TITLE:

BMI is negatively associated with telomere length; a collaborative cross-sectional meta-analysis of 72 observational studies

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The authors declare that they have no conflict of interest.

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ABSTRACT

Background

Obese persons are expected to have shorter telomeres, but the association between body-mass index (BMI) and leucocyte telomere length (TL) might differ across the lifespan, ethnicities and sexes.

Objective

A collaborative cross-sectional meta-analysis of observational studies was conducted to investigate the associations between BMI and telomere length (TL) across life span.

Design

Seventy-two distinct study populations were included in the meta-analysis capturing data from 128,673 individuals. Study-specific age and sex adjusted regression coefficients were combined using a random-effects model in which absolute (base pairs [bp]) and relative (T/S ratio) TLs were regressed against BMI. Stratified analysis was performed by three age categories ("young" ≥18 and ≤ 60 years, "middle" > 60 and ≤ 75, "old" > 75 years), sex, and ethnicity.

Results

Each unit increase in BMI corresponded to a -4.14 bp (95%C.I. -5.69, -2.59) difference in TL; among young adults -8.09 bp (95%C.I. -10.26, -5.92). Each unit increase in BMI corresponded to a -1.50 units T/S ratio (95%C.I. -2.12, -0.88) difference in age and sex adjusted relative telomere length; among young adults -2.30 units T/S ratio (95%C.I. -3.75, -0.84). The associations were stronger for whites than for African Americans. No sex differences were observed.

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Conclusions

Higher BMI is associated with shorter telomeres, especially in younger individuals. The presently observed difference is not negligible. Meta-analyses of longitudinal studies evaluating change in body weight alongside change in TL are warranted.

KEY WORDS:

BMI, telomere length, obesity, low grade inflammation, meta-analysis, observational studies

INTRODUCTION

Telomeres, the nucleoprotein structures at the ends of chromosomes, shorten with each cell division in somatic cells (1). When telomere length reaches a critical value, cells either enter a state of senescence or undergo apoptosis (2). Oxidative stress and chronic inflammation are suggested to play a role in accelerated telomere attrition (3-5). Even before the onset of age-related diseases obesity might be a contributing factor to the cumulative burden of oxidative stress and chronic inflammation throughout the life course.

Obesity is a growing health problem and worldwide its prevalence has more than doubled since 1980 (6). In addition, the burden of diabetes and cardiovascular disease is partly attributable to being overweight and obese (6). A study in the elderly found that telomere length is associated with adiposity, but not obesity (7), and a study of aging found no relation between telomere length and morbidity and mortality in the very old (8). Therefore, we hypothesize that obese persons are expected to have shorter telomeres, compared to those of normal weight of the same chronological age [3,7-15], but the association between obesity and telomere length might differ across the lifespan.

Sex and ethnicity may influence the association between BMI and telomere length. On average, women have longer telomeres than men (9-11). However, published results on sex differences in association between BMI and telomere length are inconsistent (12-14). African Americans and Native Americans have higher rates of obesity (15), and also racial differences in telomere length have frequently been reported with adult African Americans having longer telomeres than white individuals (16-20), but evidence is lacking whether the association between BMI and telomere length differs between ethnicities.

Two recent meta-analyses reported the negative association between BMI and telomere length on reported summary statistics in the literature, but could not examine sex differences nor the influence of age and ethnicity (21, 22). To further evaluate whether BMI is associated with telomere length, a large-scale collaborative cross-sectional meta-analysis was conducted across observational studies that collected information on BMI and telomere length of adult individuals. To avoid publication bias and maximize the data in the analyses, a consistent standardized analysis plan across studies was used and principal investigators (PIs) of published studies were contacted and asked to participate in the TELOMAAS group. As the relationship between telomere length and BMI could be moderated by age, sex, and ethnicity we completed additional analyses stratifying by these factors.

