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Supplementary appendix

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Supplementary material

Modifiable traits, healthy behaviours, and leucocyte telomere length: a population-based study in UK Biobank

Vasiliki Bountziouka et al.

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Supplementary methods

1. Assessment of adherence to healthy diet

Adherence to a healthy diet, is characterised by the increased consumption of fruits, nuts, vegetables, whole grains, fish, and dairy products and a reduced consumption of refined grains, processed meats, unprocessed red meats and sugar-sweetened beverages.[1] Similarly to an established rationale,[2] we identified six main food groups (vegetables (UKB field codes "1289" and "1299"), fruit ("1309" and "1319"), fish ("1329" and "1339"), type and number of slices/ bowls of bread ("1438" and "1448") and cereals ("1458" and "1468"), red meat intake ("1369", "1379", and "1389") and processed meat ("1349")), obtained via a touchscreen food frequency questionnaire, and we created an index to measure healthy diet as follows. A score of one was assigned if participants reported increased consumption of fruit (≥3 portions/day), vegetables (≥3 portions/day), fish (daily/ weekly consumption) or decreased consumption of processed meat (consumed never/ rarely) and other red meats (from never to monthly intake). A score of two was assigned if participants reported increased consumption of whole grain bread and cereals (≥3 portions/day), whilst a score of one was assigned if they reported decreased consumption of white bread and refined cereals (≤1·5 portions/day). A portion was considered to be four heaped tablespoons of vegetables, one medium-sized piece of fruit, two slices of bread and one bowl of cereals.[3] In all food groups a score of zero was assigned otherwise. A dietary index was created as the cumulative sum of these six components (theoretical range: zero to seven). Participants with scores greater than or equal to four in the diet index were considered to follow a healthy diet.

For the assessment of moderate alcohol consumption we considered participants' self–reported weekly and monthly intake in terms of glasses of red wine (UKB field codes "1568" and "4407" respectively), champagne/ white wine ("1578", "4418"), beer/ cider ("1588", "4429"), spirits ("1598", "4440"), fortified wine intake ("1608", "4451"), and other alcoholic drinks ("5364", "4462") and converted it into average daily intake by dividing by 7 or 30 accordingly. Number of drinks per day were quantified as the number of UK units of alcohol intake and then converted to grams of alcohol (1 unit=8g of alcohol).[4] Moderate alcohol intake was then considered as 5–15g of alcohol per day for women and 5–30g per day for men.[5] Alcohol intake for participants who self–reported as non–drinking were assumed to intake 0g of alcohol per day.

2. Bi-directional Mendelian Randomisation analysis

To investigate the directionality of the potential causal associations between educational attainment or smoking behaviour (initiation of regular smoking and smoking intensity) with LTL, we undertook bi–directional Mendelian randomisation (MR) using independent genetic variants and estimated weights from published large–scale genome–wide association study (GWAS) datasets.[6,7,8] For the LTL to phenotype MR we used summary statistics for genetic variants associated with LTL from a GWAS in UK Biobank that adjusted for age, sex, biobank array and the first 10 principal components (PCs), where pleiotropic variants were excluded from the MR instrument.[6] Identified variants were extracted from publicly available GWAS summary statistics for education[7] and smoking.[8] The MR estimator for each variant is derived from the Wald ratio and combined using inverse-variance weights. For the phenotype to LTL MR we used summary statistics for independent genetic variants from the same published GWAS datasets for education, adjusted for age (including a third-order polynomial in age), sex, age*sex interaction, events that may have affected access to education and the first 10 PCs[7], and smoking, adjusted for age, sex, age*sex interaction and the first 10 PCs.[8] These variants were extracted from the LTL GWAS summary statistics in UK Biobank.[6]

Under certain assumptions, namely relevance (the variants are associated with the exposure), independence (the variants are not associated with any confounders), and exclusion restriction (the variants are associated with the outcome only through the risk factor), MR is a method that intends to estimate causal effects. To examine if educational attainment was causal for a change in LTL, of the 1,271 independent variants associated with number of years spend in education (EduYears) in the educational attainment GWAS explaining 3.9% of the variance in the trait[7] we were able to match 1,267 SNP in the LTL GWAS.[6] For the reverse MR analysis (LTL to EduYears) we were able to match 87 out of 130 LTL–associated genetic variants in the educational attainment GWAS. These 130 LTL–associated variants were selected to reduce pleiotropy from 197 independent LTL associated variants that explained 4.5% of variance in LTL.[6] For the smoking phenotypes we able to match 374 of the 378 independently associated variants for smoking initiation explaining 2.3% of variance[8] and all 55 for smoking intensity explaining 1.1% of variance[8] in the LTL GWAS data. Of the 130 variants for LTL we were able to match 89 in both the smoking initiation and smoking intensity GWAS data.

For each analysis, we used the inverse–variance weighted MR method[9] allowing for a random effect to estimate the causal association and also reported the P–value for the intercept from MR Egger[10] as a check for horizontal pleiotropy. To test the robustness of the result under the key MR assumptions we ran several MR sensitivity analyses using different methods. We specifically applied the Weighted Median method[11] that is additionally robust in the presence of outliers, and the MR Raps method[12] that overcomes challenges related to measurement error, weak or invalid (due to pleiotropy)

measurements and selection bias (due to weak instrument). Therefore a combination of these methods provides the best evidence for the presence of a causal association. All MR analyses were performed in R version 3·1·6.[13]

3. Effect of healthy behaviours on the association of LTL with diseases.

To investigate whether healthy behaviours affected the association of LTL with disease, we selected 22 diseases where we had previously seem evidence of a possible causal association at either at Bonferroni ($4{\cdot}1x10^{-4}$; 12 diseases) or nominal ($5{\cdot}0x10^{-2}$; 10 diseases) significance level.[8] For all diseases there was a concordant observational association with LTL.[6] To define incident cases for each disease, we used hospital episode statistics (HES) data using primary and secondary codes from the 9th and 10th revisions of the international statistical classification of diseases and related health problems (ICD–9 & 10) and the office of population censuses and surveys classification of surgical operations versions 3 and 4 (OPCS–3 & 4) from the UK office of national statistics, as previously described.[6] We used the date of sample collection that LTL was measured as the baseline date, and censored the end of follow–up in hospital health record data as 31st March 2020. Data about deaths was also subject to censoring using the same date of 31 March 2020 used for HES records. Cases that were self–reported at baseline or had a recorded hospitalisation with any (primary or secondary) diagnosis of the disease were excluded from the analysis. Incident cases were then defined as the first recorded event (primary or secondary) of the disease occurring after the UKB baseline visit. Time–to–event is defined as the post–baseline date of the first incident hospitalisation or death, or otherwise censored at the end of study follow–up on 31 March 2020.

To examine whether the association of LTL with incident diseases varied with the number of healthy behaviours we utilised a cox-regression model adjusted for a) age, sex, ethnicity and WBC (base model), b) additionally adjusted for previously diagnosed diabetes, cancer, hypertension, vascular disease (adjusted model) and c) further adjusted for educational level, insomnia, fed–up feelings, LDL–cholesterol, C–reactive protein, estimated glomerular filtration rate (CKD-EPI) (full model), also allowing for interactions between the covariates and the primary HBI as appropriate. A Wald test was used to decide on the overall significance of the interaction terms at the 5% level. Results are given as hazard ratios (95% confidence interval), with the point estimates being corrected for the regression dilution ratio of 0·68 for LTL measurements as described elsewhere.[14] As this analysis included two models for 22 diseases, the significance level was set at $1{\cdot}14x10^{-3}$.

4. Mediation analysis

To assess the extent to which any association of healthy behaviours on life expectancy could be mediated through an effect on LTL, we first computed the association of the primary HBI score with life expectancy using public health modelling methods previously described[8] that combine cause–specific mortality rates from the general population and age–specific hazard ratios (HRs) for mortality to estimate differences in life expectancy for different primary HBI score groups using the group with a score of zero as reference. The extent of any mediation through LTL was then assessed by comparing differences in life expectancy estimated when applying HRs with/without adjustment for LTL.

We used structural equation models[15] to examine whether, and to what extent, the effect of the healthy behaviours on coronary artery disease (CAD) risk is mediated through LTL. In this analysis, the association of the primary HBI with risk of CAD are presented as a continuum i.e. per unit increase in the HB score. Results of the mediation analysis are shown as the percentage of the total effect of the primary HBI on CAD risk that could be mediated through LTL.

Supplementary References

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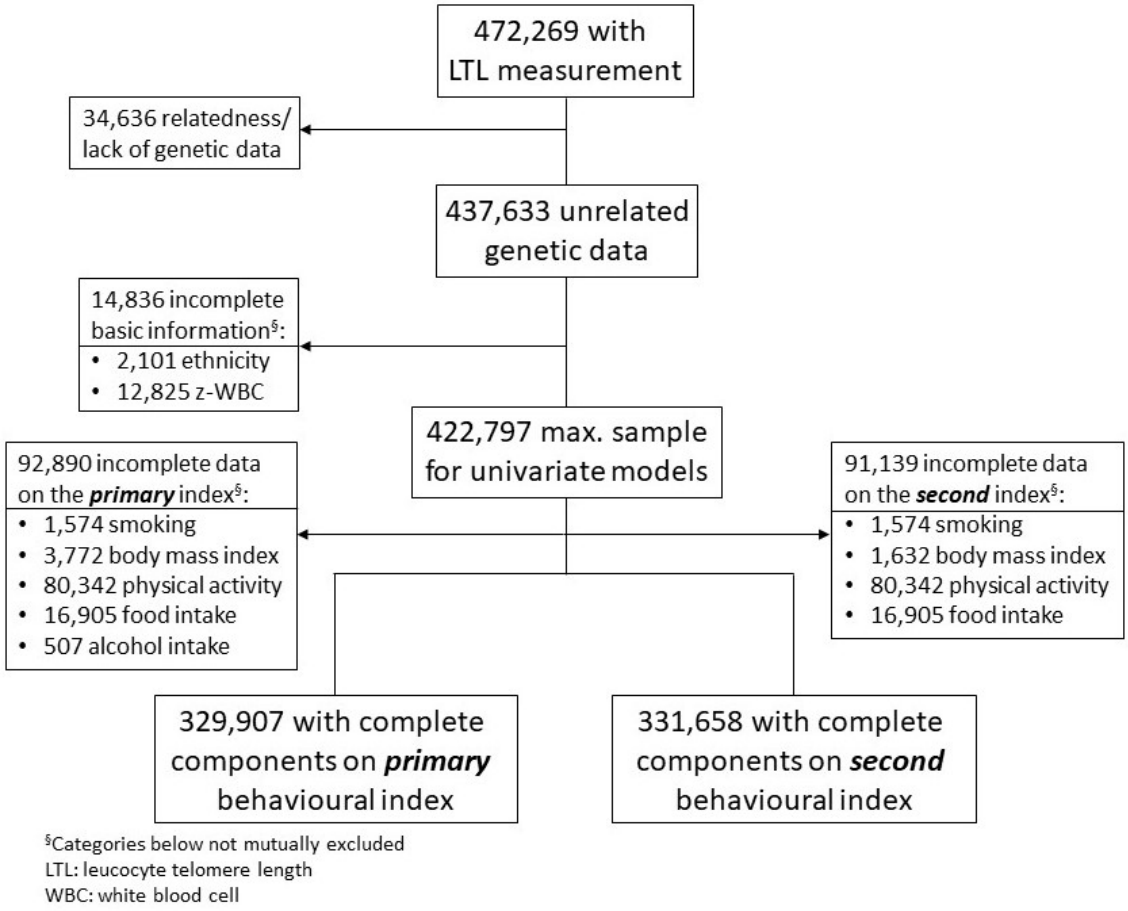
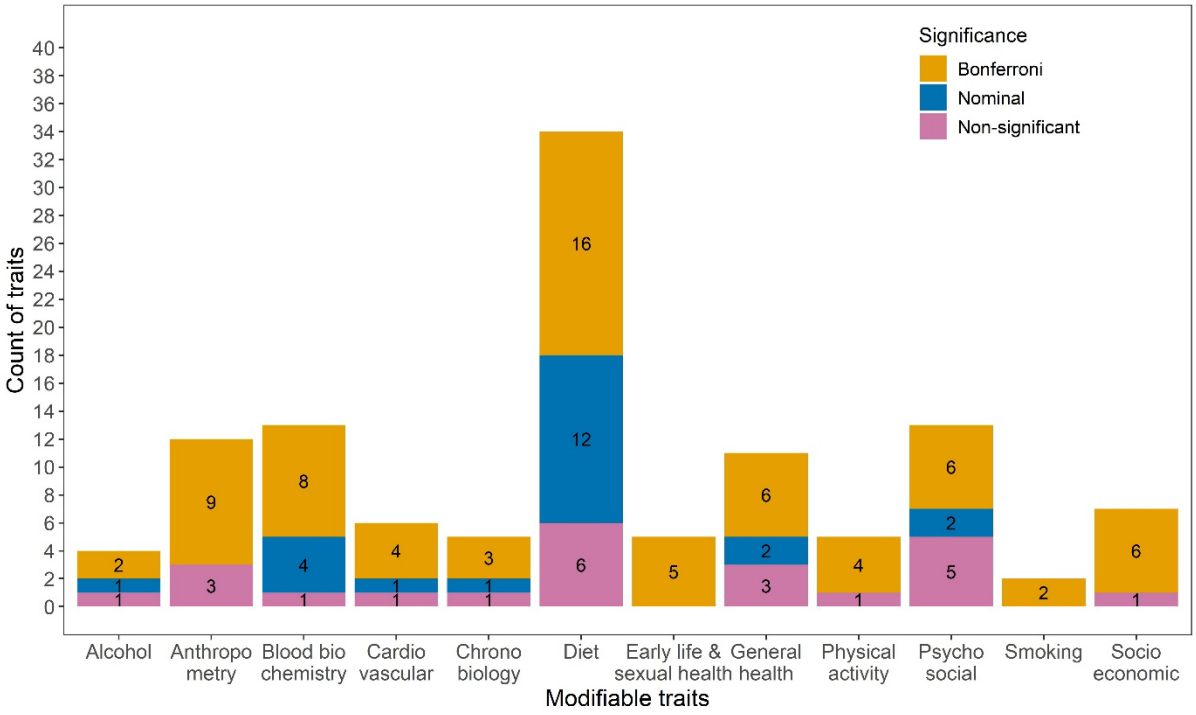
Supplementary Figures

Supplementary Figure 1. Flowchart of participants included in different analyses and reasons for exclusion.

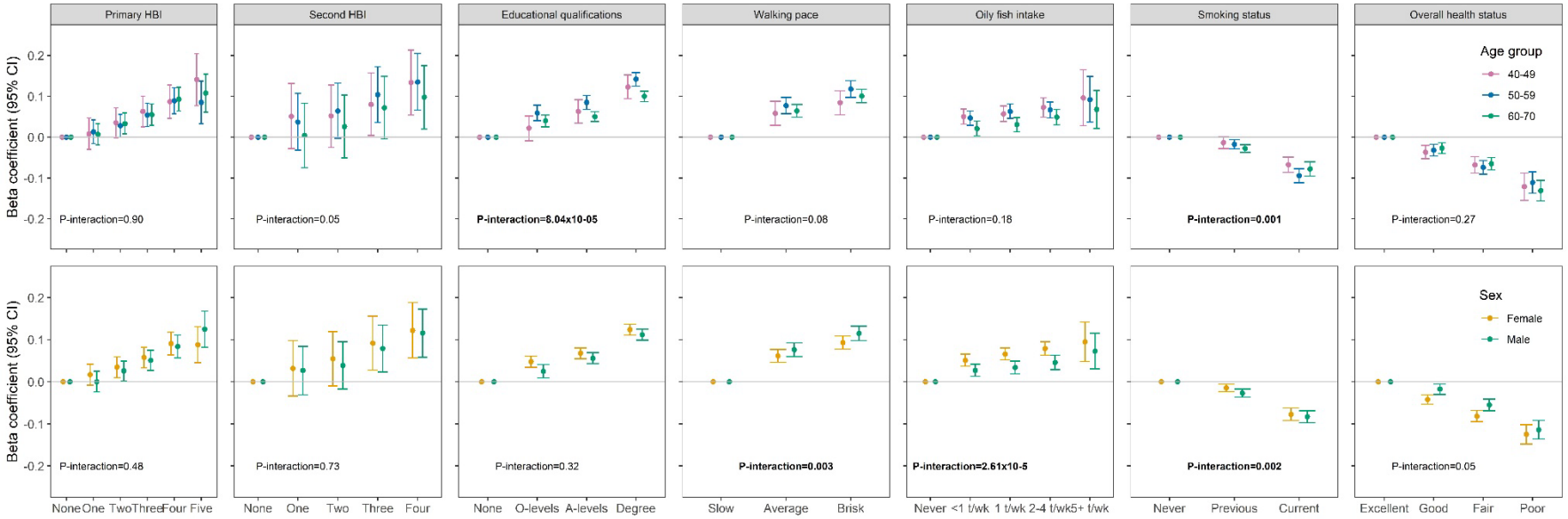


Supplementary Figure 2. Number of modifiable traits associated with leucocyte telomere length by categories and significance level.



