

Table S1

Subtelomere		Age group	35	45	55	65	P KW*	P GLM [†]
		Stat	a	b	c	d		
5p	CpG 1	Median N	0.680 (0.630-0.740) ^{b,c,d} 467	0.700 (0.640-0.760) ^{a,d} 543	0.715 (0.660-0.760) ^a 572	0.720 (0.660-0.775) ^{a,b} 548	< 0.001	< 0.001
	CpG 2	Median N	0.760 (0.695-0.810) ^d 460	0.760 (0.700-0.810) ^d 521	0.760 (0.710-0.830) 575	0.780 (0.710-0.830) ^{a,b} 540	0.014	0.037
	CpG 5	Median N	0.640 (0.560-0.700) ^{c,d} 469	0.650 (0.580-0.710) 532	0.650 (0.590-0.730) ^a 583	0.660 (0.580-0.750) ^a 557	< 0.001	< 0.001
	5p mean	Median N	0.763 (0.735-0.795) ^{c,d} 468	0.773 (0.738-0.805) ^d 537	0.778 (0.743-0.810) ^a 579	0.788 (0.750-0.818) ^{a,b} 552	< 0.001	< 0.001
21q	CpG 1.2	Median N	0.430 (0.360-0.520) 469	0.430 (0.370-0.510) 533	0.440 (0.360-0.520) 578	0.450 (0.370-0.540) 551	0.660	0.018
	CpG 3	Median N	0.480 (0.410-0.550) ^d 466	0.480 (0.420-0.560) ^d 535	0.480 (0.420-0.560) 572	0.500 (0.420-0.590) ^{a,b} 553	0.002	< 0.001
	CpG 4	Median N	0.640 (0.560-0.730) 468	0.650 (0.580-0.720) 538	0.650 (0.570-0.730) 579	0.660 (0.570-0.755) 560	0.047	0.009
	CpG 5	Median N	0.390 (0.340-0.460) ^d 467	0.400 (0.350-0.450) 535	0.400 (0.340-0.460) 577	0.410 (0.350-0.480) ^a 554	0.016	0.002
	CpG 8	Median N	0.560 (0.490-0.620) ^d 465	0.560 (0.500-0.630) ^d 534	0.570 (0.500-0.640) ^d 579	0.590 (0.510-0.670) ^{a,b,c} 556	< 0.001	< 0.001
	CpG 10-14	Median N	0.650 (0.580-0.710) ^d 468	0.650 (0.590-0.720) ^d 540	0.660 (0.590-0.730) ^d 581	0.670 (0.600-0.750) ^{a,b,c} 559	< 0.001	< 0.001
	CpG 15	Median N	0.700 (0.640-0.760) ^d 469	0.710 (0.650-0.770) ^d 540	0.710 (0.650-0.780) 583	0.730 (0.660-0.800) ^{a,b} 558	< 0.001	< 0.001
	CpG 16.17	Median N	0.580 (0.510-0.660) ^d 472	0.580 (0.520-0.655) ^d 540	0.590 (0.520-0.670) ^d 584	0.610 (0.540-0.700) ^{a,b,c} 554	< 0.001	< 0.001
	CpG 18.19	Median N	0.640 (0.580-0.700) ^{c,d} 466	0.650 (0.590-0.720) ^d 541	0.660 (0.600-0.730) ^{a,d} 581	0.670 (0.610-0.760) ^{a,b,c} 558	< 0.001	< 0.001
	CpG 20.21	Median N	0.715 (0.660-0.770) ^{c,d} 466	0.720 (0.670-0.790) ^d 537	0.730 (0.670-0.800) ^a 586	0.750 (0.680-0.820) ^{a,b} 556	< 0.001	< 0.001
	21q mean	Median N	0.616 (0.553-0.679) ^d 473	0.623 (0.569-0.690) ^d 545	0.630 (0.564-0.701) ^d 589	0.649 (0.575-0.724) ^{a,b,c} 560	< 0.001	< 0.001