METHODS

Search strategy

We performed a broad literature search up till the end of January 2016 using PUBMED, EMBASE and the Cochrane database without restrictions. Numerous studies have measured BMI and telomere length for purposes other than the association between telomere length and BMI as an outcome. Therefore, the search was rather broad and not narrowed to telomere length or BMI. Based on the existing relation between obesity, diabetes and cardiovascular diseases, and because telomere length is related to aging we completed a search in which terms related to these conditions were entered. Additionally, search items related to study design were entered. The complete search criteria are listed in Online Resource 1 (supplemental material). Citation and reference tracking were performed until no new studies were found. One author (MG) performed

the literature search and selected potentially relevant publications. Titles and abstracts of potentially relevant studies were screened. In addition, when the abstract indicated that the article was reporting a study of diabetes and/or cardiovascular disease, the full text was screened. No restrictions for study design or language were applied.

Eligibility criteria

Studies were included if height and weight or BMI was collected. The corresponding author was invited to participate in the meta-analysis and identified additional unpublished studies. PIs of these unpublished studies were also invited to participate. Only cohort studies with healthy individuals at baseline were included and if the study design was a case-control study, only controls were included in the meta-analysis. In compiling the database care was taken to exclude overlapping study cohorts. The study sample (abbreviated as study) was taken as the unit for this meta-analysis.

Data extraction

The PI of each study completed a questionnaire and additional information was extracted from the manuscript. The following data were collected: study name, study design (cohort or case-control), sample size (cohort size or control group size), presence of the variables age, sex, ethnicity (a cut off value of 70% was chosen to define a population as being white or African American, Native American, Asian, Hispanic, when at least 70% of the population was classified as white or African American, Native American, Asian, Hispanic), leucocyte telomere length, and BMI (kg/m^2), whether BMI was measured or self-reported, white blood cell types from which DNA was extracted for telomere measurements, method of telomere length measurement, and of DNA storage (Online Resource 1 (supplemental material)). Absolute telomere length in

base pairs (bp) was distinguished from relative telomere length based on T/S ratio (Telomere to Single Copy Gene ratio). The PI was free to provide the de-identified raw data or to perform analyses and provide summary statistics. If the PI provided raw data, MG conducted the linear regression analyses to obtain the summary statistics. The summary statistics included the results of twelve linear regression analyses with telomere length (bp or T/S ratio) as the outcome and BMI as the independent variable. The linear regression analyses were a combination of one of the following sex and age groups: men and women analyzed together and separately; all age groups together and analyzed in three a priori chosen subgroups ("young" ≥18 and ≤ 60 years, "middle" > 60 and ≤ 75, "old" > 75 years). When appropriate, i.e. men and women analyzed together and/or all age groups together, the analyses were corrected for sex and/or for age. If the T/S ratio was used to estimate absolute telomere length, the PI was asked to provide new analyses with the T/S ratio as the outcome. If the PI did not respond to this request absolute telomere length based on the T/S ratio was used for analyses and included in the analysis. The regression coefficients (beta estimates) and standard errors (SE) were then used in the meta-analyses. In the case of longitudinal data one randomly selected telomere length measurement along with the corresponding measurements (e.g. BMI, age) for that time point was used in the analysis.

Assessment of small study effects

To examine the potential presence of publication bias, visual inspection of funnel plots for asymmetry was performed, followed by the Egger and Begg's linear regression test for small study effects (23) and use of the Duval and Tweedie nonparametric "trim and fill" method (24).

Statistical analysis

Statistical pooling

The primary outcome of the meta-analysis was a pooled estimation of the difference in absolute telomere length in bp or relative telomere length (T/S ratio) per unit increase in BMI. Study specific regression coefficients (beta estimates) and standard errors (SE) were combined using random-effects pooling in twelve meta-analyses. Either absolute telomere length (bp) or relative telomere length (T/S ratio) was considered as the outcome measure and BMI (kg/m^2) was the independent variable.

