAIGE-HRC-X149.4_PT_MGI_20200608)</u>	53	<u>Fritsche LG et al. Am J Hum Genet (2020)</u>	32991828	No

Abbreviations: PRS, polygenic risk score; GRCh37, Genome Reference Consortium Human Build 37.

^a Published cancer site-specific PRSs included in the lasso regression were selected based on their training sample size, developing methods, test-set performance, possibility of overfit (i.e. training sample should not include UK Biobank), and the availability of SNPs and weights.

^b Breast cancer PRS was included in the lasso regression in males because there was one case of early-onset breast cancer documented in males.

* UK Biobank was included in the training set.

eTable 3. Summary of early-onset cancer spectrum in females and males, showcasing cancers with published site-specific PRSs qualified for inclusion in the lasso regression

Cancer Types with Published Site-specific PRSs qualified for inclusion in the lasso regression	Number of Cases (jn females)	Number of Cases (in males)	Number of Cases (in the total study population)
Breast	386	1	387
Melanoma	60	36	96
Colorectum	23	28	51
Brain	11	19	30
Non-Hodgkin lymphoma	7	22	29
Prostate	0	28	28
Ovary	27	0	27
Testis	0	22	22
Kidney	7	9	16
Head and neck	7	9	16
Lung	8	7	15
Endometrium	12	0	12
Thyroid	9	3	12
Multiple myeloma	4	8	12
Lymphoid leukemia	4	5	9
Cervix	8	0	8
Pancreas	5	3	8
Stomach	2	5	7
Bladder	0	6	6
Esophagus	1	2	3
Hodgkin's lymphoma	2	1	3
Larynx	0	3	3
Trachea	1	0	1
Sum	584	217	801
Others	236	210	446
Total	820	427	1,247

eTable 4. Components of female-specific HLS and male-specific HLS

Components	Categories	Score assignments
Smoking status	Current smoker Others	Smoking score 1 for current smoker 0 for others
BMI (males only) ^a	18.5≤ to <25 kg/m ² Others	BMI score 0 for 18.5≤ to <25 kg/m ² 1 for others
Physical activity	Met the guidelines ^b Didn't meet the guidelines ^b	Physical activity score 0 for met the guidelines ^b 1 for didn't meet the guidelines ^b
Alcohol consumption	Never Others	Alcohol intake score 0 for never 1 for others
Diet	<p>Fruit and vegetable intake <3 servings/day ≥3 to <5 servings/day ≥5 servings/day</p> <p><i>*Amount per serving:</i> Fresh fruit: 1 piece Dried fruit: 5 pieces Cooked vegetables: 3 heaped tablespoons Salad/raw vegetables: 3 heaped tablespoons</p> <p>Whole grain intake <2 servings/day ≥2 to <5.5 servings/day ≥5.5 servings/day</p> <p><i>*Amount per serving:</i> Cereal: 1 bowl Whole-meal bread: 1 slice Whole-grain bread: 1 slice</p>	<p>Fruit and vegetable intake 1 for <3 servings/day 0.5 for ≥3 to <5 servings/day 0 for ≥5 servings/day</p> <p>Whole grain intake 1 for <2 servings/day 0.5 for ≥2 to <5.5 servings/day 0 for ≥5.5 servings/day</p> <p>Red and processed meat intake 1 for ≥4 times/week 0.5 for ≥2 to <4 times/week 0 for <2 times/week</p> <p>Diet score (Fruit and vegetable intake score + Whole grain intake score + Red and processed meat intake score) / 3 1 for ≥0.5</p>

	<i>Brown bread: 1 slice</i> <i>Red and processed meat intake</i> ≥ 4 times/week ≥ 2 to < 4 times/week < 2 times/week	0 for < 0.5
Total Score		
<u>Female-specific HLS</u> = <i>Smoking score</i> + <i>Physical activity score</i> + <i>Alcohol intake score</i> + <i>Diet score</i> Ranging from 0 to 4, with higher scores indicating an unhealthier lifestyle. Healthy: 0 to 1 Intermediate: 2 to 3 Unhealthy: 4	<u>Male-specific HLS</u> = <i>Smoking score</i> + <i>BMI score</i> + <i>Physical activity score</i> + <i>Alcohol intake score</i> + <i>Diet score</i> Ranging from 0 to 5, with higher scores indicating an unhealthier lifestyle. Healthy: 0 to 1 Intermediate: 2 to 3 Unhealthy: 4 to 5	

Abbreviations: HLS, health-associated lifestyle score; BMI, body mass index.