Table S2

		Parametric*	Non parametric*	
5p	CpG 1	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.149 < 0.001 0.108; 0.193 2130	0.155 < 0.001 0.115; 0.199 2130
	CpG 2	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.052 0.018 0.010; 0.096 2096	0.068 0.002 0.027; 0.110 2096
	CpG 5	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.100 < 0.001 0.057; 0.142 2141	0.098 < 0.001 0.053; 0.144 2141
	Mean	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.132 < 0.001 0.090; 0.173 2136	0.140 < 0.001 0.100; 0.192 2136
21q	CpG 1.2	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.063 0.003 0.025; 0.105 2131	0.057 0.008 0.018; 0.099 2131
	CpG 3	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.087 < 0.001 0.042; 0.126 2126	0.080 < 0.001 0.035; 0.121 2126
	CpG 4	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.059 0.006 0.017; 0.102 2145	0.049 0.022 0.007; 0.095 2145
	CpG 5	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.072 0.001 0.030; 0.116 2133	0.064 0.003 0.021; 0.104 2133
	CpG 8	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.108 < 0.001 0.062; 0.149 2134	0.096 < 0.001 0.053; 0.138 2134
	10.11.12.1	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.096 < 0.001 0.055; 0.134 2148	0.091 < 0.001 0.048; 0.135 2148
	CpG 15	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.101 < 0.001 0.056; 0.141 2150	0.099 < 0.001 0.060; 0.142 2150
	CpG 16.17	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.103 < 0.001 0.062; 0.143 2150	0.098 < 0.001 0.057; 0.140 2150
	CpG 18.19	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.132 < 0.001 0.090; 0.174 2146	0.128 < 0.001 0.085; 0.166 2146
	CpG 20.21	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.118 < 0.001 0.076; 0.160 2145	0.114 < 0.001 0.072; 0.155 2145
	Mean	Correlation coefficient Sig. (2-tailed) 95% C.I. N	0.111 < 0.001 0.065; 0.156 2146	0.105 < 0.001 0.063; 0.148 2146

Table S3

	Method	Method details	R vs Age (Pearson)	p	R vs Age (Spearman)	p
1	Linear Regression	All variables entered in a single step (Enter)	0.176	< 0.001	0.174	< 0.001
2	Linear Regression	Stepwise	0.162	< 0.001	0.160	< 0.001
3	Linear Regression	Backward	0.167	< 0.001	0.163	< 0.001
4	Automatic Linear regression	Standard Model (Forward method)	0.153	< 0.001	0.155	< 0.001
5	Automatic Linear regression	Standard Model (Enter method)	0.158	< 0.001	0.156	< 0.001
6	Automatic Linear regression	Boosting (Enter method)	0.156	< 0.001	0.162	< 0.001
7	Linear Regression (after log transformation)	All variables entered in a single step (Enter)	0.172	< 0.001	0.171	< 0.001
8	Linear regression with variables selected by Principal Component Analysis	Factor Analysis	0.133	< 0.001	0.132	< 0.001

Table S4

Linear regression model*

R	R ²	Adjusted R ²	Estimate S.E.	F (anova)	Sig. (anova)
0.254	0.065	0.058	11.009	10.330	< 0.001

Coefficients		USTD		STD			Bootstrap for Coefficients			95% C.I.	
		B	S.E.	Beta	t	Sig.	Bias	S.E.	Sig.	Lower	Upper
	(Constant)	21.206	4.516		4.696	< 0.001	0.076	4.413	0.001	12.427	29.883
5p	CpG 1	17.567	3.278	0.124	5.360	< 0.001	0.012	3.224	0.001	11.500	23.882
	CpG 2	2.043	3.009	0.016	0.679	0.497	0.016	3.121	0.520	-3.603	8.159
	CpG 5	7.568	2.485	0.069	3.045	0.002	-0.031	2.504	0.001	2.641	12.413
21q	CpG 1.2	-1.100	3.830	-0.011	-0.287	0.774	-0.116	3.717	0.757	-8.739	5.916
	CpG 3	6.686	6.997	0.062	0.956	0.339	0.081	6.680	0.315	-6.970	20.291
	CpG 4	-23.427	5.246	-0.235	-4.466	< 0.001	0.133	5.047	0.001	-32.629	-13.344
	CpG 5	-1.450	7.021	-0.011	-0.207	0.836	-0.134	7.093	0.834	-14.246	11.993
	CpG 8	-2.368	11.177	-0.022	-0.212	0.832	-0.242	11.029	0.818	-23.953	18.021
	CpG 10-14	-19.228	10.812	-0.162	-1.778	0.075	-0.560	11.052	0.083	-39.824	0.334
	CpG 15	10.848	9.198	0.084	1.179	0.238	-0.111	9.173	0.250	-6.926	28.140
	CpG 16.17	-5.261	12.636	-0.048	-0.416	0.677	0.380	11.870	0.689	-28.755	18.476
	CpG 18.19	35.614	11.300	0.292	3.152	0.002	0.519	11.277	0.004	13.066	58.387
	CpG 20.21	20.190	11.534	0.151	1.751	0.080	-0.121	11.262	0.073	-1.144	41.303

Table S5

	Stat	N	Median (IQ)	P KW ^s
Age group, RASIG				
35	a	494	54.828 (53.106 - 56.465) ^{b,c,d}	<0.001
45	b	576	55.215 (53.375 - 57.389) ^{a,c,d}	
55	c	628	56.106 (54.214 - 58.007) ^{a,b,d}	
65	d	610	56.688 (54.692 - 58.741) ^{a,b,c}	
GO*	a	457	55.987 (54.188 - 57.736) ^c	0.040
SGO*	b	242	56.244 (54.433 - 57.741)	
RASIG*	c	1048	56.399 (54.421 - 58.295) ^a	
DS†	a	34	56.115 (54.611 - 58.080) ^b	0.018
RASIG†	b	197	54.977 (53.173 - 56.744) ^a	