Assessment of heterogeneity

Statistical heterogeneity was estimated by Q and I^2 statistics (25, 26) for each of the twelve meta-analyses. Low heterogeneity was indicated by I^2 up to 25%, medium heterogeneity by 25-50%, and high heterogeneity by > 50% (26). To confirm the expected differences in association for age and sex, meta-regression analysis was performed with age and sex as sources of heterogeneity. Other potential sources of heterogeneity were investigated by meta-regression analysis if medium or high heterogeneity was observed in at least one of the twelve meta-analyses. Details are given in Online Resource 1 (supplemental material)

Sensitivity analyses

The following sensitivity analyses were performed: (1) outlier analyses by omitting one study at a time, (2) omitting studies that used the relative telomere length to estimate the absolute telomere length, (3) stratification by method of measurement of telomere length (Southern blot vs. q-PCR), (4) using a cut off value of 90% for defining ethnicity. Details are given in Online Resource 1 (supplemental material).

Statistical analyses were performed using Stata software version 12.0 (StataCorp, College Station, TX, USA). All statistical tests were two-sided; p values < 0.05 were considered statistically significant, except where otherwise specified.

RESULTS

Search

The search (PUBMED, EMBASE, and Cochrane) yielded 4,282 publications, from which 158 potentially relevant publications were identified. Some authors contributed to more than one publication. As a result, 126 corresponding authors were identified and contacted. Sixty one corresponding authors responded positively, 56 authors did not respond, six declined to participate, and three authors did not have the requested data. Since one publication could include multiple studies, the PIs (if not the same as corresponding authors) of the studies were contacted. Six additional studies were identified by the corresponding authors and the PIs of these additional studies were contacted. Diversity in relative telomere length assays were used and we decided to exclude eight studies using techniques other than Southern blots and q-PCR, because the regression coefficients (beta estimates) may not be directly comparable.

In total, 72 unique studies were included in the meta-analyses. Twenty-six studies measured absolute telomere length and 46 studies used the T/S ratio. A flow chart of the inclusion procedure is presented Figure 1.

Description of studies

The characteristics of the 72 studies included in this meta-analysis are provided in Table 1. Absolute telomere lengths were obtained from 26 studies (3, 5, 12, 13, 16, 27-58) (and the unpublished data of the HyperGEN study), of which three studies estimated absolute telomere length based on the T/S ratio (18, 59-65). In 16 studies Southern blots were used (3, 5, 12, 13, 16, 27-39, 43, 44, 47-51, 54, 55, 58). Forty-six studies presented the relative telomere length (T/S

ratio) (4, 14, 66-115) (and the unpublished data of Utah Pedigree study). One PI provided the data stratified by cell type. (101) One PI provided longitudinal data (54).

The total population of this meta-analysis consisted of 128,673 adults (45% men), the young population (≥18 and ≤ 60 years) consisted of 81,540 adults (43% men), the middle aged population (> 60 and ≤ 75 years) consisted of 37,166 adults (46% men), and the old population (> 75 years) consisted of 9,948 adults (53% men). Overall, the majority of the adults were white (including Arab; 85%), followed by Asian (5%), African American (4%), Hispanic, and Native Americans (both 3%). Four studies provided data of mixed populations stratified by ethnicity (16, 68, 69, 98) (and the unpublished data of the HyperGEN study). Fifty-six studies consisted of > 70% white individuals (of which 52 had at least 90% white individuals) (3, 5, 12-14, 16, 27-33, 35-44, 47-58, 60-62, 65, 68-92, 95, 97-100, 102, 105-111, 113-115) (and unpublished data of the HyperGEN, and Utah Pedigree studies). Four studies consisted only of African Americans (16, 68, 69, 98) (and the unpublished data of the HyperGEN study); three only of Asians (34, 97, 112), one study only of Native Americans (93, 94, 103, 104), and three studies comprised only Hispanics(68, 69, 80, 81, 98).

Assessment of small study effects

Visual inspection of the funnel plots for absolute telomere length and for relative telomere length yielded symmetric plots. No publication bias was detected using Egger's test or Begg's test. The "trim and fill" method added one hypothetical study to the meta-analysis for absolute telomere length. However, the recalculated summary estimate did not change substantially and was still significant with their inclusion (beta= -4.20 (95%C.I. -5.67 to -2.72); $p < 0.001$).