^a BMI was not included as a component of female-specific HLS due to the widely recognized inverse association of BMI with the risk of early-onset/premenopausal breast cancer and the fact that early-onset total cancer in females was predominantly driven by early-onset breast cancer.

^b Met the guidelines of 150 minutes of moderate activity per week or 75 minutes of vigorous activity (or an equivalent combination).

eTable 5. Characteristics of female participants (N=34383) at baseline according to breast cancer PRS

Characteristics ^{a,b}	Breast Cancer PRS		
	Low (N=11428)	Intermediate (N=11481)	High (N=11474)
Age, mean (SD)	45.0 (2.72)	45.0 (2.73)	45.0 (2.72)
Female-specific HLS, n (%)			
Healthy	2557 (22.4%)	2504 (21.8%)	2527 (22.0%)
Intermediate	8468 (74.1%)	8524 (74.2%)	8474 (73.9%)
Unhealthy	403 (3.5%)	453 (3.9%)	473 (4.1%)
Smoking, n (%)			
Current smoker	1201 (10.5%)	1214 (10.6%)	1230 (10.7%)
Others	10227 (89.5%)	10267 (89.4%)	10244 (89.3%)
BMI, n (%)			
18.5≤ to <25 kg/m ²	5424 (47.5%)	5503 (47.9%)	5535 (48.2%)
Others	6004 (52.5%)	5978 (52.1%)	5939 (51.8%)
Physical activity, n (%)			
Met the guidelines ^c	5875 (51.4%)	5930 (51.7%)	5811 (50.6%)
Didn't meet the guidelines	5553 (48.6%)	5551 (48.3%)	5663 (49.4%)
Alcohol intake, n (%)			
Never	633 (5.5%)	591 (5.1%)	555 (4.8%)
Special occasions only	1253 (11.0%)	1322 (11.5%)	1232 (10.7%)
One to three times a month	1725 (15.1%)	1687 (14.7%)	1769 (15.4%)
Once or twice a week	3418 (29.9%)	3431 (29.9%)	3519 (30.7%)
Three or four times a week	2831 (24.8%)	2793 (24.3%)	2749 (24.0%)
Daily or almost daily	1568 (13.7%)	1657 (14.4%)	1650 (14.4%)
Fruit and vegetable intake, n (%)			
<3 servings/day	3933 (34.4%)	4157 (36.2%)	3987 (34.7%)
≥3 to <5 servings/day	4959 (43.4%)	4892 (42.6%)	5046 (44.0%)
≥5 servings/day	2536 (22.2%)	2432 (21.2%)	2441 (21.3%)
Whole grain intake, n (%)			
<2 servings/day	7273 (63.6%)	7343 (64.0%)	7277 (63.4%)
≥2 to <5.5 servings/day	4114 (36.0%)	4099 (35.7%)	4156 (36.2%)
≥5.5 servings/day	41 (0.4%)	39 (0.3%)	41 (0.4%)
Red and processed meat intake, n (%)			
<2 times/week	2344 (20.5%)	2310 (20.1%)	2312 (20.2%)
≥2 to <4 times/week	5463 (47.8%)	5437 (47.4%)	5394 (47.0%)
≥4 times/week	3621 (31.7%)	3734 (32.5%)	3768 (32.8%)
Average total household income, n (%)			
Less than 18,000	1177 (10.3%)	1172 (10.2%)	1239 (10.8%)
18,000 to 30,999	1888 (16.5%)	1922 (16.7%)	1923 (16.8%)
31,000 to 51,999	3361 (29.4%)	3303 (28.8%)	3339 (29.1%)
52,000 to 100,000	3311 (29.0%)	3361 (29.3%)	3284 (28.6%)
Greater than 100,000	926 (8.1%)	923 (8.0%)	900 (7.8%)
Prefer not to answer or do not know	765 (6.7%)	800 (7.0%)	789 (6.9%)
Family history of breast cancer, n (%)			
No	10583 (92.6%)	10315 (89.8%)	10092 (88.0%)
Yes	845 (7.4%)	1166 (10.2%)	1382 (12.0%)
Education, n (%)			
College or University degree	4649 (40.7%)	4702 (41.0%)	4660 (40.6%)