Bonferroni significance: $<4{\cdot}27x10^{-4}$; Nominal significance: $P<0{\cdot}05$; Non-significant: $P\geq0{\cdot}05$.

Supplementary Figure 3. Age and sex stratified analysis.

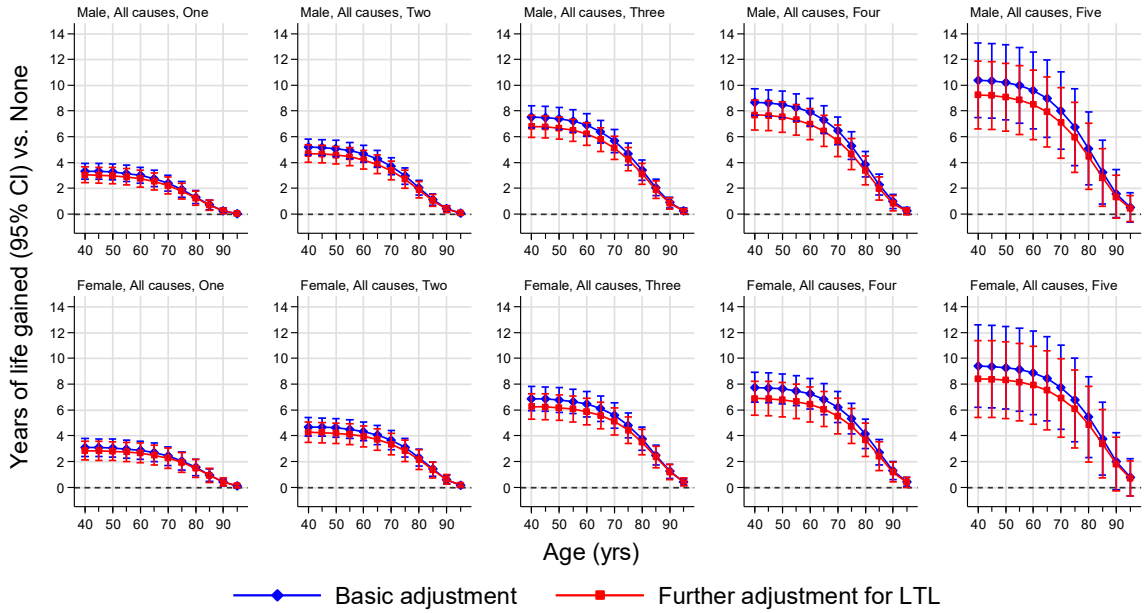


Results of the age (top panel) and sex (bottom panel) stratified analysis of the associations of leucocyte telomere length with the main traits of the study (primary and second healthy behaviour indices (HBI), educational qualifications, walking pace, oily fish intake, smoking status, and overall health status) are shown. All models were additionally adjusted for age or sex, ethnicity and white blood cell count. Bold fonts indicate significant results at the 0.05 level.

Supplementary Figure 4. Association of LTL with risk of 22 diseases across different scores for the primary healthy behaviour index.

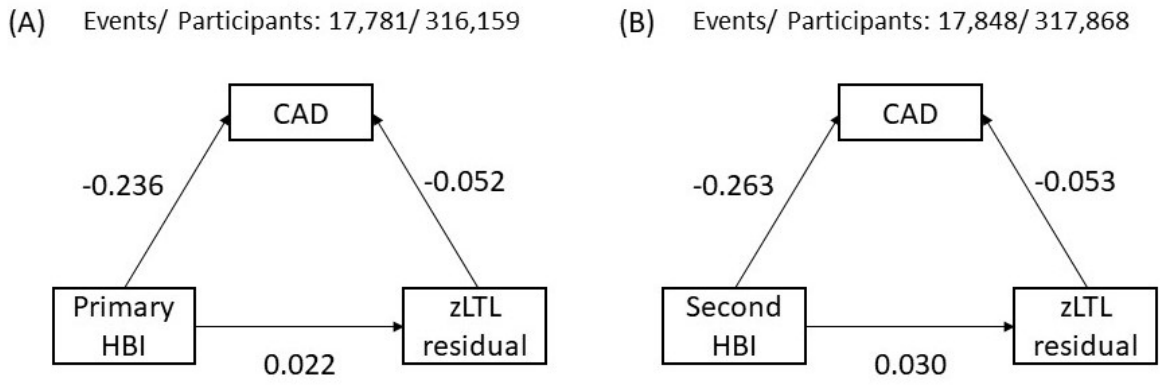
Each plot first shows the overall association of leucocyte telomere length (LTL) with risk of disease and then the associations across three scores for the primary healthy behaviour index (HBI): 0–1, 2–3, and 4–5 (all as hazard ratios per SD of longer LTL). The Base model is the model adjusted for age, sex, ethnicity and white blood cell count. The Full model is the base model additionally adjusted for self–reported doctor diagnosed history of diabetes/ cancer/ hypertension/ vascular disease, highest qualification, insomnia, fed–up feelings, low–density cholesterol, C–reactive protein, and estimated glomerular filtration rate (CKD–EPI).

Supplementary Figure 5. Years of life gained according to healthy behaviour index groups with/without adjustment for LTL as a mediator.



Years of life gained were estimated by applying hazard ratios (HRs) for cause–specific mortality calculated from UK Biobank data (specific to age–at–risk and stratified by sex and ethnic group) to population mortality rates for United Kingdom (UK) during year 2015 (by sex and 5–year age groups). Basic adjustment corresponded to age–at–risk specific HRs estimated in Cox regression (stratified by sex and ethnic group) and adjusted for white blood cell count. Further adjustment involved additional adjustment for leucocyte telomere length (LTL). The error bars are 95% confidence intervals (CI) and reflect uncertainty due to sampling variation in the HRs applied. The UK Biobank data included 329,826 participants and 19,140 deaths (comprising 4,001 vascular deaths, 10,301 cancer deaths, 4,710 non–vascular non–cancer deaths, and 128 deaths of unknown causes).

Supplementary Figure 6. Mediation analysis to examine the proportion of the association of the healthy behaviour indices with CAD that may be mediated through LTL.



Structural equation models to investigate the proportion of the effect of healthy behaviours on coronary artery disease (CAD) that is mediated through leucocyte telomere length (LTL). Model (A) is for the primary healthy behaviour index (HBI), model (B) is for the second index. zLTL residual is the standardised telomere length after removing the effect of age, sex, ethnicity and white blood cell count.

Supplementary Table 1: Association of single modifiable traits with LTL.

Group	UKB field	Trait		Available data				Imputed data (N=422,797)		
			N	Mean(SD) / N(%)	Beta (95% CI)	Pvalue	Equivalent years of age-related change in LTL	MI Beta (95% CI)	Pvalue	Equivalent years of age-related change in LTL
Alcohol	1558	Alcohol intake, frequency	422,407		*Global P:*	0·486		*Global P:*	0·475	
	1558		Never	86,777 (20·5%)	Reference			Reference		
	1558		Occasionally	98,010 (23·2%)	-0·002 (-0·016, 0·011)	0·720	-0·09	-0·003 (-0·016, 0·011)	0·706	-0·11
	1558		1-3 times/month	108,813 (25·8%)	0·000 (-0·014, 0·013)	0·954	0.00	0·000 (-0·014, 0·013)	0·945	0.00
	1558		1-2 times/week	46,768 (11·1%)	0·005 (-0·007, 0·017)	0·416	0·22	0·005 (-0·007, 0·017)	0·417	0·22
	1558		3-4 times/week	48,246 (11·4%)	0·007 (-0·006, 0·019)	0·292	0·30	0·007 (-0·006, 0·019)	0·293	0·29
	1558		Daily	33,793 (8·0%)	0·001 (-0·012, 0·014)	0·863	0·04	0·001 (-0·012, 0·014)	0·869	0·05
	1628	Alcohol comparison, 10 years	385,725		*Global P:*	9·78x10-18		*Global P:*	1·46x10-16	
	1628		About the same	146,319 (37·9%)	Reference			Reference		
	1628		Less nowadays	175,332 (45·5%)	-0·031 (-0·037, -0·024)	9·64x10-19	-1·33	-0·031 (-0·038, -0·024)	2·77x10-18	-1·34
	1628		More nowadays	64,074 (16·6%)	-0·018 (-0·027, -0·009)	7·08x10-05	-0·80	-0·020 (-0·029, -0·011)	1·00x10-05	-0·89
	20117	Drinking status	422,286		*Global P:*	0·035		*Global P:*	0·033	
	20117		Never	18,543 (4·4%)	Reference			Reference		
	20117		Previous	15,129 (3·6%)	-0·027 (-0·049, -0·006)	0·011	-1·17	-0·028 (-0·049, -0·006)	0·011	-1·21
	20117		Current	388614 (92·0%)	-0·010 (-0·025, 0·005)	0·205	-0·43	-0·010 (-0·025, 0·005)	0·173	-0·45
	Derived	Alcohol intake, g/day	327,509	18·35 (16·92)	-0·001 (-0·002, -0·001)	3·98x10-44	-0·06	-0·001 (-0·001, -0·001)	1·65x10-37	-0·05
Anthropometry	46	Hand grip strength (left)	420,875	29·63 (11·25)	0·018 (0·014, 0·022)	9·75x10-16	0·78	0·018 (0·014, 0·023)	5·16x10-16	0·79
	47	Hand grip strength (right)	420,924	31·78 (11·19)	0·017 (0·013, 0·021)	3·22x10-14	0·74	0·017 (0·013, 0·022)	1·71x10-14	0·75
	48	Waist circumference	421,919	90·32 (13·32)	-0·020 (-0·023, -0·016)	1·03x10-28	-0·87	-0·019 (-0·023, -0·016)	1·86x10-28	-0·84
	49	Hip circumference	421,877	103·35 (9·01)	-0·012 (-0·015, -0·009)	4·07x10-15	-0·52	-0·012 (-0·015, -0·009)	7·83x10-15	-0·51
	21002	Weight	421,437	78·07 (15·69)	-0·014 (-0·018, -0·011)	2·19x10-16	-0·61	-0·014 (-0·017, -0·011)	4·42x10-16	-0·61
	23099	Body fat percentage	415,106	31·38 (8·48)	-0·035 (-0·039, -0·031)	2·13x10-61	-1·52	-0·034 (-0·038, -0·029)	2·09x10-52	-1·46
	23100	Whole body fat mass	414,635	24·78 (9·36)	-0·022 (-0·025, -0·019)	2·39x10-42	-0·96	-0·021 (-0·024, -0·018)	1·30x10-39	-0·92
	23101	Whole body fat-free mass	415,295	53·31 (11·44)	0·002 (-0·004, 0·008)	0·471	0·09	0·002 (-0·004, 0·008)	0·471	0·09
	23102	Whole body water mass	415,332	39·01 (8·37)	0·002 (-0·004, 0·007)	0·527	0·09	0·002 (-0·003, 0·008)	0·432	0·10
	23104	Body mass index	421,165	27·41 (4·70)	-0·023 (-0·026, -0·020)	2·01x10-48	-1.00	-0·023 (-0·026, -0·019)	6·87x10-48	-0·98
	23105	Basal metabolic rate	415,321	6,624 (1,353)	-0·004 (-0·009, 0·001)	0·090	-0·17	-0·004 (-0·009, 0·001)	0·139	-0·16
	Derived	Waist-hip circumference	421,837	0·87 (0·09)	-0·022 (-0·026, -0·018)	1·52x10-25	-0·96	-0·021 (-0·025, -0·017)	5·17x10-25	-0·93
Blood biochemistry	30630	Apolipoprotein A	368,909	1·54 (0·27)	-0·009 (-0·013, -0·006)	8·93x10-08	-0·39	-0·009 (-0·012, -0·005)	2·44x10-07	-0·38
	30640	Apolipoprotein B	403,228	1·03 (0·24)	0·022 (0·019, 0·025)	3·34x10-46	0·96	0·021 (0·018, 0·024)	1·20x10-42	0·92
	30670	Urea	405,029	5·39 (1·31)	0·005 (0·001, 0·008)	0·005	0·22	0·004 (0·001, 0·008)	0·006	0·19
	30690	Total cholesterol	405,304	5·69 (1·13)	0·023 (0·019, 0·026)	2·23x10-47	1.00	0·022 (0·019, 0·025)	3·11x10-43	0·95
	30700	eGFR	405,094	77·39 (75·02)	-0·040 (-0·052, -0·029)	2·21x10-12	-1·74	-0·039 (-0·051, -0·028)	2·73x10-11	-1·71
	30710	CRP	404,439	2·52 (3·70)	-0·023 (-0·026, -0·020)	5·21x10-46	-1.00	-0·023 (-0·026, -0·020)	1·74x10-44	-0·99
	30740	Glucose	370,704	5·11 (1·08)	-0·004 (-0·008, -0·001)	0·006	-0·17	-0·005 (-0·008, -0·001)	0·004	-0·20