Meta-analyses

An overall summary of the meta-analysis is shown in Table 2a and Table 2b in which the beta estimates of all meta-analyses for absolute telomere length as the outcome (Table 2a) and of all meta-analyses for relative telomere length as the outcome (Table 2b) are presented. The accompanying forest plots are presented in the Online Figure 1a Absolute telomere length (Online Resource 2) and Online Figure 1b Relative telomere length (Online Resource 3).

Overall meta-analysis

Overall, sex- and age-adjusted absolute telomere length was significantly associated with BMI. Each unit increase in BMI corresponded to a -4.14 bp (95%C.I. -5.59 to -2.51; I^2= 7.1%) difference in absolute telomere length (Table 2a and Figure 2a Forest plot). For example, an estimated difference in telomere length between a normal weight individual with a BMI of 25 kg/m^2 and an obese individual with a BMI > 30 kg/m^2 is at least 20.5 bp, and, if a larger difference is used (BMI 20 kg/m^2 vs. BMI > 30 kg/m^2), 41.4 bp. The estimated difference between normal weight and morbid obesity (BMI > 40 kg/m^2) is at least 62.1 bp. Each unit increase in BMI corresponded to a -1.50 units T/S ratio (95%C.I. -2.12 to -0.88; I^2= 41.1%) difference in age- and sex-adjusted relative telomere length. An estimated difference in relative telomere length between normal weight and obesity is at least 7.5 units T/S ratio (Table 2b and Figure 2b Forest plot) and between normal weight and morbid obesity at least 22.5 units T/S ratio. The associations between BMI and telomere length did not differ significantly between men and women (see below).

Age

Analysis stratified by age category revealed that in young adults (≥18 and ≤ 60 years) a unit increase of BMI corresponded to a -8.09 bp (95%C.I. -10.26 to -5.92; I^2=15.3%) difference in absolute telomere length (Figure 3a)..

In middle age adults (> 60 and ≤ 75) the overall association between BMI and telomere length was -2.59 bp (95%C.I. -4.95 to -0.23; I^2= 0.0) per unit increase in BMI.

In old adults (> 75 years) the overall association between BMI and telomere length was -6.15 (95%C.I. -11.05 to -1.25; I^2= 11.5) per unit increase in BMI.

For relative telomere length, each unit increase in BMI corresponded to a -2.30 units T/S ratio (95%C.I. -3.755 to -0.84; I^2= 83.7%) difference in relative telomere in young adults(Table 2b and Figure 3b).

In middle age adults, the association between BMI and relative telomere length was -0.95 units T/S ratio (95%C.I. -1.68 to -0.21; I^2= 0.0) per unit increase in BMI. For old adults no statistically significant associations were found between BMI and relative telomere length.

Meta-regression and sources of heterogeneity

Age, ethnicity and study design were a source of heterogeneity at study level in the meta-regression analyses. Sex was never a source of heterogeneity (Online Resource 1 (supplemental material)). Therefore, all analyses were stratified by ethnicity and study design in addition to the originally planned analyses. With absolute telomere length as the outcome, stratified analyses revealed that for the young white population all estimates were bigger than those for the African American. With relative telomere length as the outcome, stratified analyses revealed that the estimates for the white population and Native Americans all estimates were bigger than those for the African American.

The beta estimates of the cohort studies were consistent with the estimates without stratification by study design. The beta estimates of the case-control studies were not statistically significant, except for one disproportionately large estimate (beta= -60.24 (95%C.I. -100.90 to -19.58)) in the old age category, based on a meta-analysis that included only two study samples.

Sensitivity analysis

None of the sensitivity analyses resulted in substantial change of the summary estimate ((Online Resource 1 (supplemental material)). Stratified analysis by method of measurement yielded an estimate of -4.52 bp (95%C.I. -6.77 to -2.27) for the Southern blots method and -3.93 bp (95%C.I. -5.71 to -2. 16) for q-PCR method.