Some professional qualifications	293 (2.6%)	305 (2.7%)	309 (2.7%)
Secondary education	6124 (53.6%)	6148 (53.5%)	6193 (54.0%)
Others	336 (2.9%)	302 (2.6%)	283 (2.5%)
Prefer not to answer	26 (0.2%)	24 (0.2%)	29 (0.3%)
Age at menarche, n (%)			
<12 years of age	1937 (16.9%)	1983 (17.3%)	1986 (17.3%)
12 to 13 years of age	5050 (44.2%)	5060 (44.1%)	5047 (44.0%)
≥14 years of age	4180 (36.6%)	4172 (36.3%)	4167 (36.3%)
Prefer not to answer or do not know	261 (2.3%)	266 (2.3%)	274 (2.4%)
Parity, n (%)			
Nulliparous	3059 (26.8%)	3026 (26.4%)	3111 (27.1%)
Parous	8366 (73.2%)	8453 (73.6%)	8359 (72.9%)
Prefer not to answer or do not know	3 (0.0%)	2 (0.0%)	4 (0.0%)
Age at first live birth, n (%)			
<25 years of age	2004 (17.5%)	2027 (17.7%)	1959 (17.1%)
25 to 29 years of age	2508 (21.9%)	2564 (22.3%)	2526 (22.0%)
≥30 years of age	2048 (17.9%)	2068 (18.0%)	2104 (18.3%)
Prefer not to answer or do not know	4868 (42.6%)	4822 (42.0%)	4885 (42.6%)
Oral contraceptive use, n (%)			
Yes	10473 (91.6%)	10595 (92.3%)	10569 (92.1%)
No	939 (8.2%)	878 (7.6%)	897 (7.8%)
Prefer not to answer or do not know	16 (0.1%)	8 (0.1%)	8 (0.1%)
Menopausal status and hormone replacement therapy use, n (%)			
Postmenopausal (with hormone replacement therapy)	266 (2.3%)	264 (2.3%)	254 (2.2%)
Postmenopausal (without hormone replacement therapy)	504 (4.4%)	512 (4.5%)	482 (4.2%)
Premenopausal	10641 (93.1%)	10687 (93.1%)	10723 (93.5%)
Prefer not to answer or do not know	17 (0.1%)	18 (0.2%)	15 (0.1%)
History of mammograms, n (%)			
Yes	2799 (24.5%)	2954 (25.7%)	3132 (27.3%)
No	8592 (75.2%)	8490 (73.9%)	8303 (72.4%)
Prefer not to answer or do not know	37 (0.3%)	37 (0.3%)	39 (0.3%)

Abbreviations: PRS, polygenic risk score; HLS, health-associated lifestyle score; SD, standard deviation.

^a Characteristics of eligible female participants.

^b Mean (SD) for continuous variables and n (%) for categorical variables.

^c Met the guidelines of 150 minutes of moderate activity per week or 75 minutes of vigorous activity (or an equivalent combination).

eTable 6. Characteristics of female participants (N=34383) at baseline according to female-specific HLS

Characteristics ^{a,b}	Female-specific HLS		
	Healthy (N=7588)	Intermediate (N=25466)	Unhealthy (N=1329)
Age, mean (SD)	45.0 (2.72)	45.0 (2.72)	45.0 (2.70)
Female-specific Total Cancer PRS, n (%)			
Low	2566 (33.8%)	8462 (33.2%)	416 (31.3%)
Intermediate	2515 (33.1%)	8527 (33.5%)	434 (32.7%)
High	2507 (33.0%)	8477 (33.3%)	479 (36.0%)
Smoking, n (%)			
Current smoker	36 (0.5%)	2280 (9.0%)	1329 (100%)
Others	7552 (99.5%)	23186 (91.0%)	0 (0%)
BMI, n (%)			
18.5≤ to <25 kg/m ²	4204 (55.4%)	11712 (46.0%)	546 (41.1%)
Others	3384 (44.6%)	13754 (54.0%)	783 (58.9%)
Physical activity, n (%)			
Met the guidelines ^c	7279 (95.9%)	10337 (40.6%)	0 (0%)
Didn't meet the guidelines	309 (4.1%)	15129 (59.4%)	1329 (100%)
Alcohol intake, n (%)			
Never	1132 (14.9%)	647 (2.5%)	0 (0%)
Special occasions only	701 (9.2%)	2906 (11.4%)	200 (15.0%)
One to three times a month	1008 (13.3%)	3974 (15.6%)	199 (15.0%)
Once or twice a week	2211 (29.1%)	7822 (30.7%)	335 (25.2%)
Three or four times a week	1772 (23.4%)	6307 (24.8%)	294 (22.1%)
Daily or almost daily	764 (10.1%)	3810 (15.0%)	301 (22.6%)
Fruit and vegetable intake, n (%)			
<3 servings/day	510 (6.7%)	10689 (42.0%)	878 (66.1%)
≥3 to <5 servings/day	3252 (42.9%)	11240 (44.1%)	405 (30.5%)
≥5 servings/day	3826 (50.4%)	3537 (13.9%)	46 (3.5%)
Whole grain intake, n (%)			
<2 servings/day	3413 (45.0%)	17364 (68.2%)	1116 (84.0%)
≥2 to <5.5 servings/day	4114 (54.2%)	8042 (31.6%)	213 (16.0%)
≥5.5 servings/day	61 (0.8%)	60 (0.2%)	0 (0%)
Red and processed meat intake, n (%)			
<2 times/week	3294 (43.4%)	3572 (14.0%)	100 (7.5%)
≥2 to <4 times/week	3723 (49.1%)	11961 (47.0%)	610 (45.9%)
≥4 times/week	571 (7.5%)	9933 (39.0%)	619 (46.6%)
Average total household income, n (%)			
Less than 18,000	771 (10.2%)	2576 (10.1%)	241 (18.1%)
18,000 to 30,999	1183 (15.6%)	4274 (16.8%)	276 (20.8%)
31,000 to 51,999	2131 (28.1%)	7489 (29.4%)	383 (28.8%)
52,000 to 100,000	2317 (30.5%)	7362 (28.9%)	277 (20.8%)
Greater than 100,000	625 (8.2%)	2072 (8.1%)	52 (3.9%)
Prefer not to answer or do not know	561 (7.4%)	1693 (6.6%)	100 (7.5%)
Family history of cancer, n (%)			
No	5536 (73.0%)	18226 (71.6%)	915 (68.8%)
Yes	2052 (27.0%)	7240 (28.4%)	414 (31.2%)
Education, n (%)			
College or University degree	3496 (46.1%)	10129 (39.8%)	386 (29.0%)