Blood biochemistry	30750	HbA1c		402,742	36·07 (6·14)	-0·009 (-0·012, -0·006)	2·24x10-08	-0·39	-0·009 (-0·012, -0·006)	2·41x10-08	-0·39
	30760	HDL		370,963	1·45 (0·38)	-0·005 (-0·009, -0·002)	0·004	-0·22	-0·004 (-0·007, 0·000)	0·028	-0·16
	30780	LDL		404,553	3·56 (0·86)	0·024 (0·021, 0·027)	1·01x10-56	1·04	0·024 (0·021, 0·027)	5·41x10-51	1·03
	30790	Lipoprotein A		324,102	44·58 (49·13)	0·005 (0·002, 0·008)	0·003	0·22	0·004 (0·000, 0·007)	0·026	0·17
	30870	Triglycerides		404,972	1·74 (0·99)	0·011 (0·008, 0·015)	1·53x10-12	0·48	0·011 (0·007, 0·014)	4·28x10-11	0·46
	30890	Vitamin D		386,944	48·52 (20·81)	0·001 (-0·002, 0·005)	0·375	0·04	0·001 (-0·002, 0·004)	0·508	0·05
Cardiovascular	102	Pulse rate		399,424	69·33 (11·11)	-0·009 (-0·012, -0·006)	1·44x10-08	-0·39	-0·008 (-0·012, -0·005)	1·19x10-07	-0·37
	4079	Diastolic blood pressure		399,424	82·23 (10·03)	0·007 (0·004, 0·010)	6·19x10-06	0·30	0·007 (0·004, 0·010)	3·66x10-06	0·31
	4080	Systolic blood pressure		399,421	137·81 (18·42)	0·009 (0·006, 0·013)	1·46x10-08	0·39	0·009 (0·005, 0·012)	3·09x10-07	0·38
	6032	Maximum workload (fitness)		66,110	72·03 (35·61)	0·013 (0·004, 0·022)	0·004	0·57	0·020 (0·016, 0·023)	1·61x10-19	0·85
	6033	Maximum heart rate (fitness)		66,094	110·20 (19·60)	0·001 (-0·007, 0·008)	0·880	0·04	0·003 (-0·002, 0·007)	0·231	0·11
	Derived	Pulse pressure		399,421	55·57 (13·45)	0·008 (0·004, 0·011)	1·03x10-05	0·35	0·006 (0·003, 0·010)	4·13x10-04	0·27
Chronobiology	1160	Sleep duration		420,164	7·15 (1·07)	0·000 (-0·003, 0·003)	0·876	0.00	0·000 (-0·003, 0·003)	0·876	0.00
	1170	Getting up in morning		422,066		*Global P:*	1·54x10-04		*Global P:*	1·50x10-04	
	1170		Not at all easy		16,585 (3·9%)	Reference			Reference		
	1170		Not very easy		59,231 (14·0%)	0·018 (0·001, 0·034)	0·038	0·78	0·018 (0·001, 0·035)	0·037	0·78
	1170		Fairly easy		209,653 (49·7%)	0·020 (0·005, 0·036)	0·009	0·87	0·021 (0·005, 0·036)	0·009	0·89
	1170		Very easy		136,597 (32·4%)	0·007 (-0·009, 0·023)	0·394	0·30	0·007 (-0·009, 0·023)	0·392	0·30
	1190	Day nap		422,070		*Global P:*	1·95x10-09		*Global P:*	2·06x10-09	
	1190		Never/rarely		237,109 (56·2%)	Reference			Reference		
	1190		Sometimes		162,339 (38·5%)	-0·016 (-0·023, -0·010)	2·76x10-07	-0·70	-0·016 (-0·023, -0·010)	2·89x10-07	-0·71
	1190		Usually		22,622 (5·3%)	-0·032 (-0·046, -0·019)	2·65x10-06	-1·39	-0·032 (-0·046, -0·019)	2·66x10-06	-1·40
	1200	Insomnia		422,390		*Global P:*	1·00x10-09		*Global P:*	1·10x10-09	
	1200		Never/rarely		102,340 (24·2%)	Reference			Reference		
	1200		Sometimes		201,451 (47·7%)	-0·011 (-0·018, -0·003)	0·005	-0·48	-0·011 (-0·018, -0·003)	0·005	-0·46
	1200		Usually		118,599 (28·1%)	-0·027 (-0·035, -0·018)	2·78x10-10	-1·17	-0·027 (-0·035, -0·018)	3·06x10-10	-1·15
	1220	Narcolepsy		420,565		*Global P:*	4·89x10-04		*Global P:*	7·56x10-04	
	1220		Never/rarely		319,550 (76·0%)	Reference			Reference		
	1220		Sometimes		89,228 (21·2%)	-0·007 (-0·014, 0·001)	0·073	-0·30	-0·006 (-0·014, 0·001)	0·082	-0·28
	1220		Often		11,752 (2·8%)	-0·036 (-0·054, -0·018)	8·11x10-05	-1·57	-0·036 (-0·054, -0·018)	7·46x10-05	-1·57
	1220		All of the time		35 (0·0%)	0·076 (-0·247, 0·398)	0·645	3·30	0·087 (-0·244, 0·417)	0·606	3·77
Diet	1289	Cooked vegetable intake		408,950	2·74 (1·59)	0·006 (0·003, 0·009)	5·43x10-05	0·26	0·006 (0·003, 0·009)	3·67x10-05	0·28
	1299	Raw vegetable intake		397,383	2·24 (1·88)	0·008 (0·005, 0·011)	3·21x10-07	0·35	0·008 (0·005, 0·011)	1·41x10-07	0·35
	1309	Fresh fruit intake		407,512	2·27 (1·45)	0·016 (0·013, 0·019)	3·69x10-26	0·70	0·016 (0·013, 0·019)	2·95x10-26	0·71
	1319	Dried fruit intake		384,574	0·86 (1·54)	0·025 (0·022, 0·028)	9·48x10-54	1·09	0·024 (0·021, 0·027)	1·36x10-48	1·03
	1329	Oily fish intake		420,294		*Global P:*	1·56x10-28		*Global P:*	1·93x10-28	
	1329		Never		45,794 (10·9%)	Reference			Reference		
	1329		Less than once a week		139,316 (33·1%)	0·040 (0·029, 0·050)	5·51x10-14	1·74	0·040 (0·029, 0·050)	3·92x10-14	1·73
	1329		Once a week		159,100 (37·9%)	0·051 (0·041, 0·061)	1·70x10-22	2·22	0·051 (0·041, 0·061)	8·60x10-23	2·22
	1329		2-4 times a week		72,069 (17·1%)	0·064 (0·052, 0·075)	3·51x10-27	2·78	0·064 (0·052, 0·075)	1·97x10-27	2·77

1329		5+ times a week		4,015 (1·0%)	0·085 (0·054, 0·116)	1·19x10-07	3·70	0·083 (0·051, 0·114)	3·07x10-07	3·59
1339	Non-oily fish intake		420,586		*Global P:*	0·025		*Global P:*	0·026	
1339		Never		19,725 (4·7%)	Reference			Reference		
1339		Less than once a week		122,050 (29·0%)	0·020 (0·005, 0·035)	0·007	0·87	0·021 (0·006, 0·036)	0·006	0·91
1339		Once a week		209,634 (49·8%)	0·019 (0·004, 0·033)	0·011	0·83	0·020 (0·005, 0·034)	0·008	0·85
1339		2-4 times a week		66,521 (15·8%)	0·019 (0·003, 0·034)	0·018	0·83	0·020 (0·004, 0·036)	0·013	0·87
1339		5+ times a week		2,656 (0·7%)	0·055 (0·016, 0·095)	0·006	2·39	0·052 (0·012, 0·092)	0·011	2·26
1349	Processed meat intake		421,808		*Global P:*	7·61x10-21		*Global P:*	1·35x10-21	
1349		Never		39,127 (9·3%)	Reference			Reference		
1349		Less than once a week		128,413 (30·4%)	-0·022 (-0·033, -0·011)	1·23x10-04	-0·96	-0·021 (-0·032, -0·010)	1·54x10-04	-0·93
1349		Once a week		123,038 (29·2%)	-0·042 (-0·053, -0·031)	2·70x10-13	-1·83	-0·041 (-0·053, -0·030)	4·45x10-13	-1·80
1349		2-4 times a week		114,385 (27·1%)	-0·050 (-0·062, -0·039)	1·16x10-17	-2·17	-0·050 (-0·061, -0·038)	2·20x10-17	-2·16
1349		5+ times a week		16,845 (4·0%)	-0·054 (-0·072, -0·036)	2·62x10-09	-2·35	-0·054 (-0·072, -0·036)	2·81x10-09	-2·36
1359	Poultry intake		421,939		*Global P:*	1·18x10-07		*Global P:*	1·60x10-07	
1359		Never		21,494 (5·1%)	Reference			Reference		
1359		Less than once a week		45,438 (10·8%)	-0·028 (-0·044, -0·012)	6·35x10-04	-1·22	-0·027 (-0·043, -0·011)	7·49x10-04	-1·19
1359		Once a week		151,450 (35·9%)	-0·034 (-0·048, -0·020)	1·55x10-06	-1·48	-0·034 (-0·048, -0·020)	1·94x10-06	-1·48
1359		2-4 times a week		193,971 (46·0%)	-0·041 (-0·055, -0·027)	6·29x10-09	-1·78	-0·040 (-0·054, -0·027)	8·93x10-09	-1·76
1359		5+ times a week		9,586 (2·2%)	-0·044 (-0·067, -0·020)	2·89x10-04	-1·91	-0·043 (-0·067, -0·020)	2·93x10-04	-1·89
1369	Beef intake		420,909		*Global P:*	5·60x10-08		*Global P:*	5·70x10-08	
1369		Never		46,538 (11·1%)	Reference			Reference		
1369		Less than once a week		191,645 (45·5%)	-0·020 (-0·031, -0·010)	7·65x10-05	-0·87	-0·020 (-0·030, -0·010)	1·12x10-04	-0·87
1369		Once a week		133,926 (31·8%)	-0·031 (-0·041, -0·020)	1·15x10-08	-1·35	-0·031 (-0·041, -0·020)	1·31x10-08	-1·34
1369		2-4 times a week		47,710 (11·3%)	-0·033 (-0·046, -0·020)	4·21x10-07	-1·43	-0·033 (-0·045, -0·020)	4·53x10-07	-1·42
1369		5+ times a week		1,090 (0·3%)	-0·051 (-0·110, 0·007)	0·087	-2·22	-0·054 (-0·112, 0·003)	0·064	-2·37
1379	Lamb intake		419,924		*Global P:*	0·761		*Global P:*	0·708	
1379		Never		74,379 (17·7%)	Reference			Reference		
1379		Less than once a week		237,891 (56·7%)	0·002 (-0·006, 0·010)	0·621	0·09	0·002 (-0·006, 0·010)	0·615	0·09
1379		Once a week		94,754 (22·5%)	-0·003 (-0·012, 0·007)	0·594	-0·13	-0·003 (-0·012, 0·007)	0·593	-0·11
1379		2-4 times a week		12,442 (3·0%)	0·001 (-0·018, 0·019)	0·953	0·04	0·001 (-0·018, 0·019)	0·955	0·02
1379		5+ times a week		458 (0·1%)	-0·026 (-0·116, 0·064)	0·573	-1·13	-0·033 (-0·118, 0·053)	0·452	-1·43
1389	Pork intake		420,120		*Global P:*	0·006		*Global P:*	0·008	
1389		Never		72,258 (17·2%)	Reference					
1389		Less than once a week		238,916 (56·9%)	-0·007 (-0·015, 0·001)	0·100	-0·30	-0·006 (-0·015, 0·002)	0·125	-0·28
1389		Once a week		93,869 (22·3%)	-0·017 (-0·027, -0·008)	4·00x10-04	-0·74	-0·017 (-0·027, -0·007)	5·30x10-04	-0·74
1389		2-4 times a week		14,466 (3·4%)	-0·011 (-0·028, 0·007)	0·232	-0·48	-0·010 (-0·028, 0·007)	0·250	-0·45
1389		5+ times a week		611 (0·2%)	-0·046 (-0·124, 0·031)	0·243	-2.00	-0·042 (-0·118, 0·033)	0·272	-1·84

Diet

Diet	1408	Cheese intake		411,632		*Global P:*	1·08x10-24		*Global P:*	9·56x10-25	
	1408		Never		11,265 (2·7%)	Reference			Reference		
	1408		Less than once a week		71,024 (17·3%)	0·013 (-0·007, 0·032)	0·193	0·57	0·013 (-0·006, 0·032)	0·182	0·57
	1408		Once a week		87,902 (21·3%)	0·011 (-0·008, 0·030)	0·243	0·48	0·012 (-0·007, 0·031)	0·227	0·51
	1408		2-4 times a week		186,658 (45·4%)	0·021 (0·002, 0·039)	0·027	0·91	0·021 (0·003, 0·040)	0·023	0·93
	1408		5+ times a week		54,783 (13·3%)	0·063 (0·043, 0·083)	4·55x10-10	2·74	0·063 (0·044, 0·083)	3·04x10-10	2·76
	1418	Milk type		422,450		*Global P:*	3·45x10-06		*Global P:*	3·33x10-06	
	1418		Never/rarely		14,115 (3·3%)	Reference			Reference		
	1418		Full cream		29,193 (6·9%)	-0·011 (-0·031, 0·008)	0·266	-0·48	-0·011 (-0·031, 0·008)	0·255	-0·49
	1418		Semi-skimmed		272,463 (64·5%)	-0·003 (-0·019, 0·014)	0·742	-0·12	-0·003 (-0·020, 0·013)	0·712	-0·13
	1418		Skimmed		84,692 (20·1%)	-0·002 (-0·020, 0·015)	0·803	-0·10	-0·003 (-0·020, 0·015)	0·770	-0·11
	1418		Soya		16,551 (3·9%)	0·040 (0·018, 0·062)	3·40x10-04	1·74	0·040 (0·018, 0·062)	3·71x10-04	1·73
	1418		Other type of milk		5,436 (1·3%)	-0·005 (-0·036, 0·025)	0·741	-0·22	-0·005 (-0·036, 0·025)	0·724	-0·24
	1428	Spread type		421,983		*Global P:*	0·007		*Global P:*	0·007	
	1428		Rarely use spread		45,785 (10·9%)	Reference			Reference		
	1428		Butter		153,640 (36·4%)	-0·013 (-0·023, -0·003)	0·014	-0·57	-0·013 (-0·023, -0·003)	0·014	-0·55
	1428		Flora/Benecol		2,392 (0·6%)	-0·006 (-0·046, 0·034)	0·773	-0·26	-0·005 (-0·045, 0·035)	0·801	-0·22
	1428		Other spread		220,166 (52·1%)	-0·017 (-0·027, -0·007)	5·80x10-04	-0·74	-0·017 (-0·027, -0·007)	5·76x10-04	-0·75
	1448	Bread type		407,749		*Global P:*	1·25x10-53		*Global P:*	1·36x10-52	
	1448		White		107,314 (26·3%)	Reference			Reference		
	1448		Brown		51,406 (12·6%)	0·032 (0·021, 0·042)	1·39x10-09	1·39	0·031 (0·021, 0·042)	1·82x10-09	1·37
	1448		Wholemeal		231,557 (56·8%)	0·057 (0·050, 0·065)	1·90x10-55	2·48	0·057 (0·050, 0·064)	2·65x10-55	2·48
	1448		Other type		17,472 (4·3%)	0·044 (0·028, 0·060)	3·78x10-08	1·91	0·045 (0·029, 0·061)	3·03x10-08	1·95
	1468	Cereal type		347,253		*Global P:*	2·92x10-54		*Global P:*	7·38x10-41	
	1468		Other		67,901 (19·6%)	Reference			Reference		
	1468		Bran cereal		58,374 (16·8%)	0·026 (0·016, 0·037)	1·64x10-06	1·15	0·027 (0·017, 0·038)	7·01x10-07	1·19
	1468		Biscuit cereal		61,247 (17·6%)	0·004 (-0·007, 0·014)	0·486	0·16	0·006 (-0·004, 0·016)	0·254	0·26
	1468		Oat cereal		88,946 (25·6%)	0·034 (0·024, 0·044)	1·20x10-11	1·48	0·035 (0·024, 0·045)	7·98x10-10	1·51
	1468		Muesli		70,785 (20·4%)	0·075 (0·064, 0·085)	1·11x10-45	3·24	0·070 (0·060, 0·080)	3·35x10-29	3·05
	1478	Added salt		422,709		*Global P:*	1·74x10-35		*Global P:*	2·12x10-35	
	1478		Never/rarely		234,081 (55·4%)	Reference			Reference		
	1478		Sometimes		118,724 (28·1%)	-0·024 (-0·031, -0·018)	2·43x10-12	-1·04	-0·024 (-0·031, -0·018)	2·55x10-12	-1·06
	1478		Usually		49,402 (11·7%)	-0·038 (-0·047, -0·028)	4·44x10-15	-1·65	-0·038 (-0·047, -0·028)	4·77x10-15	-1·64
	1478		Always		20,502 (4·9%)	-0·073 (-0·087, -0·059)	1·15x10-24	-3·17	-0·073 (-0·087, -0·059)	1·32x10-24	-3·17
	1488	Tea intake		408,734	3·48 (2·68)	-0·003 (-0·006, 0·000)	0·026	-0·13	-0·004 (-0·007, -0·001)	0·017	-0·16
	1498	Coffee intake		391,072	2·12 (2·00)	-0·003 (-0·006, 0·000)	0·089	-0·13	-0·002 (-0·005, 0·001)	0·221	-0·08
	1528	Water intake		391,350	2·87 (2·13)	0·009 (0·006, 0·012)	2·71x10-08	0·39	0·008 (0·005, 0·012)	1·27x10-07	0·37