DISCUSSION

This cross-sectional meta-analysis of 72 observational studies of adult populations confirmed previous observations that BMI is negatively associated with telomere length. After stratification for age and ethnicity the negative association between BMI and telomere length appeared to be stronger in "young adult" populations (age < 60 years) and in white populations, the latter of which was apparent only when absolute telomere length was measured. Differences between men and women could not be confirmed.

Based on our estimates for absolute telomere length, a ~5-unit increase in BMI appears to be equivalent to a difference in telomere length of ~21-41 bp or ~7.5-12 units T/S ratio. Compared to an estimated average yearly decrease (i.e., ~25 bp/year or ~0.01 T/S ratio/per year) of leucocyte telomere length in adults based on cross-sectional data (3, 31, 116-118), the association is not negligible. In addition, compared to accelerated attrition (i.e. 3-5 bp/year) due to smoking one pack of cigarettes daily (91, 119) the association reported in this meta-analysis appears relevant and could exceed or at least be in line with the effect of smoking. A major disadvantage of cross-sectional analysis is the impossibility to infer causation. However, the robust association

887 between higher BMI and lower telomere length found in this meta-analysis highlights another
888 potential area of concern for the obesity epidemic.
889 Since obesity, and more specifically an increase in leptin and a decrease in adiponectin have
890 been associated with low-grade inflammation and oxidative stress (120), the observed negative
891 association between BMI and leucocyte telomere length may be due in part to the chronic
892 inflammatory state associated with higher leptin. Recently, a negative association was observed
893 between age-related relative telomere length and serum leptin in seven cohorts of 11,448
894 participants, which remained significant after adjustment for BMI (100). These data suggest that
895 beyond a high BMI, especially via the increase in leptin, inflammatory conditions likely
896 contribute to telomere shortening. Since a longitudinal study found a tendency for a higher
897 reduction in BMI over a 5 year period in participants who initially had the longest telomeres (95),
898 it is also suggested that a common factor, such as chronic inflammation, is associated both with
899 leptin resistance and with telomere length.
900 The negative association between BMI and telomere length was most apparent in the younger
901 population, in which a stronger association was found for absolute and relative telomere length
902 compared to the other age groups, which highlights the urgency to address the obesity epidemic.
903 Three possible explanations could explain this observation. First, BMI could be a better marker
904 for adiposity in younger individuals aged less than 60 years compared to older individuals (21).
905 Above 65 years of age BMI may less consistently reflect obesity because of potential loss of
906 muscle and bone mass and height (21). The fact that older men weigh less than the middle-aged
907 men at a given height is attributed to older men having less lean tissue, and a lower BMI can
908 actually reflect a higher fat mass (121). Second, selective survival might be one of the causes for
909 the stronger association found in the younger age category. As Manson et al. state “obesity in
910 one’s 40s contributes to the onset of type 2 diabetes in one’s 50s, which leads to myocardial

infarction (MI) in one's 60s, heart failure and weight loss due to debilitation and muscle wasting at age 70, and death at age 75" (122). People who suffered from age-related diseases may have died and those who survived may therefore differ from those who died. (123) Third, older people are more likely to have chronic diseases that lead to weight loss and people with chronic diseases are probably less likely to participate in studies (122).

The negative association between BMI and leucocyte telomere length was found predominantly amongst white populations. One possible explanation could be that telomere length differs between different cell types (124) and that leucocyte cell subpopulations(125) differ between whites and African Americans. However, more research is required to resolve whether this observation explains the racial differences in association between telomere length and BMI for white and African Americans. Second, it was recently reported that the estimation of visceral adipose tissue, the most relevant tissue that determines the risk to develop chronic metabolic diseases, was different in white and African American adults (126). At higher BMI or increased waist circumference (WC), white adults had higher levels of visceral adipose tissue than African American adults (120). Since the presence of leptin resistance or markers of inflammation were not included in these studies, it remains to be determined whether the relation between BMI, leptin resistance, inflammation and telomere attrition is different for African Americans from whites. Surprisingly, the one study consisting of 3,256 Native Americans showed similar trends as found for the white populations (104). The majority of this study sample was centrally obese, and leucocyte telomere length was negatively correlated with C-reactive protein.