Some professional qualifications	208 (2.7%)	647 (2.5%)	52 (3.9%)
Secondary education	3674 (48.4%)	13993 (54.9%)	798 (60.0%)
Others	186 (2.5%)	645 (2.5%)	90 (6.8%)
Prefer not to answer	24 (0.3%)	52 (0.2%)	3 (0.2%)
Age at menarche, n (%)			
<12 years of age	1313 (17.3%)	4352 (17.1%)	241 (18.1%)
12 to 13 years of age	3376 (44.5%)	11233 (44.1%)	548 (41.2%)
≥14 years of age	2741 (36.1%)	9261 (36.4%)	517 (38.9%)
Prefer not to answer or do not know	158 (2.1%)	620 (2.4%)	23 (1.7%)
Parity, n (%)			
Nulliparous	2267 (29.9%)	6531 (25.6%)	398 (29.9%)
Parous	5317 (70.1%)	18933 (74.3%)	928 (69.8%)
Prefer not to answer or do not know	4 (0.1%)	2 (0.0%)	3 (0.2%)
Age at first live birth, n (%)			
<25 years of age	1202 (15.8%)	4450 (17.5%)	338 (25.4%)
25 to 29 years of age	1656 (21.8%)	5731 (22.5%)	211 (15.9%)
≥30 years of age	1340 (17.7%)	4756 (18.7%)	124 (9.3%)
Prefer not to answer or do not know	3390 (44.7%)	10529 (41.3%)	656 (49.4%)
Oral contraceptive use, n (%)			
Yes	6877 (90.6%)	23510 (92.3%)	1250 (94.1%)
No	702 (9.3%)	1933 (7.6%)	79 (5.9%)
Prefer not to answer or do not know	9 (0.1%)	23 (0.1%)	0 (0%)
Menopausal status and hormone replacement therapy use, n (%)			
Postmenopausal (with hormone replacement therapy)	168 (2.2%)	565 (2.2%)	51 (3.8%)
Postmenopausal (without hormone replacement therapy)	339 (4.5%)	1069 (4.2%)	90 (6.8%)
Premenopausal	7070 (93.2%)	23796 (93.4%)	1185 (89.2%)
Prefer not to answer or do not know	11 (0.1%)	36 (0.1%)	3 (0.2%)
History of mammograms, n (%)			
Yes	1982 (26.1%)	6562 (25.8%)	341 (25.7%)
No	5580 (73.5%)	18821 (73.9%)	984 (74.0%)
Prefer not to answer or do not know	26 (0.3%)	83 (0.3%)	4 (0.3%)

Abbreviations: PRS, polygenic risk score; HLS, health-associated lifestyle score; SD, standard deviation.

^a Characteristics of eligible female participants.

^b Mean (SD) for continuous variables and n (%) for categorical variables.