	2654	Vegetable spread type	219,677		*Global P:*	7·44x10-18		*Global P:*	4·12x10-15	
	2654	Olive oil based spread		54,213 (24·7%)	Reference			Reference		
	2654	Flora/Benecol		33,876 (15·4%)	-0·008 (-0·021, 0·005)	0·238	-0·35	-0·002 (-0·014, 0·011)	0·789	-0·08
	2654	Soft (tub) margarine		28,194 (12·8%)	-0·066 (-0·080, -0·052)	3·32x10-20	-2·88	-0·063 (-0·077, -0·049)	2·99x10-18	-2·73
	2654	Hard (block) margarine		341 (0·2%)	0·011 (-0·093, 0·114)	0·838	0·47	0·008 (-0·033, 0·049)	0·697	0·35
	2654	Polyunsaturated/sunflower		73,234 (33·3%)	-0·022 (-0·033, -0·012)	4·87x10-05	-0·97	-0·022 (-0·033, -0·011)	5·99x10-05	-0·96
	2654	Other low/reduced fat spread		21,789 (9·9%)	-0·028 (-0·044, -0·013)	2·62x10-04	-1·24	-0·018 (-0·028, -0·009)	1·86x10-04	-0·79
	2654	Other type of spread		8,030 (3·7%)	-0·024 (-0·047, -0·001)	0·037	-1·05	-0·015 (-0·035, 0·006)	0·169	-0·63
	6155	Vitamin supplement	434,860							
	6155_1	Vitamin A (yes vs no)		8,799 (2·0%)	0·015 (-0·006, 0·036)	0·159	0·65	0·015 (-0·006, 0·036)	0·159	0·65
	6155_2	Vitamin B (yes vs no)		18,809 (4·3%)	-0·004 (-0·018, 0·011)	0·599	-0·17	-0·004 (-0·018, 0·011)	0·610	-0·16
	6155_3	Vitamin C (yes vs no)		38,414 (8·8%)	0·016 (0·006, 0·027)	0·002	0·70	0·016 (0·006, 0·027)	0·002	0·71
	6155_4	Vitamin D (yes vs no)		17,567 (4·0%)	0·021 (0·006, 0·036)	0·005	0·91	0·021 (0·006, 0·036)	0·006	0·92
	6155_5	Vitamin E (yes vs no)		13,338 (3·1%)	0·019 (0·002, 0·036)	0·030	0·83	0·019 (0·002, 0·036)	0·029	0·82
	6155_6	Folic acid (vit B9) (yes vs no)		9,880 (2·3%)	-0·022 (-0·042, -0·002)	0·030	-0·96	-0·022 (-0·041, -0·002)	0·033	-0·94
	6155_7	Multivitamins (yes vs no)		95,930 (22·1%)	0·011 (0·004, 0·018)	0·002	0·48	0·011 (0·004, 0·018)	0·002	0·49
	6179	Mineral supplement	435,861							
	6179_1	Fish oil (yes vs no)		136,848 (31·4%)	0·006 (0·000, 0·013)	0·057	0·26	0·006 (0·000, 0·013)	0·054	0·28
	6179_2	Glucosamine (yes vs no)		83,394 (19·1%)	0·014 (0·007, 0·022)	1·93x10-04	0·61	0·014 (0·007, 0·022)	1·83x10-04	0·63
	6179_3	Calcium (yes vs no)		30,660 (7·0%)	0·012 (0·000, 0·024)	0·048	0·52	0·012 (0·000, 0·024)	0·045	0·52
	6179_4	Zinc (yes vs no)		18,045 (4·1%)	0·018 (0·004, 0·033)	0·014	0·78	0·018 (0·004, 0·033)	0·015	0·80
	6179_5	Iron (yes vs no)		14,515 (3·3%)	0·012 (-0·005, 0·028)	0·157	0·52	0·012 (-0·005, 0·028)	0·165	0·51
	6179_6	Selenium (yes vs no)		10,516 (2·4%)	0·028 (0·008, 0·047)	0·005	1·22	0·028 (0·009, 0·047)	0·004	1·21
Early life and sexual health	1677	Breastfed as a baby	323,147	233,570 (72·3%)	0·034 (0·027, 0·042)	2·39x10-18	1·48	0·029 (0·022, 0·037)	7·91x10-12	1·28
	1787	Maternal smoking around birth	364,690	107,180 (29·4%)	-0·054 (-0·061, -0·047)	2·94x10-52	-2·35	-0·050 (-0·057, -0·043)	9·02x10-44	-2·16
	2139	Age first sexual intercourse	367,951	19·10 (3·66)	0·035 (0·032, 0·038)	1·54x10-99	1·52	0·033 (0·030, 0·036)	5·17x10-58	1·44
	2754	Age first live birth	153,938	25·37 (4·59)	0·045 (0·040, 0·050)	5·87x10-69	1·96	0·034 (0·029, 0·038)	1·10x10-15	1·47
	2764	Age last live birth	153,638	30·31 (4·86)	0·032 (0·027, 0·037)	1·23x10-36	1·39	0·023 (0·019, 0·028)	5·51x10-14	1·02
General health	78	Bone mineral density	237,905	-0·34 (1·19)	0·001 (-0·003, 0·005)	0·605	0·04	0·000 (-0·003, 0·004)	0·874	0.00
	2178	Overall health status	420,835		*Global P:*	2·13x10-70		*Global P:*	1·63x10-70	
	2178	Excellent		69,612 (16·5%)	Reference			Reference		
	2178	Good		244,178 (58·0%)	-0·030 (-0·039, -0·022)	3·80x10-13	-1·3	-0·030 (-0·039, -0·022)	3·93x10-13	-1·32
	2178	Fair		88,236 (21·0%)	-0·068 (-0·078, -0·058)	2·86x10-42	-2·96	-0·068 (-0·078, -0·058)	1·41x10-42	-2·97
	2178	Poor		18,809 (4·5%)	-0·120 (-0·136, -0·104)	5·97x10-50	-5·22	-0·120 (-0·135, -0·104)	7·65x10-50	-5·20
	3064	Peak expiratory flow	385,708	408·89 (125·34)	0·024 (0·020, 0·028)	2·54x10-30	1·04	0·024 (0·021, 0·028)	2·38x10-34	1·06
	6149	Dental problems	421,450							
	6149_1	Mouth ulcers (yes vs no)		42,691 (10·1%)	0·014 (0·005, 0·024)	0·004	0·63	0·015 (0·005, 0·024)	0·004	0·63
	6149_2	Painful gums (yes vs no)		12,855 (3·1%)	-0·023 (-0·041, -0·006)	0·007	-1·02	-0·023 (-0·041, -0·006)	0·007	-1·02
	6149_3	Bleeding gums (yes vs no)		56,496 (13·4%)	0·018 (0·009, 0·027)	5·48x10-05	0·78	0·018 (0·009, 0·026)	6·02x10-05	0·77
	6149_4	Loose teeth (yes vs no)		18,402 (4·4%)	-0·061 (-0·076, -0·047)	1·02x10-16	-2·66	-0·061 (-0·075, -0·047)	1·38x10-16	-2·65

General health	6149_5	Toothache (yes vs no)		18,831 (4·5%)	0·000 (-0·014, 0·015)	0·953	0·02	0·000 (-0·014, 0·015)	0·952	0·02
	6149_6	Dentures (yes vs no)		69,920 (16·6%)	-0·063 (-0·071, -0·054)	1·94x10-50	-2·72	-0·062 (-0·071, -0·054)	3·74x10-50	-2·71
	30520	Potassium in urine	409,917	63·10 (33·63)	0·002 (-0·001, 0·005)	0·118	0·09	0·002 (-0·001, 0·005)	0·131	0·10
	30530	Sodium in urine	409,928	77·40 (44·03)	-0·007 (-0·010, -0·004)	3·68x10-06	-0·30	-0·007 (-0·010, -0·004)	5·58x10-06	-0·31
Physical activity	924	Walking pace	419,819		*Global P:*	8·95x10-73		*Global P:*	3·00x10-74	
	924	Slow pace		33,821 (8·1%)	Reference			Reference		
	924	Average pace		221,482 (52·8%)	0·068 (0·057, 0·080)	5·72x10-33	2·96	0·069 (0·058, 0·080)	3·21x10-34	3.00
	924	Brisk pace		164,516 (39·1%)	0·103 (0·092, 0·115)	6·23x10-68	4·48	0·104 (0·092, 0·115)	4·97x10-70	4·51
	22037	METs walking	342,455	1,038·14 (1,085·23)	-0·009 (-0·012, -0·005)	3·02x10-07	-0·39	-0·006 (-0·009, -0·003)	4·81x10-05	-0·28
	22038	METs moderate activity	342,455	931·92 (1,224·55)	-0·009 (-0·012, -0·006)	1·27x10-07	-0·39	-0·006 (-0·009, -0·003)	5·89x10-05	-0·27
	22039	METs vigorous activity	342,455	666·76 (1,140·98)	0·011 (0·008, 0·015)	8·58x10-12	0·48	0·014 (0·010, 0·017)	2·29x10-16	0·59
	22040	Total METs	342,455	2,636·47 (2,657·64)	0·003 (-0·001, 0·006)	0·114	0·13	0·006 (0·003, 0·009)	4·01x10-05	0·28
Psychosocial	1920	Mood swings	411,691	186,961 (45·4%)	-0·028 (-0·034, -0·022)	9·72x10-20	-1·22	-0·027 (-0·033, -0·021)	2·84x10-18	-1·16
	1930	Miserableness	415,000	176,981 (42·7%)	-0·021 (-0·027, -0·015)	2·63x10-11	-0·91	-0·020 (-0·026, -0·014)	6·28x10-11	-0·89
	1940	Irritability	403,170	113,003 (28·0%)	-0·009 (-0·016, -0·002)	0·008	-0·39	-0·009 (-0·016, -0·003)	0·006	-0·40
	1950	Sensitivity/ hurt feelings	410,054	227,262 (55·4%)	-0·015 (-0·021, -0·009)	2·26x10-06	-0·65	-0·014 (-0·020, -0·008)	4·56x10-06	-0·62
	1960	Fed-up feelings	413,210	167,429 (40·5%)	-0·033 (-0·039, -0·027)	7·30x10-26	-1·43	-0·032 (-0·038, -0·026)	7·26x10-25	-1·39
	1970	Nervous feelings	411,223	96,822 (23·5%)	0·000 (-0·007, 0·007)	0·899	0.00	0·000 (-0·007, 0·007)	0·982	0.00
	1980	Worrier/ anxious feelings	411,254	232,064 (56·4%)	0·001 (-0·006, 0·007)	0·867	0·04	0·001 (-0·006, 0·007)	0·859	0·02
	1990	Tense/ 'highly strung'	407,212	72,141 (17·7%)	-0·011 (-0·019, -0·003)	0·008	-0·48	-0·010 (-0·018, -0·003)	0·008	-0·45
	2000	Worry too long after embarrassment	404,972	192,982 (47·7%)	0·000 (-0·006, 0·006)	0·914	0.00	0·000 (-0·006, 0·006)	0·992	0.00
	2020	Loneliness, isolation	415,520	76,486 (18·4%)	-0·018 (-0·025, -0·010)	5·77x10-06	-0·78	-0·017 (-0·025, -0·010)	7·71x10-06	-0·76
	2030	Guilty feelings	410,889	118,149 (28·8%)	-0·006 (-0·012, 0·001)	0·094	-0·26	-0·007 (-0·013, 0·000)	0·054	-0·28
	2040	Risk taking	406,629	110,057 (27·1%)	-0·005 (-0·012, 0·002)	0·162	-0·22	-0·005 (-0·012, 0·002)	0·173	-0·21
	20127	Neuroticism score	339,183	4·11 (3·27)	-0·009 (-0·012, -0·006)	1·29x10-07	-0·39	-0·009 (-0·012, -0·006)	2·15x10-09	-0·40
Smoking	20116	Smoking	421,223		*Global P:*	8·77x10-53		*Global P:*	4·91x10-52	
	20116	Never		230,529 (54·7%)	Reference			Reference		
	20116	Previous		146,351 (34·7%)	-0·022 (-0·029, -0·016)	1·36x10-11	-0·96	-0·022 (-0·029, -0·016)	1·51x10-11	-0·97
	20116	Current		44,343 (10·5%)	-0·079 (-0·089, -0·069)	4·71x10-52	-3·43	-0·079 (-0·089, -0·068)	3·15x10-51	-3·42
	20161	Pack years of smoking	127,781	23·20 (18·01)	-0·035 (-0·041, -0·030)	4·52x10-35	-1·52	-0·027 (-0·032, -0·023)	1·81x10-14	-1·18
Socioeconomic	189	Townsend deprivation index at recruitment	422,260	-1·32 (3·08)	-0·014 (-0·017, -0·011)	1·46x10-19	-0·61	-0·014 (-0·017, -0·011)	1·37x10-19	-0·61
	806	Standing job	242,435		*Global P:*	2·57x10-26		*Global P:*	3·00x10-15	
	806	Never/rarely		85,691 (35·3%)	Reference			Reference		
	806	Sometimes		74,453 (30·7%)	-0·020 (-0·030, -0·011)	2·78x10-05	-0·87	-0·014 (-0·023, -0·006)	0·002	-0·63
	806	Usually		35,773 (14·8%)	-0·028 (-0·040, -0·016)	5·21x10-06	-1·22	-0·022 (-0·033, -0·011)	1·62x10-04	-0·96
	806	Always		46,518 (19·2%)	-0·062 (-0·073, -0·051)	4·33x10-28	-2·70	-0·045 (-0·054, -0·035)	2·27x10-15	-1·94
	816	Manual job	242,483		*Global P:*	4·93x10-28		*Global P:*	4·39x10-15	
	816	Never/rarely		158,031 (65·2%)	Reference			Reference		
	816	Sometimes		52,058 (21·5%)	-0·038 (-0·048, -0·029)	5·42x10-15	-1·65	-0·033 (-0·042, -0·023)	8·42x10-09	-1·42
	816	Usually		16,416 (6·8%)	-0·061 (-0·077, -0·045)	2·29x10-14	-2·65	-0·043 (-0·058, -0·028)	3·51x10-07	-1·86

Socioeconomic	816		Always		15,978 (6·6%)	-0·055 (-0·071, -0·040)	7·59x10-12	-2·39	-0·047 (-0·062, -0·032)	1·05x10-07	-2·04
	826	Shift job		242,179		*Global P:*	4·45x10-11		*Global P:*	6·68x10-09	
	826		Never/rarely		200,323 (82·7%)	Reference			Reference		
	826		Sometimes		18,059 (7·5%)	-0·027 (-0·042, -0·012)	3·57x10-04	-1·17	-0·026 (-0·040, -0·012)	2·98x10-04	-1·13
	826		Usually		5,168 (2·1%)	-0·048 (-0·075, -0·021)	4·22x10-04	-2·09	-0·041 (-0·065, -0·016)	0·002	-1·76
	826		Always		18,629 (7·7%)	-0·042 (-0·057, -0·028)	1·40x10-08	-1·83	-0·038 (-0·052, -0·024)	1·55x10-06	-1·66
	6138	Educational qualifications		418,349		*Global P:*	2·94x10-154		*Global P:*	1·40x10-152	
	6138		None		71,004 (17·0%)	Reference			Reference		
	6138		O-levels/CSE		70,325 (16·8%)	0·038 (0·028, 0·048)	4·64x10-13	1·19	0·037 (0·027, 0·048)	1·12x10-12	1·63
	6138		A-levels/NVQ/Other		138,330 (33·1%)	0·061 (0·052, 0·070)	5·96x10-40	2·65	0·060 (0·051, 0·069)	3·28x10-39	2·62
	6138		Degree		138,690 (33·2%)	0·116 (0·107, 0·125)	2·40x10-137	5·04	0·115 (0·106, 0·124)	4·85x10-136	5.00
	6141	Marital status		419,742	307,527 (73·3%)	0·000 (-0·007, 0·007)	0·984	0.00	0·001 (-0·006, 0·007)	0·817	0·03
	24004	Air pollution		416,537	43·84 (14·65)	-0·005 (-0·008, -0·002)	3·84x10-04	-0·22	-0·005 (-0·008, -0·002)	3·66x10-04	-0·24

Models are adjusted for age, sex, ethnicity and white blood cell count. LTL, leucocyte telomere length; UKB field, UK Biobank code from which the trait data are derived; N, available sample size for the trait; Values are shown as mean (SD) for continuous traits and as frequencies (%) for categorical variables. Reference indicates the reference category for categorical traits. For categorical variables with more than two categories a Global P has been estimated using a likelihood ratio test and P value given in the P value column. Note that the Bonferonni corrected P value for the number of tests carried out is 4·27x10-4. Traits that were significant are highlighted in green. Equivalent years of age-related change in LTL is the ratio of the trait beta and the absolute value of age beta (-0·023). Colour coding is to help identify those with effect ≥ 1 year age-related change (in absolute value) in LTL.