Although just one author performed the literature search and selected potentially relevant publications, which is a limitation of this meta-analysis, one of the main strengths of this study is that we did not rely on publications. Instead we contacted PIs, which in turn have pointed us

towards important studies we may have missed, to obtain the regression coefficients for the meta-analysis. Also we incorporated several potential confounders (age and sex) and sources of heterogeneity (ethnicity and study design). The response rate of the originally contacted PIs was 55% with a final count of 72 unique studies and over 120,000 individuals. Although it is impossible to make a direct comparison with the unpublished beta estimates of the non-responders, we assume, also based on the absence of significant publication bias, that the studies in this meta-analysis are a random selection of all studies conducted and that we present a valid representation of the association between BMI and telomere length. Because of the large variation in adult telomere length, as well as biological and measurement variation (q-PCR), large sample sizes are needed, especially in cross-sectional studies, to detect modest effects (29). In this meta-analysis we were able to detect a statistically significant association of -4.14 bp or -1.50 units T/S ratio per unit increase BMI, despite the use of cross-sectional data, and the large biological and measurement variation. Since 35% of the analyses showed a statistically significant association with estimates of the same magnitude (except for one), we assume that false positive reporting is only of minor concern.

Two recently meta-analyses, which relied on published data, also reported negative associations between BMI and telomere length. The first reported negative regression coefficients on the association between telomere length and BMI (21), (in total 7,530 individuals), of which five studies were also included in this meta-analysis (12, 13, 18, 79, 127). The larger scale meta-analysis reported a weak negative correlation (48,334 individuals), a standardized mean differences of 0.84 (95%C.I. 0.22 to 1.46) between obese individuals (n= 1,947) and normal weight individuals (n= 6,063) and an odds ratio of 1.39 (95%C.I. 1.15 to1.69) (n= 4250) (22). Of the 45 samples that met our inclusion criteria 33 collaborated in our analysis. This shows that, despite the fact that different statistical techniques were used and slightly different populations

were analyzed, the results between the meta-analyses are consistent and very robust. Although age and ethnicity were taken into account, it should be mentioned that the older study sample was relatively small (~ 10,000 individuals), and that the majority of the individuals were white (85%). Unfortunately, we did not include smoking in the meta-analysis. Smoking is generally associated with a lower BMI and shorter telomere length (3, 119, 122), which may have caused an underestimation of the inverse association between BMI and telomere length. Also inflammation was not directly measured. We were also not able to measure telomere attrition as we did not incorporate longitudinal data and reverse causation cannot be excluded. However, there are very few large scale studies with repeated measures of telomere length.

The issue of inter and intra assay measurement variation (inter and intra assay CV) is relevant when combining data from different techniques and laboratories. Inter assay CV is higher for q-PCR (T/S ratio) than for Southern blots (bp) (128) and although the method of measurement of telomere length was not detected as a large source of heterogeneity, we stratified the analyses by method of measurement and indeed the estimate of the Southern blots method and of q-PCR differed slightly. However, we did not take intra assay CV into account. Two other weaknesses were that we did not take into account the DNA extraction method, although DNA extraction method has been found to influence the telomere length (129-131), and that we did not use standardized betas in the regression analysis for a more accurate comparison between white blood cell types, because telomere length differs across white blood cell types. Leucocytes are a mixture of cells that may actually change with increasing inflammation. Control for differential counts would have improved the accuracy of the associations. However, cell type was not a source of heterogeneity and additional stratification by cell type did not change the results (data not shown).

The lengths of telomeres at different ages are highly correlated, and it has been suggested that most of the variation in leucocyte telomere length in adults is a result of telomere length at birth and that therefore the impact of environmental and lifestyle factors is rather small (119, 132). Benetos et al. described that ranking of individuals into deciles according to their telomere length barely changes across adult life. They showed that around half of the individuals stay in the same decile, whereas 17.9% showed a downwards shift and 20.7% showed an upward shift of one decile (119). Our meta-analysis shows that five units increase in BMI corresponds to ~25 bp or even ~40 bp change in the young population, which is equivalent to at least a yearly decrease irrespective of ranking. This could be an additional argument to tackle the obesity epidemic.