Table S6

	MAST vs age		MAST vs telomere length		Telomere length vs age	
	Spearman	Pearson	Spearman	Pearson	Spearman	Pearson
Correl. coeff.	0.269	0.274	-0.049	-0.071	-0.151	-0.153
Sig. (2-tailed)	< 0.001	< 0.001	0.050	0.005	< 0.001	< 0.001
95% C.I.	0.219; 0.311	0.229; 0.317	-0.103; -0.004	-0.122; -0.019	-0.201; -0.102	-0.201; -0.105
N	1596		1596		1596	

Table S7

Factor	Stat	N	Median (IQ)	MAST	
				P KW* (ϵ^2)	P GLM† (η^2)
Recruitment centre					
Finland	a	93	56.159 (54.040 - 58.251) ^c	<0.001 (0.016)	<0.001 (0.015) [§]
Italy	b	398	55.650 (53.568 - 57.638)		
Austria	c	399	54.865 (52.980 - 57.068) ^{a,d,e,f,g}		
Greece	d	392	55.972 (54.238 - 57.958) ^c		
Poland	e	406	56.039 (54.052 - 57.895) ^c		
Belgium	f	262	55.971 (54.050 - 57.419) ^c		
Germany	g	358	55.838 (54.113 - 57.668) ^c		
Sex					
F	a	1189	55.865 (53.826 - 57.800)	0.153 (0.002)	0.054 (0.002) [‡]
M	b	1119	55.722 (53.761 - 57.555)		
Classes of BMI (Kg/m²)					
< 25	a	1032	55.530 (53.577 - 57.378)	0.002 (0.007)	0.085 (0.009) [°]
25 to < 30	b	872	56.048 (54.131 - 57.866) ^c		
30 and over	c	399	55.845 (53.963 - 58.077) ^b		

Table S8

Factor	Stat	N	Median (IQ)	MAST		
				P KW* (ϵ^2)	P GLM† (η^2)	
Vegetables consumption	< 1 serv./day	a	902	55.702 (53.818 - 57.437)	0.378 (0.001)	0.884 (0.002)
	= 1 serv./day	b	1049	55.852 (53.831 - 57.855)		
	≥ 2 serv./day	c	357	55.722 (53.674 - 57.585)		
Fruit consumption	< 1 serv./day	a	810	55.600 (53.718 - 57.488)	0.083 (0.003)	0.975 (0.002)
	= 1 serv./day	b	926	55.852 (53.869 - 57.739)		
	≥ 2 serv./day	c	572	56.002 (53.712 - 57.834)		
Meat consumption	≤ 1 serv./week	a	183	55.726 (54.069 - 58.235)	0.381 (0.001)	0.7 (0.002)
	2-6 serv./week	b	1838	55.844 (53.825 - 57.698)		
	≥ 7 serv./week	c	287	55.484 (53.528 - 57.295)		
Vitamin consumption	No serv./day	a	1441	55.771 (53.719 - 57.636)	0.469 (0.001)	0.906 (0.003)
	< 1 serv./day	b	570	55.813 (53.831 - 57.723)		
	≥ 1 serv./day	c	296	55.918 (54.156 - 57.784)		
Dairy products consumption	< 1 serv./weekly or never	a	267	55.588 (53.992 - 57.537)	0.306 (0.001)	0.537 (0.003)
	= 1-6 serv./weekly	b	771	55.777 (53.665 - 57.458)		
	≥ 1 serv./day	c	1270	55.832 (53.847 - 57.800)		
Eggs consumption	< 1 serv./weekly or never	a	1036	55.835 (53.812 - 57.809)	0.504 (< 0.001)	0.22 (0.002)
	≥ 1 serv./weekly	b	1272	55.788 (53.775 - 57.606)		
Fish consumption	< 1 serv./weekly or never	a	1044	55.778 (53.807 - 57.819)	0.771 (< 0.001)	0.089 (0.002)
	≥ 1 serv./weekly	b	1256	55.828 (53.776 - 57.541)		
French fries consumption	never	a	617	56.077 (54.062 - 58.115) _{c,b}	0.002 (0.006)	0.08 (0.008)
	< 1 serv./week	b	1315	55.745 (53.765 - 57.535) _a		
	≥ 1 serv./week	c	357	55.671 (53.470 - 57.181) _a		
Brown bread Consumption	< 1 serv./weekly or never	a	1154	55.794 (53.933 - 57.636)	0.065 (0.003)	0.189 (0.007)
	= 1-6 serv./weekly	b	641	55.563 (53.652 - 57.560)		
	≥ 1 serv./day	c	513	56.107 (53.784 - 57.983)		
White bread consumption	< 1 serv./weekly or never	a	863	55.942 (54.023 - 57.896)	0.002 (0.007)	0.034 (0.010)
	= 1-6 serv./weekly	b	805	55.401 (53.599 - 57.400) _c		
	≥ 1 serv./day	c	629	55.916 (54.039 - 57.785) _b		
Whole bread consumption	< 1 serv./weekly or never	a	326	55.930 (53.736 - 58.064)	0.055 (0.003)	0.614 (0.005)
	= 1-6 serv./weekly	b	1575	55.863 (53.865 - 57.770)		
	≥ 1 serv./day	c	405	55.365 (53.637 - 57.057)		
Alcohol consumption	never	a	917	55.736 (53.761 - 57.776)	0.023 (0.004)	0.001 (0.006)
	Moderate consumption (max 7 serv /week)	b	816	55.615 (53.726 - 57.437) _c		
	> 7 serv /week	c	560	56.050 (54.198 - 57.819) _b		
Smoke habits	never	a	1170	55.850 (53.767 - 57.674)	0.364 (0.001)	0.936 (0.004)
	former	b	708	55.835 (53.896 - 57.775)		
	current	c	430	55.605 (53.613 - 57.535)		