Gradient in years of age-related change (in absolute value) in LTL	1-1·99	2-2·99	3-3·99	4+

Supplementary Table 2: Scoring system for the primary and second healthy behaviour indices.

Component	UKB field code	Classification	Scoring for	
			Primary healthy index	Second healthy index
Body mass index	23104	<18·5 kg/m2	excluded	1
		18·5-24·9 kg/m2	1	1
		25·0-29·9 kg/m2	0	1
		≥30 kg/m^2	0	0
Smoking	20116	Never	1	1
		Previous	0	1
		Current	0	0
Diet score	Derived from touchscreen	0-3	0	0
	food frequency questionnaire	4-7	1	1
Physical activity	22040	<735 MET min/week	0	-
		≥735 MET min/week	1	-
	22032	low	-	0
		moderate	-	1
		high	-	1
Alcohol intake	Derived from weekly	Female: <5 or >15 g/day	0	-
	alcohol questionnaire	Male: <5 or >30 g/day	0	-
		Female: 5-15 g/day	1	-
		Male: 5-30 g/day	1	-

Supplementary Table 3: Multivariable analysis of 17 traits with strongest association with LTL.

			Single trait			Multiple traits					
			Available data (N=84,462)			Available data (N=84,462)			Imputed data (N=422,797)		
Group	UKB field	Trait	Beta (95% CI)	Pvalue	Equivalent years of age-related change in LTL	Beta (95% CI)	Pvalue	Equivalent years of age-related change in LTL	Beta (95% CI)	Pvalue	Equivalent years of age-related change in LTL
Diet	1329	Oily fish intake	*Global P:*	7·34x10-07		*Global P:*	0·001		*Global P:*	4·49x10-08	
	1329	Never	Reference			Reference			Reference		
	1329	Less than once a week	0·033 (0·011, 0·055)	0·004	1·43	0·027 (0·005, 0·050)	0·019	1·17	0·025 (0·014, 0·035)	3·47x10-06	1·09
	1329	Once a week	0·048 (0·026, 0·070)	1·87x10-05	2·09	0·035 (0·012, 0·058)	0·003	1·52	0·028 (0·017, 0·038)	2·11x10-07	1·22
	1329	2-4 times a week	0·071 (0·045, 0·097)	7·15x10-08	3·09	0·055 (0·028, 0·082)	5·53x10-05	2·39	0·036 (0·024, 0·047)	3·72x10-09	1·57
	1329	5+ times a week	0·083 (0·004, 0·162)	0·039	3·61	0·059 (-0·020, 0·138)	0·143	2·57	0·053 (0·022, 0·085)	9·40x10-04	2·30
	1349	Processed meat intake	*Global P:*	1·17x10-04		*Global P:*	0·173		*Global P:*	1·89x10-05	
	1349	Never	Reference			Reference			Reference		
	1349	Less than once a week	-0·033 (-0·059, -0·007)	0·013	-1·43	-0·020 (-0·046, 0·007)	0·152	-0·87	-0·016 (-0·027, -0·004)	0·007	-0·70
	1349	Once a week	-0·052 (-0·078, -0·026)	1·00x10-04	-2·26	-0·031 (-0·058, -0·004)	0·026	-1·35	-0·027 (-0·039, -0·015)	4·99x10-06	-1·17
	1349	2-4 times a week	-0·058 (-0·085, -0·032)	1·78x10-05	-2·52	-0·031 (-0·059, -0·004)	0·027	-1·35	-0·027 (-0·039, -0·015)	8·83x10-06	-1·17
	1349	5+ times a week	-0·059 (-0·099, -0·019)	0·004	-2·57	-0·031 (-0·072, 0·009)	0·132	-1·35	-0·025 (-0·044, -0·007)	0·006	-1·09
	1408	Cheese intake	*Global P:*	7·76x10-10		*Global P:*	1·88x10-05		*Global P:*	2·64x10-08	
	1408	Never	Reference			Reference			Reference		
	1408	Less than once a week	-0·011 (-0·058, 0·036)	0·645	-0·48	-0·022 (-0·069, 0·025)	0·361	-0·96	0·001 (-0·018, 0·021)	0·888	0·04
	1408	Once a week	-0·036 (-0·082, 0·010)	0·128	-1·57	-0·045 (-0·091, 0·001)	0·054	-1·96	0·002 (-0·018, 0·021)	0·875	0·09
	1408	2-4 times a week	-0·010 (-0·055, 0·034)	0·648	-0·43	-0·028 (-0·073, 0·017)	0·223	-1·22	0·002 (-0·017, 0·021)	0·839	0·09
	1408	5+ times a week	0·046 (-0·002, 0·093)	0·060	2.00	0·015 (-0·033, 0·063)	0·542	0·65	0·031 (0·011, 0·051)	0·002	1·35
	1448	Bread type	*Global P:*	8·07x10-11		*Global P:*	0·034		*Global P:*	2·24x10-04	
	1448	White	Reference			Reference			Reference		
	1448	Brown	0·048 (0·025, 0·071)	2·99x10-05	2·09	0·030 (0·007, 0·052)	0·011	1·30	0·012 (0·002, 0·022)	0·023	0·52
	1448	Wholemeal	0·058 (0·042, 0·074)	2·05x10-12	2·52	0·023 (0·005, 0·040)	0·010	1.00	0·017 (0·010, 0·025)	1·08x10-05	0·74
	1448	Other type	0·040 (0·003, 0·077)	0·034	1·74	0·016 (-0·021, 0·053)	0·391	0·70	0·017 (0·001, 0·033)	0·041	0·74
	1468	Cereal type	*Global P:*	3·43x10-13		*Global P:*	0·002		*Global P:*	1·01x10-06	
	1468	Other	Reference			Reference			Reference		
	1468	Bran cereal	0·021 (0·000, 0·042)	0·055	0·90	-0·001 (-0·023, 0·021)	0·926	-0·04	0·002 (-0·009, 0·012)	0·765	0·09
	1468	Biscuit cereal	0·005 (-0·016, 0·026)	0·645	0·21	-0·004 (-0·025, 0·017)	0·681	-0·19	-0·006 (-0·017, 0·004)	0·245	-0·26
	1468	Oat cereal	0·034 (0·014, 0·054)	7·90x10-04	1·50	0·011 (-0·009, 0·032)	0·287	0·49	0·006 (-0·004, 0·017)	0·249	0·26
	1468	Muesli	0·075 (0·055, 0·096)	8·82x10-13	3·27	0·034 (0·013, 0·056)	0·002	1·50	0·024 (0·013, 0·035)	1·97x10-05	1·04
	1478	Added salt	*Global P:*	3·40x10-04		*Global P:*	0·227		*Global P:*	7·25x10-07	
	1478	Never/rarely	Reference			Reference			Reference		
	1478	Sometimes	-0·022 (-0·037, -0·007)	0·005	-0·96	-0·010 (-0·025, 0·005)	0·187	-0·43	-0·013 (-0·020, -0·006)	2·09x10-04	-0·57
	1478	Usually	-0·016 (-0·039, 0·007)	0·167	-0·70	0·001 (-0·022, 0·024)	0·948	0·04	-0·019 (-0·028, -0·009)	1·24x10-04	-0·83
	1478	Always	-0·068 (-0·106, -0·030)	4·23x10-04	-2·96	-0·034 (-0·072, 0·005)	0·087	-1·48	-0·028 (-0·043, -0·014)	9·89x10-05	-1·22
	2654	Vegetable spread type	*Global P:*	2·77x10-04		*Global P:*	0·466		*Global P:*	0·190	
	2654	Olive oil based spread	Reference			Reference			Reference		
	2654	Flora/Benecol	-0·018 (-0·040, 0·004)	0·107	-0·78	-0·010 (-0·033, 0·012)	0·354	-0·45	-0·002 (-0·015, 0·011)	0·739	-0·09
	2654	Soft (tub) margarine	-0·050 (-0·073, -0·027)	2·16x10-05	-2·16	-0·012 (-0·035, 0·012)	0·329	-0·51	-0·020 (-0·034, -0·005)	0·007	-0·87
	2654	Hard (block) margarine	0·003 (-0·197, 0·202)	0·978	0·12	0·022 (-0·177, 0·222)	0·825	0·98	0·011 (-0·031, 0·052)	0·607	0·48
	2654	Polyunsaturated/sunflower	-0·034 (-0·051, -0·017)	7·40x10-05	-1·48	-0·019 (-0·036, -0·002)	0·027	-0·83	-0·008 (-0·019, 0·003)	0·136	-0·35
	2654	Other low/reduced fat spread	-0·030 (-0·054, -0·005)	0·017	-1·30	-0·008 (-0·032, 0·017)	0·542	-0·33	-0·003 (-0·013, 0·007)	0·546	-0·13
	2654	Other type of spread	-0·042 (-0·081, -0·003)	0·036	-1·83	-0·025 (-0·064, 0·015)	0·219	-1·07	-0·001 (-0·022, 0·020)	0·935	-0·04

Early life and sexual health	1787	Maternal smoking around birth		-0·043 (-0·057, -0·028)	5·51x10-09	-1·87		-0·029 (-0·043, -0·014)	9·14x10-05	-1·26		-0·036 (-0·043, -0·029)	1·55x10-24	-1·57
General health	2178	Overall health status		*Global P:*	4·35x10-10			*Global P:*	0·003			*Global P:*	2·16x10-07	
	2178	Excellent		Reference				Reference				Reference		
	2178	Good		-0·039 (-0·057, -0·021)	1·31x10-05	-1·70		-0·021 (-0·038, -0·003)	0·024	-0·91		-0·012 (-0·020, -0·003)	0·006	-0·52
	2178	Fair		-0·059 (-0·080, -0·037)	1·16x10-07	-2·57		-0·023 (-0·046, -0·001)	0·045	-1.00		-0·024 (-0·034, -0·014)	5·70x10-06	-1·04
	2178	Poor		-0·135 (-0·184, -0·086)	7·31x10-08	-5·87		-0·091 (-0·142, -0·041)	4·11x10-04	-3·96		-0·045 (-0·062, -0·027)	4·18x10-07	-1·96
	6149	Dental problems												
	6149_4	Loose teeth (yes vs no)		-0·041 (-0·078, -0·004)	0·028	-1·78		-0·020 (-0·057, 0·017)	0·290	-0·87		-0·035 (-0·049, -0·020)	3·25x10-06	-1·52
	6149_6	Dentures (yes vs no)		-0·046 (-0·068, -0·024)	3·91x10-05	-2.00		-0·018 (-0·041, 0·004)	0·115	-0·78		-0·029 (-0·038, -0·021)	9·20x10-12	-1·26
Physical activity	924	Walking pace		*Global P:*	6·06x10-07			*Global P:*	0·195			*Global P:*	8·55x10-14	
	924	Slow pace		Reference				Reference				Reference		
	924	Average pace		0·035 (-0·001, 0·071)	0·055	1·52		0·015 (-0·022, 0·052)	0·435	0·65		0·035 (0·023, 0·048)	9·10x10-09	1·52
	924	Brisk pace		0·067 (0·031, 0·103)	3·11x10-04	2·91		0·025 (-0·012, 0·063)	0·187	1·09		0·050 (0·037, 0·063)	3·28x10-14	2·17
Smoking	20116	Smoking		*Global P:*	7·19x10-05			*Global P:*	0·045			*Global P:*	8·37x10-17	
	20116	Never		Reference				Reference				Reference		
	20116	Previous		-0·012 (-0·026, 0·003)	0·117	-0·52		-0·004 (-0·019, 0·010)	0·551	-0·17		-0·013 (-0·020, -0·006)	1·08x10-04	-0·57
	20116	Current		-0·056 (-0·081, -0·030)	1·68x10-05	-2·43		-0·033 (-0·058, -0·007)	0·013	-1·43		-0·045 (-0·056, -0·035)	3·54x10-17	-1·96
Socioeconomic	806	Standing job		*Global P:*	5·68x10-08			*Global P:*	0·251			*Global P:*	0·159	
	806	Never/rarely		Reference				Reference				Reference		
	806	Sometimes		-0·022 (-0·038, -0·006)	0·008	-0·96		-0·011 (-0·027, 0·006)	0·212	-0·48		-0·009 (-0·019, 0·000)	0·047	-0·39
	806	Usually		-0·046 (-0·066, -0·025)	1·03x10-05	-2.00		-0·023 (-0·045, 0·000)	0·048	-1.00		-0·008 (-0·020, 0·004)	0·173	-0·35
	806	Always		-0·051 (-0·070, -0·032)	8·97x10-08	-2·22		-0·012 (-0·037, 0·012)	0·322	-0·52		-0·012 (-0·026, 0·001)	0·075	-0·52
	816	Manual job		*Global P:*	3·90x10-11			*Global P:*	0·079			*Global P:*	0·789	
	816	Never/rarely		Reference				Reference				Reference		
	816	Sometimes		-0·046 (-0·062, -0·030)	2·51x10-08	-2.00		-0·017 (-0·036, 0·002)	0·082	-0·74		-0·005 (-0·016, 0·006)	0·380	-0·22
	816	Usually		-0·067 (-0·093, -0·041)	5·23x10-07	-2·91		-0·026 (-0·056, 0·005)	0·096	-1·13		-0·006 (-0·025, 0·013)	0·534	-0·26
	816	Always		-0·039 (-0·066, -0·012)	0·005	-1·70		0·010 (-0·023, 0·043)	0·568	0·43		0·000 (-0·020, 0·020)	0·999	0.00
	826	Shift job		*Global P:*	0·013			*Global P:*	0·539			*Global P:*	0·570	
	826	Never/rarely		Reference				Reference				Reference		
	826	Sometimes		-0·034 (-0·060, -0·009)	0·008	-1·48		-0·014 (-0·040, 0·012)	0·301	-0·61		-0·006 (-0·019, 0·008)	0·413	-0·26
	826	Usually		-0·027 (-0·074, 0·020)	0·263	-1·17		0·001 (-0·046, 0·048)	0·961	0·04		-0·013 (-0·037, 0·011)	0·274	-0·57
	826	Always		-0·025 (-0·049, 0·000)	0·050	-1·09		0·012 (-0·014, 0·038)	0·369	0·52		-0·005 (-0·020, 0·010)	0·502	-0·22
	6138	Educational qualifications		*Global P:*	3·72x10-30			*Global P:*	1·44x10-09			*Global P:*	1·28x10-38	
	6138	None		Reference				Reference				Reference		
	6138	O-levels/CSE		0·022 (-0·005, 0·049)	0·108	0·96		0·005 (-0·022, 0·033)	0·715	0·22		0·014 (0·004, 0·025)	0·007	0·61
	6138	A-levels/NVQ/Other		0·054 (0·029, 0·078)	1·54x10-05	2·35		0·031 (0·006, 0·056)	0·015	1·35		0·030 (0·021, 0·040)	1·39x10-10	1·30
	6138	Degree		0·113 (0·088, 0·137)	1·70x10-19	4·91		0·065 (0·039, 0·092)	1·63x10-06	2·83		0·063 (0·052, 0·073)	1·03x10-33	2·74

LTL, leucocyte telomere length; UKB field, UK Biobank code from which the trait data are derived. Results are shown for both the subset of participants (n=84,462) with available data for all 17 traits that were Bonferroni significant and had an association with LTL equivalent to an age effect on LTL of ≥2 years and for imputed data for all participants. In addition, the single trait results for the subset of participants are also shown to compare with the single trait findings shown in Supplementary Table 1. Models are adjusted for age, sex, ethnicity and white blood cell count. UKB field, UK Biobank code from which the trait data are derived; N, available sample size for the trait; Values are shown as mean (SD) for continuous traits and as frequencies (%) for categorical variables. Reference indicates the reference category for categorical traits. For categorical variables with more than two categories a Global P has been estimated using a likelihood ratio test and P value given in the P value column. The Bonferonni corrected P value for the number of tests carried out is 4·27x10-4.