In summary, a higher BMI is associated with shorter telomeres, especially in the younger population. Although no causal inference can be drawn and the possibility of residual confounding is always a possibility, the results were robust across a variety of potential confounders. Given this, we could possibly infer that the obesity epidemic may be contributing to an increased biological aging of the population. However, meta-analyses of longitudinal studies that can evaluate change in body weight alongside change in telomere length are warranted.

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Table 1 Characteristics of included Study samples

ref	Study Name	all	men	women	18 - 60 yrs	> 60 - 75 yrs	> 75 yrs	Cell type	TL measure	DNA	BMI	Data	Design	Ethnicity (proportion) White/ Black/ Asian/ Hispanic/ Native American
		n	n	n	n	n	n							
absolute TL bp														
(3, 27-30)	TwinsUK	3236	286	2950	2630	574	32	Leucocytes	Southern Blot RF	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(16, 31-33)	Bogalusa	635	635	0	635	0	0	Leucocytes	Southern Blot RF	unknown	measured	raw	cohort	0.71 / 0.29 / 0 / 0 / 0
(133)	India CURES Study	40	20	20	37	3	0	Leucocytes	Southern Blot RF	stored	measured	raw	case-control	0 / 0 / 1 / 0 / 0
(35)	Campania	528	251	277	320	100	108	Leucocytes	Southern Blot RF	stored	measured	raw	cohort	1 / 0 / 0 / 0 / 0
(13, 36-38)	Asklepios	2509	1218	1291	2509	0	0	Leucocytes	Southern Blot RF	stored	measured	raw	cohort	1 / 0 / 0 / 0 / 0
(5, 12, 39)	Framingham	1146	557	589	658	444	44	Leucocytes	Southern Blot RF		measured	summary	cohort	1 / 0 / 0 / 0 / 0
(41)	COPD	178	89	89	113	60	5	Leucocytes	Real Time PCR		measured	raw	case-control	1 / 0 / 0 / 0 / 0
(42)	Crete	109	109	0	0	0	109	Leucocytes	Real Time PCR		measured	raw	cohort	1 / 0 / 0 / 0 / 0
(40)	Zutphen	189	189	0	0	68	121	Leucocytes	Real Time PCR		measured	raw	cohort	1 / 0 / 0 / 0 / 0
(16)	Family Heart African American	625	216	409	459	148	18	Leucocytes	Southern Blot RF		measured	summary	cohort	0 / 1 / 0 / 0 / 0
(16)	Family Heart White	2603	1170	1433	1419	997	187	Leucocytes	Southern Blot RF		measured	summary	cohort	1 / 0 / 0 / 0 / 0
Not publ	HyperGEN African American	224	108	116	172	51	1	Leucocytes	Southern Blot RF		measured	summary	cohort	0 / 1 / 0 / 0 / 0
Not publ	HyperGEN White	1240	612	628	799	426	15	Leucocytes	Southern Blot RF		measured	summary	cohort	1 / 0 / 0 / 0 / 0
(43, 44)	LSADT	525	171	354	0	82	443	Leucocytes	Southern Blot RF		measured	summary	cohort	1 / 0 / 0 / 0 / 0
(45, 46)	Heart and Soul	954	777	177	274	451	229	Leucocytes	Real Time PCR	unknown	measured	summary	cohort	0.60 / 0.16 / 0.12 / 0.09 / 0.03
(56, 57)	Lothian	1057	530	527	0	1057	0	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(47, 48)	WarTwins	639	639	0	0	86	553	Leucocytes	Southern Blot RF	stored	reported	raw	cohort	1 / 0 / 0 / 0 / 0
(54)	Jerusalem LRC	620	413	207	620	0	0	Leucocytes	Southern Blot RF	Buffy coat stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(55)	Jerusalem Palestinians	939	498	441	336	306	0	Leukocytes	Southern Blot RF	Buffy coat stored	measured	summary	Cross-sectional	1 / 0 / 0 / 0 / 0
(49-51)	Helsinki Businessmen Study (HBS)	487	487	0	0	250	237	Leucocytes	Southern Blot RF	stored	reported	raw	cohort	1 / 0 / 0 / 0 / 0
(52)	Copenhagen General Population Study	45069	20422	24647	26040	14525	4504	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(53)	SOLVABLE	152	0	152	136	16	0	PBMC	Real Time PCR	stored	measured	summary	case-control	0.70 / 0.22 / 0.03 / 0.05 / 0
(58)	ZTL2008	25	17	8	24	1	0	PBMC	Southern Blot RF	stored	measured	raw	cohort	1 / 0 / 0 / 0 / 0
absolute TL estimated from T/S ratio														
(18, 59, 63, 64)	South Carolina	323	145	178	305	18	0	Leucocytes	Real Time PCR	unknown	measured	summary	cohort	0.57 / 0.41 / 0.01 / 0.01 / 0