Table S9

Variable	Stat	N	Median (IQ)	MAST		
				P KW* (ϵ^2)	P GLM† (η^2)	
Glucose (mmol/L) quartiles	≤ 4.65	a	443	55.671 (53.764 - 57.310) ^d	<0.001 (0.014)	0.062 (0.020)
	4.66 - 5.09	b	436	55.433 (53.391 - 57.277) ^d		
	5.10 - 5.57	c	418	55.953 (53.881 - 57.805)		
	≥ 5.58	d	356	56.324 (54.227 - 58.592) ^{a,b}		
Glycosylated haemoglobin A1C (%) quartiles	≤ 5.64	a	479	55.996 (54.181 - 57.512)	0.062 (0.005)	< 0.001 (0.006)
	5.65 - 5.95	b	451	56.070 (53.902 - 58.030)		
	5.96 - 6.29	c	426	55.348 (53.358 - 57.406)		
	≥ 6.30	d	398	55.732 (53.826 - 57.809)		
Total cholesterol (mg/dL) tertiles	≤ 220	a	515	55.622 (53.576 - 57.190)	0.009 (0.006)	0.080 (0.009)
	221-257	b	547	55.662 (53.764 - 57.730)		
	≥ 258	c	561	56.054 (54.137 - 58.019)		
Triglycerides (mmol/L) quartiles	< 0.78	a	429	55.353 (53.514 - 57.316) ^{d,b}	<0.001 (0.013)	0.001 (0.018)
	0.78 - 1.05	b	398	55.690 (53.625 - 57.730) ^a		
	1.06 - 1.50	c	401	55.805 (53.955 - 57.404) ^d		
	≥ 1.51	d	425	56.200 (54.275 - 58.287) ^{a,c}		
High density lipoprotein cholesterol (mmol/L) quartiles	≤ 1.20	a	428	55.771 (53.932 - 57.491)	0.252 (0.003)	0.112 (0.007)
	1.21 - 1.47	b	402	56.012 (53.933 - 58.101)		
	1.48 - 1.80	c	411	55.828 (53.847 - 57.776)		
	> 1.80	d	411	55.591 (53.576 - 57.629)		
Low density lipoprotein cholesterol (mmol/L) quartiles	≤ 2.7	a	416	55.707 (53.625 - 57.672)	0.008 (0.008)	0.038 (0.011)
	2.71 - 3.29	b	421	55.207 (53.591 - 57.500)		
	3.30 - 3.84	c	410	55.775 (53.859 - 57.536)		
	≥ 3.86	d	406	56.168 (54.254 - 58.137)		
Free fatty acids (mg/dL) quartiles	< 0.45	a	420	55.649 (53.608 - 57.246) ^d	0.041 (0.006)	0.357 (0.009)
	0.45 - 0.60	b	411	55.814 (53.745 - 58.038)		
	0.61 - 0.79	c	420	55.622 (53.684 - 57.566)		
	≥ 0.80	d	400	56.097 (54.213 - 58.223) ^a		
Homocysteine (μmol/L) quartiles	≤ 11.05	a	464	55.840 (53.992 - 57.668)	0.605 (0.001)	0.078 (0.003)
	11.06 - 14.22	b	430	55.955 (53.875 - 57.667)		
	14.23 - 18.27	c	437	55.892 (53.793 - 57.842)		
	> 18.27	d	437	55.679 (53.822 - 57.595)		
Fibrinogen (mg/ml) quartiles	<2.538	a	547	54.994 (53.304 - 56.971) ^{b,c,d}	<0.001 (0.024)	0.008 (0.026)
	2.538-3.279	b	550	55.738 (53.672 - 57.599) ^{a,d}		
	3.280-4.197	c	554	56.086 (53.994 - 57.896) ^a		
	>4.197	d	548	56.195 (54.428 - 58.137) ^{a,b}		
C-reactive protein (mg/l) quartiles	<0.57	a	577	56.220 (54.317 - 57.684)	0.110 (0.008)	0.272 (0.010)
	0.57-1.17	b	576	56.378 (54.397 - 58.094)		
	1.18-2.42	c	571	56.682 (54.936 - 59.002)		
	>2.42	d	576	56.495 (54.463 - 58.388)		