Gradient in years of age-related change (in absolute value) in LTL: 1-1·99 | 2-2·99 | 3-3·99 | 4+

Supplementary Table 4. Association of educational attainment with LTL after adjustment for potential confounders.

	Base model	Base model with complete data for additional confounders	Base model with additional confounders
Available data	n=418,349	n=328,978	
Educational qualifications, vs None			
Global P	*2·94x10-154*	*7·28x10-114*	*1·10x10-86*
O-levels/CSE	0·038 (0·028; 0·048)	0·032 (0·020; 0·044)	0·026 (0·014; 0·038)
A-levels/NVQ/Other	0·061 (0·052; 0·070)	0·057 (0·046; 0·068)	0·050 (0·039; 0·061)
Degree	0·116 (0·107; 0·125)	0·112 (0·101; 0·123)	0·099 (0·088; 0·110)
Imputed data		n=422,797	
Educational qualifications, vs None			
Global P	*1·40x10-152*	-	*7·83x10-115*
O-levels/CSE	0·037 (0·027, 0·048)	-	0·031 (0·021; 0·041)
A-levels/NVQ/Other	0·060 (0·051, 0·069)	-	0·052 (0·043; 0·062)
Degree	0·115 (0·106, 0·124)	-	0·101 (0·092; 0·111)

Base model is adjusted for age, sex, ethnicity and white blood cell. LTL, leucocyte telomere length. Additional confounders are: Townsend index of deprivation, smoking status, drinking status, body-mass index classification, physical activity status, and adherence to a healthy diet.

Supplementary Table 5: Association of primary healthy behaviour index with LTL.

	Base model				Adjusted model				Final model			
	Available data (N=329,907)		Imputed data (N=422,797)		Available data (N=328,229)		Imputed data (N=422,797)		Available data (N=306,345)		Imputed data (N=422,797)	
	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue
No of healthy behaviours, vs None	*Global P:*	*1·94x10-48*	*Global P:*	*4·35x10-61*	*Global P:*	*5·32x10-44*	*Global P:*	*1·81x10-56*	*Global P:*	*1·06x10-22*	*Global P:*	*5·81x10-26*
One	0·009 (-0·009, 0·026)	0·326	0·013 (-0·002, 0·029)	0·089	0·005 (-0·012, 0·023)	0·561	0·010 (-0·005, 0·025)	0·198	-0·002 (-0·020, 0·016)	0·845	0·003 (-0·012, 0·018)	0·703
Two	0·030 (0·014, 0·047)	3·67x10-04	0·040 (0·026, 0·054)	4·72x10-08	0·026 (0·009, 0·043)	0·003	0·035 (0·021, 0·049)	1·18x10-06	0·018 (0·000, 0·035)	0·048	0·021 (0·007, 0·035)	3·24x10-03
Three	0·055 (0·038, 0·072)	2·52x10-10	0·065 (0·051, 0·079)	5·33x10-18	0·049 (0·032, 0·066)	2·14x10-08	0·060 (0·046, 0·074)	1·44x10-15	0·034 (0·016, 0·052)	2·39x10-04	0·038 (0·024, 0·053)	3·42x10-07
Four	0·088 (0·069, 0·107)	6·61x10-20	0·096 (0·080, 0·112)	6·17x10-29	0·082 (0·063, 0·101)	2·22x10-17	0·091 (0·075, 0·108)	3·36x10-26	0·061 (0·041, 0·081)	2·28x10-09	0·062 (0·045, 0·079)	8·55x10-13
Five	0·107 (0·077, 0·137)	5·10x10-12	0·114 (0·086, 0·142)	2·66x10-15	0·103 (0·072, 0·133)	3·89x10-11	0·109 (0·081, 0·137)	3·90x10-14	0·072 (0·041, 0·104)	7·68x10-06	0·074 (0·046, 0·103)	3·39x10-07
Age, per year	-0·023 (-0·024, -0·023)	<1·00x10-300	-0·023 (-0·024, -0·023)	<1·00x10-300	-0·023 (-0·024, -0·023)	<1·00x10-300	-0·023 (-0·024, -0·023)	<1·00x10-300	-0·023 (-0·023, -0·022)	<1·00x10-300	-0·023 (-0·023, -0·022)	<1·0x10-300
Males vs Females	-0·175 (-0·181, -0·168)	<1·00x10-300	-0·174 (-0·180, -0·168)	<1·00x10-300	-0·171 (-0·177, -0·164)	<1·00x10-300	-0·170 (-0·176, -0·164)	<1·0x10-300	-0·234 (-0·261, -0·207)	7·82x10-65	-0·239 (-0·262, -0·216)	2·33x10-84
Ethnicity, vs White												
Mixed	0·132 (0·088, 0·176)	2·99x10-09	0·127 (0·089, 0·165)	7·51x10-11	0·133 (0·089, 0·176)	3·02x10-09	0·128 (0·090, 0·166)	4·55x10-11	0·118 (0·072, 0·163)	3·86x10-07	0·126 (0·088, 0·164)	9·49x10-11
Asian/ Asian British	0·024 (-0·002, 0·050)	0·066	0·031 (0·010, 0·052)	0·004	0·032 (0·006, 0·058)	0·016	0·039 (0·017, 0·060)	3·63x10-04	0·027 (0·000, 0·054)	0·054	0·036 (0·015, 0·057)	8·27x10-04
Black/ Black British	0·389 (0·360, 0·418)	2·13x10-152	0·392 (0·369, 0·416)	1·57x10-227	0·394 (0·365, 0·423)	5·24x10-154	0·395 (0·371, 0·419)	2·76x10-229	0·364 (0·330, 0·398)	1·35x10-96	0·367 (0·340, 0·394)	1·14x10-154
Chinese	0·346 (0·286, 0·407)	4·46x10-29	0·365 (0·314, 0·417)	8·64x10-44	0·347 (0·285, 0·408)	1·38x10-28	0·367 (0·315, 0·419)	3·55x10-44	0·322 (0·257, 0·388)	3·00x10-22	0·349 (0·298, 0·401)	3·23x10-40
Other ethnic group	0·157 (0·120, 0·194)	7·44x10-17	0·179 (0·148, 0·210)	2·19x10-30	0·159 (0·122, 0·196)	5·63x10-17	0·182 (0·151, 0·213)	2·24x10-31	0·152 (0·113, 0·191)	2·60x10-14	0·174 (0·143, 0·205)	8·72x10-29
WBC, per one SD higher level	-0·042 (-0·045, -0·039)	1·41x10-128	-0·043 (-0·046, -0·040)	1·98x10-172	-0·041 (-0·044, -0·037)	1·71x10-118	-0·042 (-0·045, -0·039)	9·86x10-161	-0·034 (-0·038, -0·031)	7·84x10-74	-0·035 (-0·038, -0·032)	1·76x10-105
Diabetes vs No	-		-		-0·051 (-0·067, -0·035)	2·39x10-10	-0·047 (-0·061, -0·034)	1·10x10-11	-0·028 (-0·045, -0·011)	0·001	-0·023 (-0·037, -0·009)	9·66x10-04
Cancer vs No	-		-		0·006 (-0·007, 0·018)	0·385	0·011 (0·000, 0·022)	0·056	0·008 (-0·005, 0·021)	0·232	0·012 (0·001, 0·024)	0·030
Hypertension vs No	-		-		0·019 (0·011, 0·027)	2·26x10-06	0·021 (0·014, 0·028)	1·95x10-09	0·031 (0·022, 0·039)	4·10x10-13	0·033 (0·026, 0·040)	4·79x10-20
Vascular disease vs No	-		-		-0·078 (-0·094, -0·063)	1·61x10-24	-0·081 (-0·094, -0·068)	3·12x10-34	-0·051 (-0·067, -0·035)	3·30x10-10	-0·054 (-0·067, -0·041)	1·93x10-15
Highest qualification, vs None			-		-		-					
O-level/(G)CSE	-		-		-		-		0·024 (0·011, 0·037)	2·31x10-04	0·027 (0·017, 0·038)	1·79x10-07
A-levels/NVQ/Other	-		-		-		-		0·047 (0·036, 0·058)	2·32x10-16	0·048 (0·039, 0·057)	1·36x10-25
Degree	-		-		-		-		0·095 (0·083, 0·106)	6·21x10-60	0·096 (0·086, 0·105)	5·20x10-91
Suffer from insomnia, vs Never			-				-					
Sometimes	-		-		-		-		-0·003 (-0·011, 0·006)	0·510	-0·004 (-0·012, 0·003)	0·246
Usually	-		-		-		-		-0·012 (-0·022, -0·002)	0·017	-0·011 (-0·019, -0·002)	0·013
Fed up feelings: Yes versus No	-		-		-		-		-0·013 (-0·021, -0·006)	3·96x10-04	-0·015 (-0·021, -0·008)	4·90x10-06
LDL, per one SD higher level	-		-		-		-		0·024 (0·020, 0·027)	1·92x10-36	0·023 (0·020, 0·026)	3·22x10-44
CRP, per one SD higher level	-		-		-		-		-0·015 (-0·019, -0·011)	2·52x10-14	-0·017 (-0·020, -0·013)	4·16x10-23
eGFR, per one SD higher level	-		-		-		-		-0·030 (-0·044, -0·017)	1·03x10-05	-0·034 (-0·045, -0·022)	9·59x10-09

LTL, leucocyte telomere length. Findings are shown for the subset of participants with available data to compute the index (white columns) and for the imputed data in the full cohort (blue shaded columns). The base model includes the primary healthy behaviour index, age, sex, ethnicity and white blood cell (WBC) count, while the adjusted model additionally includes self-reported diseases diagnosed by doctor (diabetes, cancer, hypertension and vascular diseases). The final model, in addition to the parameters included in the adjusted model, is also adjusted for highest educational qualification, suffering from insomnia, fed-up feelings, low-density lipoprotein (LDL), C-reactive protein (CRP) and estimated glomerular filtration rate (CKD-EPI; eGFR). All beta coefficients are for z-standardised LTL with the comparator groups specified in the table. A Global P has been estimated across the levels of the primary healthy behaviour index using a likelihood ratio test and its P value given in the P value column.

Supplementary Table 6: Participant demographics by healthy behaviour groups of the second health behaviour index.

n (%)	Overall 331,658	None 2,069 (0·62)	One 25,220 (7·60)	Two 96,777 (29·2)	Three 169,664 (51·2)	Four 37,928 (11·4)	Pvalue
zLTL	0·007 (1·00)	-0·06 (0·96)	-0·05 (1·01)	-0·02 (1·00)	0·03 (1·00)	0·03 (0·99)	8·52x10-49
Age, years	56·3 (8·06)	54·3 (7·72)	55·7 (7·84)	56·0 (8·01)	56·4 (8·13)	57·6 (7·91)	2·45x10-278
Sex, n (%)							6·45x10-136
Female	171,770 (51·8)	895 (43·3)	11,965 (47·4)	47,559 (49·1)	91,369 (53·9)	19,982 (52·7)	
Male	159,888 (48·2)	1,174 (56·7)	13,255 (52·6)	49,218 (50·9)	78,295 (46·2)	17,946 (47·3)	
Ethnicity, n (%)							4·95x10-47
White	315,856 (95·2)	1,950 (94·3)	23,825 (94·5)	91,526 (94·6)	162,164 (95·6)	36,391 (96·0)	
Mixed	1,939 (0·58)	18 (0·87)	181 (0·72)	665 (0·69)	917 (0·54)	158 (0·42)	
Asian	5,711 (1·72)	25 (1·21)	449 (1·78)	1,794 (1·85)	2,835 (1·67)	608 (1·60)	
Black	4,436 (1·34)	45 (2·17)	491 (1·95)	1,697 (1·75)	1,839 (1·08)	364 (0·96)	
Chinese	1,006 (0·30)	4 (0·19)	41 (0·16)	230 (0·24)	635 (0·37)	96 (0·25)	
Other	2,710 (0·82)	27 (1·30)	233 (0·92)	865 (0·89)	1,274 (0·75)	311 (0·82)	
White blood cell count, 10^9 cells/Litre	6·83 (1·72)	8·58 (2·01)	7·69 (1·93)	7·16 (1·79)	6·60 (1·59)	6·41 (1·54)	<1·00x10-300
Highest education, n (%)							<1·00x10-300
None	46,900 (14·1)	492 (23·9)	4,793 (19·1)	15,593 (16·2)	21,538 (12·8)	4,484 (11·9)	
O-levels/CSE/GCSE	54,143 (16·3)	414 (20·1)	4,674 (18·7)	16,688 (17·4)	27,032 (16·0)	5,335 (14·2)	
A-levels/NVQ/Other	110,429 (33·3)	688 (33·5)	8,859 (35·4)	33,338 (34·7)	55,793 (33·1)	11,751 (31·2)	
Degree	118,081 (35·6)	463 (22·5)	6,715 (26·8)	30,476 (31·7)	64,312 (38·1)	16,115 (42·8)	
Missing	*2,105 (0·63)*						
Insomnia, n (%)							3·36x10-151
Never/rarely	84,046 (25·3)	418 (20·2)	5,695 (22·6)	23,707 (24·5)	43,982 (25·9)	10,244 (27·0)	
Sometimes	157,395 (47·5)	863 (41·7)	11,071 (43·9)	45,327 (46·9)	82,025 (48·4)	18,109 (47·8)	
Usually	90,083 (27·2)	787 (38·1)	8,443 (33·5)	27,699 (28·6)	43,603 (25·7)	9,551 (25·2)	
Missing	*134 (0·04)*						
Fed-up feelings, n (%)							<1·00x10-300
No	199,467 (60·1)	794 (39·1)	12,056 (48·5)	53,518 (56·2)	107,749 (64·5)	25,350 (67·9)	
Yes	126,902 (38·3)	1,239 (60·9)	12,780 (51·5)	41,705 (43·8)	59,203 (35·5)	11,975 (32·1)	
Missing	*5,289 (1·59)*						

LDL cholesterol, mmol/L							3·95x10-27
	Mean (SD)	3·55 (0·85)	3·60 (0·94)	3·54 (0·90)	3·57 (0·87)	3·56 (0·84)	3·48 (0·83)	
	Missing, n (%)	*14,333 (4·32)*						
C-reactive protein, mg/L							<1·00x10-300
	Mean (SD)	2·42 (3·59)	4·94 (4·87)	4·15 (4·72)	3·00 (3·92)	1·98 (3·16)	1·68 (2·90)	
	Missing, n (%)	*14,421 (4·35)*						
eGFR, mg/dL							1·74x10-71
	Mean (SD)	74·5 (75·0)	61·3 (73·5)	68·6 (76·1)	70·7 (75·4)	77·7 (74·8)	74·9 (73·6)	
	Missing, n (%)	*13,912 (4·19)*						
Diabetes GP, n (%)							<1·00x10-300
	No	314,558 (94·8)	1,794 (87·4)	22,306 (88·8)	90,072 (93·3)	163,759 (96·7)	36,627 (96·7)	
	Yes	16,441 (4·96)	259 (12·6)	2,811 (11·2)	6,471 (6·70)	5,637 (3·33)	1,263 (3·33)	
	Missing	*659 (0·20)*						
Cancer GP, n (%)							0·009
	No	306,080 (92·3)	1,923 (93·3)	23,244 (92·5)	89,311 (92·6)	156,812 (92·6)	34,790 (91·9)	
	Yes	24,790 (7·47)	139 (6·74)	1,882 (7·49)	7,181 (7·44)	12,513 (7·39)	3,075 (8·12)	
	Missing	*788 (0·24)*						
Hypertension GP, n (%)							<1·00x10-300
	No	243,930 (73·6)	1,296 (62·8)	15,271 (60·7)	66,286 (68·6)	131,553 (77·6)	29,524 (78·0)	
	Yes	87,302 (26·3)	768 (37·2)	9,907 (39·4)	30,352 (31·4)	37,923 (22·4)	8,352 (22·1)	
	Missing	*426 (0·13)*						
Vascular disease GP, n (%)							6·06x10-207
	No	313,050 (94·4)	1,804 (87·4)	22,875 (90·9)	90,356 (93·5)	162,089 (95·6)	35,926 (94·9)	
	Yes	18,182 (5·48)	260 (12·6)	2,303 (9·15)	6,282 (6·50)	7,387 (4·36)	1,950 (5·15)	
	Missing	*426 (0·13)*						

Values are shown as mean (SD) for continuous traits and as frequencies (%) for categorical variables. zLTL, Z-standardised leukocyte $\log_e$ telomere length; LDL, low-density lipoproteins; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate (CKD-EPI); diseases are self-reported as diagnosed by doctor. P values are estimated using the Jonckheere-Terpstra test for trend for both continuous and categorical traits.