^c Met the guidelines of 150 minutes of moderate activity per week or 75 minutes of vigorous activity (or an equivalent combination).

eTable 7. Characteristics of male participants (N=31925) at baseline according to male-specific HLS

Characteristics ^{a,b}	Male-specific HLS		
	Healthy (N=2277)	Intermediate (N=19821)	Unhealthy (N=9827)
Age, mean (SD)	44.9 (2.76)	44.9 (2.74)	45.0 (2.74)
Male-specific Total Cancer PRS, n (%)			
Low	792 (34.8%)	6625 (33.4%)	3184 (32.4%)
Intermediate	740 (32.5%)	6560 (33.1%)	3307 (33.7%)
High	745 (32.7%)	6636 (33.5%)	3336 (33.9%)
Smoking, n (%)			
Current smoker	13 (0.6%)	1356 (6.8%)	3297 (33.6%)
Others	2264 (99.4%)	18465 (93.2%)	6530 (66.4%)
BMI, n (%)			
18.5≤ to <25 kg/m ²	2116 (92.9%)	6246 (31.5%)	428 (4.4%)
Others	161 (7.1%)	13575 (68.5%)	9399 (95.6%)
Physical activity, n (%)			
Met the guidelines ^c	2235 (98.2%)	14948 (75.4%)	1351 (13.7%)
Didn't meet the guidelines	42 (1.8%)	4873 (24.6%)	8476 (86.3%)
Alcohol intake, n (%)			
Never	407 (17.9%)	791 (4.0%)	44 (0.4%)
Special occasions only	101 (4.4%)	1118 (5.6%)	631 (6.4%)
One to three times a month	223 (9.8%)	2258 (11.4%)	1146 (11.7%)
Once or twice a week	680 (29.9%)	6249 (31.5%)	2911 (29.6%)
Three or four times a week	587 (25.8%)	5747 (29.0%)	2715 (27.6%)
Daily or almost daily	279 (12.3%)	3658 (18.5%)	2380 (24.2%)
Fruit and vegetable intake, n (%)			
<3 servings/day	184 (8.1%)	7968 (40.2%)	6330 (64.4%)
≥3 to <5 servings/day	959 (42.1%)	7676 (38.7%)	2967 (30.2%)
≥5 servings/day	1134 (49.8%)	4177 (21.1%)	530 (5.4%)
Whole grain intake, n (%)			
<2 servings/day	479 (21.0%)	10211 (51.5%)	6809 (69.3%)
≥2 to <5.5 servings/day	1530 (67.2%)	9050 (45.7%)	2941 (29.9%)
≥5.5 servings/day	268 (11.8%)	560 (2.8%)	77 (0.8%)
Red and processed meat intake, n (%)			
<2 times/week	738 (32.4%)	1993 (10.1%)	254 (2.6%)
≥2 to <4 times/week	1150 (50.5%)	7426 (37.5%)	2926 (29.8%)
≥4 times/week	389 (17.1%)	10402 (52.5%)	6647 (67.6%)
Average total household income, n (%)			
Less than 18,000	182 (8.0%)	1378 (7.0%)	881 (9.0%)
18,000 to 30,999	344 (15.1%)	2949 (14.9%)	1365 (13.9%)
31,000 to 51,999	658 (28.9%)	6140 (31.0%)	2936 (29.9%)
52,000 to 100,000	720 (31.6%)	6408 (32.3%)	3255 (33.1%)
Greater than 100,000	248 (10.9%)	1840 (9.3%)	875 (8.9%)
Prefer not to answer or do not know	125 (5.5%)	1106 (5.6%)	515 (5.2%)
Family history of cancer, n (%)			
No	1659 (72.9%)	14243 (71.9%)	6995 (71.2%)
Yes	618 (27.1%)	5578 (28.1%)	2832 (28.8%)
Education, n (%)			
College or University degree	1216 (53.4%)	7960 (40.2%)	3445 (35.1%)

Some professional qualifications	28 (1.2%)	332 (1.7%)	184 (1.9%)
Secondary education	970 (42.6%)	10666 (53.8%)	5656 (57.6%)
Others	58 (2.5%)	779 (3.9%)	523 (5.3%)
Prefer not to answer	5 (0.2%)	84 (0.4%)	19 (0.2%)

Abbreviations: PRS, polygenic risk score; HLS, health-associated lifestyle score; SD, standard deviation.

^a Characteristics of eligible male participants.

^b Mean (SD) for continuous variables and n (%) for categorical variables.

^c Met the guidelines of 150 minutes of moderate activity per week or 75 minutes of vigorous activity (or an equivalent combination).