Table S10

Variable	Stat	N	MAST		
			Median (IQ)	P KW* (e^2)	P GLM† (η^2)
Relative DNMT1 expression, quartiles	0.046-0.0980	a	460	55.826 (53.655 - 57.679) ^d	0.001 (0.010) 0.001 (0.015)
	0.0980-0.1293	b	418	55.416 (53.77 - 57.197) ^d	
	0.1294-0.1704	c	465	55.735 (53.712 - 57.666) ^d	
	>0.1704	d	420	56.363 (54.433 - 58.16) ^{abc}	
Relative DNMT3B expression, quartiles	0.014-0.155	a	446	56.018 (54.042 - 57.821)	0.181 (0.003) 0.754 (0.004)
	0.156-0.205	b	413	56.002 (53.764 - 57.732)	
	0.206-0.281	c	450	55.967 (53.843 - 57.708)	
	>0.282	d	452	55.335 (53.866 - 57.448)	
Relative DNMT3A expression, tertiles	< 2.93	a	49	53.214 (51.367 - 54.866) ^c	0.017 (0.228) 0.001 (0.291)
	2.93-4.75	b	54	54.195 (53.147 - 56.331)	
	> 4.75	c	50	56.181 (54.169 - 58.329) ^a	
Relative TET1 expression, tertiles	0.047-0.149	a	49	55.623 (53.028 - 56.907)	0.529 (0.009) 0.134 (0.038)
	0.149-0.209	b	54	55.687 (54.417 - 57.398)	
	>0.209	c	50	55.548 (53.117 - 57.897)	
Relative TET2 expression, tertiles	0.616-3.604	a	53	56.312 (53.497 - 57.486)	0.282 (0.016) 0.524 (0.036)
	3.605-5.855	b	50	55.358 (53.029 - 57.398)	
	>5.855	c	50	55.364 (53.210 - 57.505)	
Relative TET3 expression, tertiles	1.366-2.638	a	51	56.166 (53.966 - 57.888) ^c	0.027 (0.043) 0.024 (0.068)
	2.639-3.363	b	54	55.971 (53.400 - 57.323)	
	>3.363	c	48	54.449 (52.590 - 56.808) ^a	
Relative TDG expression, tertiles	0.095-0.158	a	48	55.971 (53.764 - 57.78)	0.583 (0.007) 0.837 (0.014)
	0.159-0.209	b	42	55.364 (53.400 - 56.933)	
	>0.209	c	47	54.954 (53.029 - 57.486)	

Table S11

Variable	Stat	N	MAST		
			Median (IQ)	P KW* (ϵ^2)	P GLM† (η^2)
White blood cell count ($n^* \times 10^9/l$)	< 5.00	a	613	55.585 (53.655 - 57.636)	0.288 (0.002) 0.621 (0.003)
	5.00 - 5.89	b	542	55.851 (53.978 - 57.601)	
	5.90 - 6.91	c	551	55.973 (53.955 - 57.805)	
	> 6.91	d	582	55.707 (53.769 - 57.639)	
Monocyte count ($n^*/\mu l$)	< 364	a	477	55.624 (53.568 - 57.666)	0.322 (0.002) 0.645 (0.002)
	364 - 452	b	505	55.890 (53.909 - 57.658)	
	452 - 566	c	758	55.682 (53.736 - 57.668)	
	> 566	d	515	55.916 (54.113 - 57.8)	
Lymphocyte count ($n^*/\mu l$)	< 1540	a	530	55.146 (53.381 - 57.303) ^{b,d}	0.001 (0.011) <0.001 (0.008)
	1540 - 1890	b	499	55.994 (53.739 - 57.647) ^a	
	1891 - 2281	c	759	55.662 (53.794 - 57.732)	
	> 2281	d	468	56.120 (54.375 - 57.946) ^a	
Lymphocytes to monocytes ratio	< 3.35	a	522	55.415 (53.518 - 57.297) ^d	0.035 (0.004) 0.001 (0.009)
	3.35-4.20	b	520	55.687 (53.947 - 57.599)	
	4.20-5.24	c	773	55.798 (53.763 - 57.742)	
	> 5.24	d	441	56.033 (54.259 - 58.007) ^a	
Neutrophil count ($n^* \times 10^9/l$)	< 2.56	a	480	56.104 (53.992 - 58.053) ^d	0.024 (0.005) 0.026 (0.009)
	2.56-3.20	b	508	55.616 (53.736 - 57.415)	
	3.20-3.90	c	775	55.808 (53.902 - 57.729)	
	≥ 3.99	d	500	55.481 (53.503 - 57.378) ^a	
Eosinophil count ($n^*/\mu l$)	≥ 100	a	523	55.755 (53.774 - 57.464)	0.507 (0.001) 0.758 (0.003)
	101-151	b	502	55.892 (53.707 - 57.895)	
	152-230	c	776	55.616 (53.670 - 57.666)	
	≥ 231	d	460	55.885 (54.210 - 57.453)	
Basophil count ($n^*/\mu l$)	≤ 20.4	a	531	55.784 (53.827 - 57.325)	0.636 (0.001) 0.882 (0.002)
	20.5-32.4	b	590	55.839 (53.950 - 57.895)	
	32.5-48.8	c	562	55.622 (53.585 - 57.729)	
	> 48.8	d	573	55.824 (53.833 - 57.611)	