Supplementary Table 7: Association of second healthy behaviour index with LTL.

	Base model				Adjusted model				Final model			
	Available data (N=331,658)		Imputed data (N=422,797)		Available data (N=329,962)		Imputed data (N=422,797)		Available data (N=307,935)		Imputed data (N=422,797)	
	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue	Beta (95% CI)	Pvalue
No of healthy behaviours, vs None	*Global P:*	*1·98x10-48*	*Global P:*	*5·59x10-64*	*Global P:*	*1·49x10-44*	*Global P:*	*4·96x10-59*	*Global P:*	*3·48x10-23*	*Global P:*	*1·22x10-28*
One	0·028 (-0·016, 0·071)	0·213	0·030 (-0·004, 0·064)	0·085	0·025 (-0·019, 0·069)	0·259	0·026 (-0·008, 0·060)	0·136	0·019 (-0·027, 0·064)	0·417	0·019 (-0·015, 0·053)	0·270
Two	0·045 (0·003, 0·087)	0·038	0·062 (0·028, 0·095)	3·27x10-04	0·040 (-0·003, 0·082)	0·067	0·055 (0·022, 0·089)	0·001	0·027 (-0·017, 0·072)	0·229	0·037 (0·003, 0·070)	0·031
Three	0·083 (0·041, 0·125)	1·21x10-04	0·097 (0·064, 0·130)	9·01x10-09	0·077 (0·034, 0·119)	4·20x10-4	0·090 (0·057, 0·123)	1·05x10-07	0·057 (0·012, 0·101)	0·012	0·062 (0·029, 0·095)	2·68x10-04
Four	0·117 (0·074, 0·160)	1·06x10-07	0·131 (0·097, 0·165)	8·97x10-14	0·111 (0·068, 0·155)	5·03x10-07	0·124 (0·090, 0·158)	1·56x10-12	0·084 (0·039, 0·129)	2·91x10-04	0·090 (0·056, 0·124)	2·83x10-07
Age, per year	-0·024 (-0·024, -0·023)	<1·00x10-300	-0·024 (-0·024, -0·023)	<1·00x10-300	-0·023 (-0·024, -0·023)	<1·00x10-300	-0·024 (-0·024, -0·023)	<1·00x10-300	-0·023 (-0·023, -0·022)	<1·00x10-300	-0·023 (-0·023, -0·022)	<1·00x10-300
Males vs Females	-0·175 (-0·181, -0·168)	<1·00x10-300	-0·174 (-0·180, -0·168)	<1·00x10-300	-0·170 (-0·177, -0·164)	<1·00x10-300	-0·170 (-0·176, -0·164)	<1·00x10-300	-0·233 (-0·260, -0·206)	1·51x10-64	-0·239 (-0·262, -0·216)	1·24x10-83
Ethnicity, vs White												
Mixed	0·128 (0·085, 0·172)	6·72x10-09	0·126 (0·088, 0·164)	1·10x10-10	0·130 (0·086, 0·173)	5·69x10-09	0·127 (0·089, 0·165)	6·81x10-11	0·116 (0·071, 0·161)	5·16x10-07	0·125 (0·087, 0·163)	1·28x10-10
Asian/ Asian British	0·021 (-0·004, 0·047)	0·103	0·028 (0·007, 0·050)	0·008	0·029 (0·003, 0·055)	0·027	0·036 (0·015, 0·057)	8·45x10-04	0·025 (-0·003, 0·052)	0·078	0·034 (0·013, 0·055)	0·002
Black/ Black British	0·388 (0·359, 0·417)	1·04x10-151	0·394 (0·370, 0·418)	4·46x10-229	0·392 (0·363, 0·421)	4·07x10-153	0·396 (0·372, 0·420)	1·83x10-230	0·363 (0·329, 0·397)	2·32x10-96	0·367 (0·340, 0·394)	7·01x10-155
Chinese	0·344 (0·284, 0·405)	3·11x10-29	0·365 (0·313, 0·416)	1·10x10-43	0·344 (0·283, 0·404)	1·34x10-28	0·366 (0·315, 0·418)	4·86x10-44	0·321 (0·256, 0·385)	2·18x10-22	0·349 (0·298, 0·401)	3·69x10-40
Other ethnic group	0·158 (0·122, 0·195)	2·88x10-17	0·176 (0·145, 0·206)	2·53x10-29	0·160 (0·123, 0·197)	2·06x10-17	0·179 (0·148, 0·209)	2·95x10-30	0·155 (0·116, 0·194)	7·28x10-15	0·171 (0·141, 0·202)	5·76x10-28
WBC, per one SD higher level	-0·041 (-0·045, -0·038)	4·69x10-122	-0·042 (-0·045, -0·039)	2·40x10-158	-0·040 (-0·043, -0·037)	6·89x10-113	-0·041 (-0·044, -0·037)	2·66x10-148	-0·034 (-0·037, -0·030)	1·57x10-71	-0·034 (-0·037, -0·031)	1·99x10-99
Diabetes vs No	-		-		-0·049 (-0·065, -0·033)	9·74x10-10	-0·045 (-0·059, -0·031)	9·07x10-11	-0·027 (-0·043, -0·010)	0·002	-0·022 (-0·036, -0·008)	0·002
Cancer vs No	-		-		0·005 (-0·008, 0·017)	0·467	0·011 (-0·001, 0·022)	0·065	0·007 (-0·006, 0·020)	0·285	0·012 (0·001, 0·023)	0·034
Hypertension vs No	-		-		0·019 (0·011, 0·027)	2·59x10-06	0·021 (0·014, 0·028)	2·14x10-09	0·031 (0·022, 0·039)	4·24x10-13	0·033 (0·026, 0·040)	6·68x10-20
Vascular disease vs No	-		-		-0·081 (-0·096, -0·066)	6·80x10-26	-0·082 (-0·095, -0·069)	5·21x10-35	-0·053 (-0·069, -0·037)	6·11x10-11	-0·055 (-0·068, -0·041)	7·58x10-16
Highest qualification, vs None			-		-		-					
O-level/(G)CSE	-		-		-		-		0·024 (0·012, 0·037)	1·76x10-04	0·027 (0·017, 0·038)	2·06x10-07
A-levels/NVQ/Other	-		-		-		-		0·048 (0·037, 0·059)	3·72x10-17	0·048 (0·039, 0·057)	1·53x10-25
Degree	-		-		-		-		0·097 (0·085, 0·108)	1·12x10-62	0·096 (0·087, 0·106)	1·87x10-92
Suffer from insomnia, vs Never			-				-					
Sometimes	-		-		-		-		-0·004 (-0·012, 0·005)	0·377	-0·005 (-0·012, 0·003)	0·223
Usually	-		-		-		-		-0·013 (-0·023, -0·003)	0·010	-0·011 (-0·020, -0·003)	0·009
Fed up feelings vs No	-		-		-		-		-0·013 (-0·020, -0·006)	5·18x10-04	-0·014 (-0·020, -0·008)	9·23x10-06
LDL, per one SD higher level	-		-		-		-		0·023 (0·020, 0·027)	5·97x10-36	0·023 (0·020, 0·026)	1·29x10-43
CRP, per one SD higher level	-		-		-		-		-0·015 (-0·018, -0·011)	6·28x10-14	-0·016 (-0·020, -0·013)	4·69x10-22
eGFR, per one SD higher level	-		-		-		-		-0·030 (-0·043, -0·016)	1·50x10-05	-0·034 (-0·045, -0·022)	9·88x10-09

LTL, leucocyte telomere length. Findings are shown for the subset of participants with available data to compute the index (white columns) and for the imputed data in the full cohort (blue shaded columns). The base model includes the second healthy behaviour index, age, sex, ethnicity and white blood cell (WBC) count, while the adjusted model additionally includes self-reported diseases diagnosed by doctor (diabetes, cancer, hypertension and vascular diseases). The final model, in addition to the parameters included in the adjusted model, is also adjusted for highest educational qualification, suffering from insomnia, fed-up feelings, low-density lipoprotein (LDL), C-reactive protein (CRP) and estimated glomerular filtration rate (CKD-EPI; eGFR). All beta coefficients are for z-standardised LTL with the comparator groups specified in the table. A Global P has been estimated across the levels of the second healthy behaviour index using a likelihood ratio test and its P value given in the P value column.

Supplementary Table 8. Association of single traits with LTL after excluding prevalent cancer cases.

		Base model		P
		complete available data beta (95% CI)	excl. prevalent cancer cases beta (95% CI)	
Primary index				
No of healthy behaviours vs None, n		329,907	298,930	
	One	0·009 (-0·009; 0·026)	0·011 (-0·008; 0·029)	0·88
	Two	0·030 (0·014; 0·047)	0·031 (0·014; 0·049)	0·94
	Three	0·055 (0·038; 0·072)	0·056 (0·038; 0·074)	0·95
	Four	0·088 (0·069; 0·107)	0·086 (0·066; 0·106)	0·90
	Five	0·107 (0·077; 0·137)	0·113 (0·081; 0·145)	0·79
Second index				
No of healthy behaviours vs None, n		331,658	300,527	
	One	0·028 (-0·016; 0·071)	0·027 (-0·019; 0·073)	0·98
	Two	0·045 (0·003; 0·087)	0·044 (-0·001; 0·088)	0·97
	Three	0·083 (0·041; 0·125)	0·084 (0·039; 0·128)	0·98
	Four	0·117 (0·074; 0·160)	0·115 (0·069; 0·160)	0·94
Educational qualifications vs None, n		418,349	378,651	
	O-levels/CSE	0·038 (0·028; 0·048)	0·038 (0·027; 0·049)	0·99
	A-levels/NVQ/Other	0·061 (0·052; 0·070)	0·062 (0·052; 0·071)	0·90
	Degree	0·116 (0·107; 0·125)	0·118 (0·108; 0·127)	0·81
Walking pace vs Slow, n		419,819	379,962	
	Average pace	0·068 (0·057; 0·080)	0·069 (0·057; 0·081)	0·97
	Brisk pace	0·103 (0·092; 0·115)	0·103 (0·091; 0·116)	1.00
Oily fish intake vs Never, n		420,294	380,341	
	Less than once a week	0·040 (0·029; 0·050)	0·041 (0·031; 0·052)	0·81
	Once a week	0·051 (0·041; 0·061)	0·052 (0·041; 0·063)	0·88
	2-4 times a week	0·064 (0·052; 0·075)	0·064 (0·052; 0·076)	0·93
	5+ times a week	0·085 (0·054; 0·116)	0·092 (0·059; 0·125)	0·78
Smoking status vs Never, n		421,223	381,232	
	Previous	-0·022 (-0·029; -0·016)	-0·022 (-0·029; -0·015)	0·98
	Current	-0·079 (-0·089; -0·069)	-0·079 (-0·090; -0·068)	0·92
Overall health status vs Excellent, n		420,835	380,878	
	Good	-0·030 (-0·039; -0·022)	-0·031 (-0·040; -0·022)	0·93
	Fair	-0·068 (-0·078; -0·058)	-0·068 (-0·078; -0·058)	1.00
	Poor	-0·120 (-0·136; -0·104)	-0·125 (-0·142; -0·108)	0·68

LTL, leucocyte telomere length. Base model was adjusted for age, sex, ethnicity and white blood cell. Two-sample t-test with equal variances was used to derive the Pvalues for the difference between the regression coefficients of the two models. We identified 40,165 cases who reported, at recruitment, a history of one or more of 19 different cancer types (i.e., bladder, ovary, brain, breast, cervical, colorectal, head and neck, kidney, liver, lung, esophageal, pancreas, prostate, skin, small intestine, stomach, testicular, thyroid, uterus).

Supplementary Table 9: Bi-directional Mendelian Randomisation analysis of the association between LTL and years spent in education (Supplementary Table 9a); smoking initiation (Supplementary Table 9b); and smoking burden (Supplementary Table 9c).

a Years spent in education on LTL - 1267 SNPs

Method of estimation	Beta (95% CI)	Pvalue	I2
Inverse-variance weighted	0·096 (0·080, 0·113)	3·19x10-30	51·4
Egger (for pleiotropy)	-	0·146	
Weighted median	0·089 (0·071, 0·108)	5·36x10-21	
Robust adjusted profile score	0·101 (0·089, 0·112)	<1·00x10-300	

LTL on years spent in education - 87 SNPs

Method of estimation	Beta (95% CI)	Pvalue	I2
Inverse-variance weighted	0·005 (-0·020, 0·030)	0·702	63·9
Egger (for pleiotropy)	-	0·018	
Weighted median	-0·009 (-0·036, 0·018)	0·497	
Robust adjusted profile score	0·005 (-0·010, 0·020)	0·517	

b Initiation of regular smoking on LTL - 374 SNPs

Method of estimation	Beta (95% CI)	Pvalue	I2
Inverse-variance weighted	-0·057 (-0·074, -0·040)	1·42x10-10	52·6
Egger (for pleiotropy)	-	0·794	
Weighted median	-0·062 (-0·081, -0·043)	1·03x10-10	
Robust adjusted profile score	-0·060 (-0·072, -0·048)	<1·00x10-300	

LTL on initiation of regular smoking - 89 SNPs

Method of estimation	Beta (95% CI)	Pvalue	I2
Inverse-variance weighted	0·007 (-0·018, 0·032)	0·608	9·8
Egger (for pleiotropy)	-	0·326	
Weighted median	-0·005 (-0·042, 0·032)	0·789	
Robust adjusted profile score	0·007 (-0·017, 0·031)	0·589	

c Smoking intensity on LTL - 55 SNPs

Method of estimation	Beta (95% CI)	Pvalue	I2
Inverse-variance weighted	-0·064 (-0·103, -0·026)	0·001	62·2
Egger (for pleiotropy)	-	0·186	
Weighted median	-0·057 (-0·099, -0·015)	0·008	
Robust adjusted profile score	-0·066 (-0·090, -0·043)	3·67x10-8	

LTL on smoking intensity - 89 SNPs

Method of estimation	Beta (95% CI)	Pvalue	I2
Inverse-variance weighted	-0·019 (-0·073, 0·036)	0·502	23·9
Egger (for pleiotropy)	-	0·887	
Weighted median	-0·029 (-0·109, 0·051)	0·480	
Robust adjusted profile score	-0·019 (-0·067, 0·029)	0·440	

LTL, leucocyte telomere length. In each table the results are shown for LTL as the outcome and LTL as the predictor with the corresponding number of genetic variants (SNPs) used in each analysis. The results of different MR tests are shown (see Supplementary Methods for explanation of each test).

Supplementary Table 10: Association of selected diseases with LTL overall and stratified by number of healthy behaviours.