Table S12

Model	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
N	1961	1961	1961	1916	1916	1916	1914	1913	1908	1801	1800	1552	1447	1915	1901	1900	1801	1801	1789	1758	1434
	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.
Age group	134.571 < 0.001	133.299 < 0.001	134.080 < 0.001	130.890 < 0.001	131.350 < 0.001	131.054 < 0.001	133.570 < 0.001	111.090 < 0.001	127.429 < 0.001	116.492 < 0.001	117.190 < 0.001	101.278 < 0.001	72.680 < 0.001	116.452 < 0.001	119.128 < 0.001	131.372 < 0.001	115.957 < 0.001	105.258 < 0.001	115.782 < 0.001	81.760 < 0.001	64.037 < 0.001
Recruitment center		2.203 0.138	2.181 0.140	3.533 0.060	3.503 0.061	3.509 0.061	4.205 0.040	4.426 0.064	4.146 0.042	3.598 0.074	3.094 0.079	2.764 0.096	2.635 0.105	4.426 0.035	3.347 0.067	3.107 0.078	2.989 0.084	3.763 0.052	3.868 0.049	5.008 0.025	3.647 0.056
Sex			3.773 0.052	3.348 0.067	3.275 0.070	3.265 0.071	1.373 0.241	2.009 0.156	3.662 0.056	4.866 0.027	5.616 0.018	1.058 0.604	0.935 0.334	4.461 0.035	2.270 0.132	3.564 0.059	3.800 0.051	5.691 0.017	4.200 0.040	4.074 0.044	2.250 0.134
Lymphocytes to monocytes ratio				3.310 0.069	3.371 0.066	3.334 0.068	3.345 0.067	3.289 0.070	3.194 0.074	2.839 0.092	2.525 0.112	2.353 0.125	1.779 0.182	3.720 0.054	2.690 0.101	3.309 0.069	2.731 0.098	2.572 0.109	3.126 0.077	2.554 0.110	1.935 0.164
Neutrophils					0.644 0.422								0.552 0.450							0.453 0.501	0.426 0.514
Lymphocytes						0.271 0.603							0.201 0.654							0.101 0.751	0.118 0.731
Alcohol consumption							6.426 0.011						4.011 0.045							4.952 0.026	3.820 0.050
Fibrinogen								6.457 0.011					3.604 0.058							2.517 0.113	2.296 0.130
White bread consumption									0.724 0.395				0.032 0.858							0.337 0.562	0.187 0.666
LDL-Cholesterol										4.864 0.027			1.850 0.174							1.747 0.186	0.630 0.427
Triglycerides											2.899 0.089		1.825 0.177							0.178 0.673	0.514 0.474
Relative DNMT1 expression												7.481 0.006	4.578 0.032								4.398 0.036
BMI														5.978 0.014						1.343 0.247	0.793 0.373
French fries consumption															2.841 0.092					1.349 0.245	1.210 0.271
Glycated haemoglobin (HbA1c)																1.576 0.209				9.273 0.002	9.015 0.003
Cholesterol																2.208 0.137				0.325 0.569	0.028 0.868
Glucose																		5.014 0.025		7.886 0.005	7.609 0.006
Free fatty acids																			1.638 0.201	0.874 0.350	0.287 0.592

Table S13

Model	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22			
N	1408	1408	1408	1408	1361	1361	1359	1358	1358	1307	1307	1307	1118	1069	1360	1350	1347	1307	1307	1304	1273	1057			
	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.	Wald Sig.			
Subject group (GO, SGO, RASIG)	12.935 0.002	13.170 0.001	13.503 0.001	12.483 0.002	12.504 0.002	12.511 0.002	12.504 0.002	11.126 0.004	11.842 0.003	13.598 0.001	10.497 0.005	9.892 0.007	10.960 0.004	8.485 0.014	10.894 0.004	11.247 0.004	12.013 0.002	10.420 0.005	9.627 0.008	10.350 0.006	6.224 0.045	5.480 0.065			
Recruitment centre		1.330 0.249	1.219 0.270	1.495 0.222	0.675 0.411	0.673 0.412	0.672 0.412	0.427 0.513	0.521 0.470	0.660 0.417	0.283 0.595	0.295 0.587	0.028 0.867	0.153 0.695	0.304 0.581	0.461 0.497	0.080 0.777	0.279 0.598	0.064 0.786	0.245 0.621	1.987 0.159	5.047 0.025			
Sex			1.441 0.230	1.810 0.178	1.673 0.196	1.681 0.195	1.679 0.195	1.875 0.171	0.933 0.334	1.207 0.272	1.789 0.181	2.121 0.145	0.585 0.444	0.518 0.472	2.079 0.149	1.731 0.188	0.866 0.352	1.505 0.220	2.448 0.118	2.057 0.152	2.045 0.153	1.238 0.266			
Age				16.330 < 0.001	15.993 < 0.001	15.974 < 0.001	15.968 < 0.001	16.303 < 0.001	15.533 < 0.001	15.842 < 0.001	15.947 < 0.001	14.917 < 0.001	13.841 < 0.001	12.077 0.001	15.652 < 0.001	17.048 < 0.001	13.121 < 0.001	15.265 < 0.001	13.623 < 0.001	14.737 < 0.001	12.592 < 0.001	11.409 0.001			
Lymphocytes to monocytes ratio					3.638 0.056	3.634 0.057	3.636 0.057	3.496 0.062	3.826 0.050	3.723 0.054	2.663 0.103	2.773 0.096	6.827 0.009	4.671 0.031	3.652 0.056	3.864 0.049	3.231 0.072	2.732 0.098	2.729 0.099	2.811 0.094	2.549 0.110	5.096 0.024			
Neutrophils						0.011 0.915								0.358 0.550								0.165 0.685	0.616 0.433		
Lymphocytes							0.007 0.931							0.344 0.557									0.159 0.690	0.601 0.438	
White bread consumption								0.346 0.556						0.013 0.909									0.630 0.427	0.179 0.673	
Alcohol consumption									2.051 0.152					1.345 0.246									0.476 0.490	0.937 0.333	
Fibrinogen										1.972 0.160				2.584 0.108									0.514 0.473	0.947 0.331	
LDL-Cholesterol											2.699 0.100			0.962 0.327									1.397 0.237	0.938 0.333	
Triglycerides												0.225 0.635		0.019 0.890									0.371 0.542	0.180 0.672	
Relative DNMT1 expression													4.086 0.043	4.369 0.037										3.209 0.073	
BMI															7.329 0.007									6.073 0.014	5.417 0.020
Glycated haemoglobin (HbA1c)															0.174 0.676									4.108 0.043	5.145 0.023
French fries consumption																	8.602 0.003							6.698 0.010	5.804 0.016
Cholesterol																		0.829 0.362						0.294 0.588	0.227 0.633
Glucose																				2.462 0.117				4.540 0.033	5.262 0.022
Free fatty acids																					0.056 0.812			0.304 0.581	0.088 0.767

Legends to supplementary tables

Table S1

Subtelomeric DNA methylation in the RASIG population stratified by age

*KW test: nonparametric comparison by the Kruskal–Wallis test of the CpG methylation level between age groups. Data are reported as median and interquartile range (IQ). Pairwise comparisons, adjusted for multiple comparisons, were performed by the Mann–Whitney U-test (comparisons with $p < 0.05$ are marked by the associated superscripts).

†GLM test: groups comparison by generalized linear model analysis. The model included the effects of sex, recruitment centre and age as covariates (p values refer to age groups). Bold text indicates a statistically significant p value. Definition of abbreviations is provided in the supplementary list.

Table S2

Correlation between subtelomeric DNA methylation and age in the RASIG population

*The confidence intervals for both Pearson (parametric) and Spearman (non-parametric) correlation coefficients are based on 1000 bootstrap re-samples. Stratification was by sex and recruitment centre. Bold text indicates a statistically significant p value.

Table S3

Comparison of different linear regression models for subtelomeric DNA methylation to age in the RASIG population

Bold text indicates a statistically significant p value.

Table S4

Linear regression model

*The standard errors and confidence intervals for Pearson correlation coefficients are based on 1000 bootstrap re-samples. Stratification was by sex and recruitment centre. Bold text indicates a statistically significant p value.

Table S5

MAST in age-stratified RASIG, GO, SGO and DS

[§]KW test: nonparametric comparison by the Kruskal–Wallis test of MAST between age groups (RASIG) and between subject groups (RASIG, GO, SGO and DS). Data are reported as median and interquartile range (IQ). Pairwise comparisons, adjusted for multiple comparisons, were performed by the Mann–Whitney U-test (comparisons with $p < 0.05$ are marked by the associated superscripts). Bold text indicates a statistically significant p value.

*Age range was 55-75 years.

†Age range was 35-54 years.

Table S6

Correlation between MAST and telomere length in RASIG

Confidence intervals for correlation coefficients are based on 1000 bootstrap re-samples. Stratification was by sex and recruitment centre (MAST vs age and telomere length vs age) and by sex recruitment centre and age (MAST vs telomere length). Bold text indicates a statistically significant p value.