		Base				Full			
Diseases		**Overall**	**HBI: 0-1**	**HBI: 2-3**	**HBI: 4-5**	**Overall**	**HBI: 0-1**	**HBI: 2-3**	**HBI: 4-5**
Not sex specific									
Melanoma	N	327,212	83,033	203,393	40,786	303,876	76,876	188,890	38,110
	n (%) incident cases	1,782 (0·54)	397 (0·48)	1,148 (0·56)	237 (0·58)	1,666 (0·55)	367 (0·48)	1,072 (0·57)	227 (0·60)
	HR (95% CI)	1·12 (1·05, 1·21)	1·10 (0·95, 1·28)	1·13 (1·04, 1·24)	1·10 (0·91, 1·34)	1·14 (1·06, 1·23)	1·15 (0·98, 1·34)	1·13 (1·04, 1·24)	1·13 (0·93, 1·38)
	Interaction P	-	-	0·693	0·701	-	-	0·911	0·943
Brain cancer	N	329,677	83,597	204,931	41,149	306,140	77,384	190,310	38,446
	n (%) incident cases	623 (0·19)	176 (0·21)	377 (0·18)	70 (0·17)	586 (0·19)	163 (0·21)	356 (0·19)	67 (0·17)
	HR (95% CI)	1·25 (1·11, 1·41)	1·29 (1·03, 1·61)	1·24 (1·07, 1·45)	1·20 (0·84, 1·71)	1·26 (1·12, 1·42)	1·32 (1·05, 1·66)	1·25 (1·07, 1·46)	1·18 (0·82, 1·69)
	Interaction P	-	-	0·599	0·644	-	-	0·469	0·528
Kidney cancer	N	329,397	83,501	204,769	41,127	305,868	77,294	190,154	38,420
	n (%) incident cases	1,088 (0·33)	379 (0·45)	635 (0·31)	74 (0·18)	1,002 (0·33)	351 (0·45)	584 (0·31)	67 (0·17)
	HR (95% CI)	1·20 (1·10, 1·32)	1·33 (1·15, 1·55)	1·14 (1·02, 1·29)	1·21 (0·86, 1·71)	1·22 (1·11, 1·34)	1·34 (1·15, 1·57)	1·15 (1·02, 1·30)	1·26 (0·88, 1·81)
	Interaction P	-	-	0·084	0·298	-	-	0·084	0·436
Thyroid cancer	N	329,568	83,574	204,868	41,126	306,036	77,363	190,252	38,421
	n (%) incident cases	248 (0·08)	65 (0·08)	160 (0·08)	23 (0·06)	226 (0·07)	58 (0·07)	149 (0·08)	19 (0·05)
	HR (95% CI)	1·53 (1·27, 1·83)	1·50 (1·05, 2·13)	1·51 (1·21, 1·90)	1·73 (0·95, 3·15)	1·51 (1·25, 1·82)	1·51 (1·04, 2·19)	1·45 (1·14, 1·83)	2·05 (1·10, 3·84)
	Interaction P	-	-	0·900	0·621	-	-	0·968	0·357
Sarcoma	N	329,673	83,595	204,938	41,140	306,126	77,383	190,310	38,433
	n (%) incident cases	242 (0·07)	65 (0·08)	153 (0·07)	24 (0·06)	223 (0·07)	61 (0·08)	138 (0·07)	24 (0·06)
	HR (95% CI)	1·24 (1·03, 1·50)	1·56 (1·10, 2·23)	1·31 (1·04, 1·66)	0·47 (0·27, 0·84)	1·23 (1·01, 1·50)	1·54 (1·07, 2·22)	1·31 (1·03, 1·68)	0·47 (0·26, 0·83)
	Interaction P	-	-	0·445	0·002	-	-	0·519	0·002
Coronary artery disease	N	316,160	78,508	197,440	40,212	293,685	72,719	183,398	37,568
	n (%) incident cases	17,782 (5·62)	5,825 (7·42)	10,542 (5·34)	1,415 (3·52)	16,401 (5·58)	5,383 (7·40)	9,696 (5·29)	1,322 (3·52)
	HR (95% CI)	0·92 (0·90, 0·94)	0·94 (0·90, 0·98)	0·92 (0·90, 0·95)	0·89 (0·83, 0·97)	0·94 (0·91, 0·96)	0·95 (0·92, 0·99)	0·93 (0·91, 0·96)	0·90 (0·83, 0·98)
	Interaction P	-	-	0·562	0·301	-	-	0·414	0·228
Coeliac disease	N	328,544	83,362	204,184	40,998	305,081	77,166	189,613	38,302
	n (%) incident cases	891 (0·27)	217 (0·26)	543 (0·27)	131 (0·32)	817 (0·27)	200 (0·26)	496 (0·26)	121 (0·32)
	HR (95% CI)	0·82 (0·74, 0·90)	0·86 (0·71, 1·05)	0·79 (0·69, 0·89)	0·85 (0·66, 1·11)	0·80 (0·72, 0·89)	0·86 (0·70, 1·06)	0·77 (0·68, 0·88)	0·84 (0·64, 1·11)
	Interaction P	-	-	0·386	0·907	-	-	0·326	0·985
Liver cirrhosis	N	328,686	83,162	204,422	41,102	305,213	76,979	189,834	38,400
	n (%) incident cases	1,366 (0·42)	631 (0·76)	693 (0·34)	42 (0·10)	1,247 (0·41)	578 (0·75)	631 (0·33)	38 (0·10)
	HR (95% CI)	0·69 (0·64, 0·75)	0·73 (0·65, 0·82)	0·68 (0·61, 0·76)	0·64 (0·40, 1·01)	0·72 (0·67, 0·78)	0·75 (0·66, 0·85)	0·72 (0·64, 0·80)	0·70 (0·43, 1·15)
	Interaction P	-	-	0·387	0·388	-	-	0·594	0·46

Colorectal polyps	N	322,398	81,101	200,730	40,567	299,429	75,083	186,441	37,905
	n (%) incident cases	24,066 (7·46)	7,652 (9·44)	14,283 (7·12)	2,131 (5·25)	22,306 (7·45)	7,102 (9·46)	13,214 (7·09)	1,990 (5·25)
	HR (95% CI)	1·02 (1·00, 1·04)	1·01 (0·98, 1·05)	1·03 (1·01, 1·06)	1·02 (0·96, 1·09)	1·03 (1·01, 1·05)	1·03 (0·99, 1·06)	1·04 (1·01, 1·07)	1·03 (0·96, 1·10)
	Interaction P	-	-	0·487	0·681	-	-	0·644	0·854
Hypothyroidism	N	314,247	78,940	195,560	39,747	291,822	73,098	181,597	37,127
	n (%) incident cases	6,153 (1·96)	1,801 (2·28)	3,785 (1·94)	567 (1·43)	5,673 (1·94)	1,650 (2·26)	3,493 (1·92)	530 (1·43)
	HR (95% CI)	0·90 (0·87, 0·94)	0·85 (0·79, 0·91)	0·94 (0·89, 0·98)	0·87 (0·77, 0·99)	0·92 (0·88, 0·95)	0·85 (0·79, 0·92)	0·95 (0·91, 1·00)	0·89 (0·78, 1·01)
	Interaction P	-	-	0·025	0·684	-	-	0·026	0·729
Kidney stones	N	325,081	82,246	202,095	40,740	301,874	76,141	187,668	38,065
	n (%) incident cases	3,530 (1·09)	1,080 (1·31)	2,156 (1·07)	294 (0·72)	3,264 (1·08)	988 (1·30)	1,998 (1·06)	278 (0·73)
	HR (95% CI)	1·07 (1·01, 1·12)	1·08 (0·99, 1·18)	1·04 (0·97, 1·10)	1·32 (1·11, 1·57)	1·08 (1·03, 1·14)	1·10 (1·00, 1·21)	1·04 (0·97, 1·11)	1·39 (1·17, 1·66)
	Interaction P	-	-	0·324	0·071	-	-	0·181	0·055
Atopic dermatitis	N	320,561	81,192	199,432	39,937	297,608	75,149	185,145	37,314
	n (%) incident cases	582 (0·18)	146 (0·18)	361 (0·18)	75 (0·19)	554 (0·19)	141 (0·19)	344 (0·19)	69 (0·18)
	HR (95% CI)	0·87 (0·77, 0·98)	0·91 (0·71, 1·16)	0·85 (0·73, 0·99)	0·88 (0·63, 1·25)	0·86 (0·76, 0·98)	0·88 (0·69, 1·14)	0·85 (0·72, 1·00)	0·89 (0·62, 1·28)
	Interaction P	-	-	0·518	0·725	-	-	0·791	0·825
Rheumatoid arthritis	N	326,068	82,281	202,878	40,909	302,798	76,188	188,398	38,212
	n (%) incident cases	2,958 (0·91)	1,041 (1·27)	1,708 (0·84)	209 (0·51)	2,722 (0·90)	959 (1·26)	1,566 (0·83)	197 (0·52)
	HR (95% CI)	0·93 (0·88, 0·98)	0·97 (0·89, 1·06)	0·91 (0·85, 0·98)	0·95 (0·77, 1·16)	0·96 (0·91, 1·02)	0·99 (0·89, 1·08)	0·95 (0·88, 1·02)	1·01 (0·82, 1·25)
	Interaction P	-	-	0·246	0·527	-	-	0·375	0·933
Multiple sclerosis	N	328,870	83,303	204,471	41,096	305,381	77,118	189,871	38,392
	n (%) incident cases	284 (0·09)	97 (0·12)	161 (0·08)	26 (0·06)	270 (0·09)	90 (0·12)	154 (0·08)	26 (0·07)
	HR (95% CI)	1·30 (1·10, 1·55)	1·27 (0·95, 1·71)	1·29 (1·03, 1·62)	1·62 (0·92, 2·85)	1·33 (1·11, 1·58)	1·31 (0·96, 1·78)	1·31 (1·03, 1·65)	1·61 (0·91, 2·83)
	Interaction P	-	-	1.000	0·612	-	-	0·917	0·678
Meniere's disease	N	328,912	83,367	204,472	41,073	305,410	77,169	189,871	38,370
	n (%) incident cases	357 (0·11)	97 (0·12)	219 (0·11)	41 (0·10)	332 (0·11)	92 (0·12)	200 (0·11)	40 (0·10)
	HR (95% CI)	1·10 (0·94, 1·28)	1·04 (0·77, 1·40)	1·15 (0·94, 1·41)	0·96 (0·60, 1·52)	1·11 (0·95, 1·31)	1·07 (0·78, 1·45)	1·17 (0·95, 1·44)	0·96 (0·59, 1·54)
	Interaction P	-	-	0·483	0·810	-	-	0·591	0·712
Men specific									
Prostate	N	156,898	41,939	96,447	18,512	145,664	38,781	89,578	17,305
	n (%) incident cases	6,502 (4·14)	1,678 (4·00)	4,048 (4·20)	776 (4·19)	6,017 (4·13)	1,546 (3·99)	3,742 (4·18)	729 (4·21)
	HR (95% CI)	1·16 (1·12, 1·21)	1·20 (1·11, 1·29)	1·14 (1·09, 1·20)	1·19 (1·07, 1·32)	1·15 (1·11, 1·20)	1·18 (1·10, 1·27)	1·13 (1·08, 1·19)	1·20 (1·08, 1·34)
	Interaction P	-	-	0·213	0·756	-	-	0·411	0·796

Bening prostatic hyperplasia	N	151,782	40,596	93,298	17,888	140,954	37,570	86,658	16,726
	n (%) incident cases	10,871 (7·16)	3,146 (7·75)	6,583 (7·06)	1,142 (6·38)	10,038 (7·12)	2,897 (7·71)	6,078 (7·01)	1,063 (6·36)
	HR (95% CI)	1·11 (1·08, 1·15)	1·14 (1·08, 1·20)	1·10 (1·06, 1·14)	1·16 (1·06, 1·27)	1·12 (1·09, 1·15)	1·14 (1·08, 1·20)	1·10 (1·06, 1·14)	1·19 (1·09, 1·31)
	Interaction P	-	-	0·197	0·851	-	-	0·268	0·583
Women specific									
Ovarian cyst	N	162,515	38,939	102,091	21,485	150,926	36,069	94,789	20,068
	n (%) incident cases	2,239 (1·38)	581 (1·49)	1,394 (1·37)	264 (1·23)	2,071 (1·37)	545 (1·51)	1,284 (1·35)	242 (1·21)
	HR (95% CI)	1·10 (1·03, 1·17)	1·21 (1·07, 1·37)	1·07 (0·99, 1·16)	1·04 (0·86, 1·24)	1·11 (1·04, 1·18)	1·21 (1·07, 1·37)	1·09 (1·00, 1·18)	1·04 (0·86, 1·25)
	Interaction P	-	-	0·074	0·108	-	-	0·168	0·127
Breast cyst	N	165,844	39,971	104,163	21,710	154,023	37,044	96,706	20,273
	n (%) incident cases	493 (0·30)	132 (0·33)	295 (0·28)	66 (0·30)	452 (0·29)	122 (0·33)	269 (0·28)	61 (0·30)
	HR (95% CI)	1·10 (0·96, 1·26)	1·21 (0·94, 1·57)	1·14 (0·96, 1·35)	0·79 (0·55, 1·14)	1·12 (0·97, 1·28)	1·17 (0·89, 1·53)	1·19 (1·00, 1·42)	0·76 (0·52, 1·11)
	Interaction P	-	-	0·628	0·053	-	-	0·852	0·117
Bening breast lump	N	168,144	40,520	105,589	22,035	156,160	37,542	98,046	20,572
	n (%) incident cases	676 (0·40)	171 (0·42)	439 (0·42)	66 (0·30)	625 (0·40)	162 (0·43)	401 (0·41)	62 (0·30)
	HR (95% CI)	1·14 (1·02, 1·28)	0·98 (0·78, 1·23)	1·16 (1·01, 1·33)	1·56 (1·09, 2·24)	1·16 (1·03, 1·31)	1·04 (0·82, 1·31)	1·15 (1·00, 1·33)	1·64 (1·14, 2·37)
	Interaction P	-	-	0·928	0·013	-	-	0·377	0·024
Uterine polyps	N	163,956	39,482	102,867	21,607	152,278	36,574	95,528	20,176
	n (%) incident cases	3,723 (2·27)	980 (2·48)	2,370 (2·30)	373 (1·73)	3,443 (2·26)	905 (2·47)	2,189 (2·29)	349 (1·73)
	HR (95% CI)	1·16 (1·10, 1·22)	1·24 (1·13, 1·36)	1·12 (1·06, 1·19)	1·22 (1·05, 1·42)	1·17 (1·11, 1·23)	1·26 (1·14, 1·39)	1·13 (1·06, 1·20)	1·20 (1·03, 1·41)
	Interaction P	-	-	0·143	0·937	-	-	0·121	0·873
Uterine fibroid	N	158,962	38,160	99,791	21,011	147,673	35,360	92,693	19,620
	n (%) incident cases	3,130 (1·97)	779 (2·04)	1,997 (2·00)	354 (1·68)	2,917 (1·98)	738 (2·09)	1,855 (2·00)	324 (1·65)
	HR (95% CI)	1·28 (1·22, 1·35)	1·31 (1·18, 1·46)	1·29 (1·21, 1·37)	1·20 (1·02, 1·40)	1·30 (1·23, 1·37)	1·31 (1·18, 1·46)	1·31 (1·23, 1·40)	1·20 (1·02, 1·42)
	Interaction P	-	-	0·640	0·308	-	-	0·716	0·234

LTL, leucocyte telomere length. The base model is adjusted for age, sex, ethnicity and white blood cell count, whereas the full model is additionally adjusted for self-reported diseases diagnosed by doctor (diabetes, cancer, hypertension, vascular disease), educational level, insomnia, fed-up feelings, and low-density cholesterol, C-reactive protein, estimated glomerular filtration rate (CKD-EPI). N, available sample size; n, number of cases. The P value of the interaction term between the telomere length and the number of healthy behaviours is given in the "Interaction P" row. The selected diseases were those previously identified (Codd V, et al. *Nat Gen* . 2021) to be directionally concordant between mendelian randomisation and observational data analyses at Bonferroni (4·10x10-4) or nominal (5·00x10-2) significance level. In this analysis we examined 22 diseases during two modelling procedures, therefore the Bonferroni significance level was set at 1·14x10-3.