Table S7

Effect of recruitment centre, sex and BMI on MAST in RASIG

*KW test: nonparametric comparison by the Kruskal–Wallis test of MAST level between sample groups categorized by recruitment centre, sex and BMI. Data are reported as median and interquartile range (IQ). Pairwise comparisons, adjusted for multiple comparisons, were performed by the Mann–Whitney U-test (comparisons with $p < 0.05$ are marked by the associated superscripts).

†GLM test: groups comparison by generalized linear model analysis. The models included the effects of sex ([§]), recruitment centre ([‡]) or both (^ª) as covariates (p values refer to the categories). Bold text indicates a statistically significant p value. Definition of abbreviations is provided in the supplementary list.

Table S8

Influence of dietary habits and lifestyle on MAST in RASIG

*KW test: nonparametric comparison by the Kruskal–Wallis test of MAST level between sample groups categorized by the indicated factor intervals. Data are reported as median and interquartile range (IQ). Pairwise comparisons, adjusted for multiple comparisons, were performed by the Mann–Whitney U-test (comparisons with $p < 0.05$ are marked by the associated superscripts).

†GLM test: groups comparison by generalized linear model analysis. The models included the effects of sex and recruitment centre as covariates (p values refer to the categories). Data were obtained after questionnaires as described in Moreno-Villanueva et al. [33]. Bold text indicates a statistically significant p value.

Table S9

Influence of cardiovascular and diabetes risk biomarkers on MAST in RASIG

*KW test: nonparametric comparison by the Kruskal–Wallis test of MAST level between sample groups categorized by the indicated variable intervals. Data are reported as median and interquartile range (IQ). Pairwise comparisons, adjusted for multiple comparisons, were performed by the Mann–Whitney U-test (comparisons with $p < 0.05$ are marked by the associated superscripts).

†GLM test: groups comparison by generalized linear model analysis. The models included the effects of sex and recruitment centre as covariates (p values refer to the categories). Bold text indicates a statistically significant p value. Definition of abbreviations is provided in the supplementary list. Details about the analytic procedures for the measurement of the parameters are given in Moreno-Villanueva et al. [32].

Table S10

Influence of the expression of DNA methylation machinery components on MAST in RASIG

*KW test: nonparametric comparison by the Kruskal–Wallis test of MAST level between sample groups categorized by the indicated variable intervals. Data are reported as median and interquartile range (IQ). Pairwise comparisons, adjusted for multiple comparisons, were performed by the Mann–Whitney U-test (comparisons with $p < 0.05$ are marked by the associated superscripts).

†GLM test: groups comparison by generalized linear model analysis. The models included the effects of sex and recruitment centre as covariates (p values refer to the categories). Bold text indicates a statistically significant p value. Definition of abbreviations is provided in the supplementary list. Details about the analytic procedures for the measurement of the parameters are given in Ciccarone et al. [36] and in Valentini et al. [67].

Table S11

Influence of haematological factors on MAST in RASIG

*KW test: nonparametric comparison by the Kruskal–Wallis test of MAST level between sample groups categorized by the indicated variable intervals. Data are reported as median and interquartile range (IQ). Pairwise comparisons, adjusted for multiple comparisons, were performed by the Mann–Whitney U-test (comparisons with $p < 0.05$ are marked by the associated superscripts).

†GLM test: groups comparison by generalized linear model analysis. The models included the effects of sex and recruitment centre as covariates (p values refer to the categories). Bold text indicates a statistically significant p value. Definition of abbreviations is provided in the supplementary list. Details about the analytic procedures for the measurement of the parameters are given in Moreno-Villanueva et al. [32].

Table S12

Contribution of selected variables and covariates on age-related changes of MAST in RASIG

Models: MAST (s), response variable; age group (o), factor variable; sex (n), recruitment centre (n), white bread consumption (s), alcohol consumption (s), triglycerides (s), LDL cholesterol (s), lymphocytes (s), ratio of lymphocyte to monocyte (s), neutrophils (s), fibrinogen (s), DNMT1 expression (s), BMI (s), French fries consumption (s), glycated haemoglobin (s), cholesterol (s), serum glucose (s) and free fatty acids (s) were included as covariates (o = ordinal variable; n = nominal variable; s = scale variable). Bold text indicates a statistically significant p value.

Table S13

Contribution of selected variables and covariates on group-related (GO, SGO and RASIG) changes of MAST in individuals aged > 54 years.

Models: MAST (s), response variable; subject group (o), factor variable; age (s), sex (n), recruitment centre (n), white bread consumption (s), alcohol consumption (s), triglycerides (s), LDL cholesterol (s), lymphocytes (s), ratio of lymphocyte to monocyte (s), neutrophils (s), fibrinogen (s), DNMT1 expression (s), BMI (s), French fries consumption (s), glycated haemoglobin (s), cholesterol (s), serum glucose (s) and free fatty acids (s) were included as covariates (o = ordinal variable; n = nominal variable; s = scale variable).