(60, 61, 65)	Bruneck	800	395	405	363	315	122	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(62)	RPCI	174	0	174	111	47	16	Leucocytes	Real Time PCR	stored	reported	raw	case-control	0.93 / 0.05 / 0 / 0 / 0.02
Telomere length T/S ratio														
(14)	MONICA	511	183	328	419	92	0	Leucocytes	Real Time PCR		measured	raw	cohort	1 / 0 / 0 / 0 / 0
(14)	MDCC	476	330	146	199	277	0	granulocytes	Real Time PCR		measured	raw	cohort	1 / 0 / 0 / 0 / 0
Not publ	Utah Pedigree Study	964	493	471	725	183	56	Leucocytes	Real Time PCR		measured	summary	cohort	1 / 0 / 0 / 0 / 0
(68, 69)	MESA White	182	89	93	80	80	22	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(68, 69)	MESA African American	278	125	153	141	109	28	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0 / 1 / 0 / 0 / 0
(68, 69)	MESA Hispanic	518	252	266	245	231	42	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0 / 0 / 0 / 1 / 0
(70)	EARSII T/S controls	395	395	0	395	0	0	Leucocytes	Real Time PCR	unknown	measured	raw	case-control	1 / 0 / 0 / 0 / 0
(71)	UCLA MacArthur	233	115	118	0	144	89	Leucocytes	Real Time PCR		reported	summary	cohort	1 / 0 / 0 / 0 / 0
(72)	Ashkenazi	359	191	168	50	179	130	Leucocytes	Real Time PCR	stored	measured	raw	cohort	1 / 0 / 0 / 0 / 0
(73)	Warsaw	714	246	468	235	411	68	Leucocytes	Real Time PCR	stored	measured	raw	case-control	1 / 0 / 0 / 0 / 0
(74)	Finland Health 2000 cohort	938	350	588	754	137	47	Leucocytes	Real Time PCR	stored	unknown	summary	cohort	1 / 0 / 0 / 0 / 0
(75)	Sister Study I (Vanguard sample)	644	0	644	475	169	0	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0.83 / 0.07 / 0.02 / 0.02 / 0.05
(111)	Sister Study II (Genetic Study subcohort)	734	0	734	548	186	0	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0.92 / 0.04 / 0 / 0.02 / 0.02
(76)	CAS controls	183	96	87	112	53	18	Leucocytes	Real Time PCR	stored	measured	raw	case-control	1 / 0 / 0 / 0 / 0
(77)	PATH 40	331	151	180	331	0	0	Leucocytes	Real Time PCR	stored	reported	raw	cohort	0.95 / 0 / 0.03 / 0 / 0.02
(77)	PATH 60	294	157	137	0	294		Leucocytes	Real Time PCR	stored	reported	raw	cohort	0.97 / 0 / 0.02 / 0 / 0.01
(78)	Italy alcohol controls	258	258	0	255	3	0	Leucocytes	Real Time PCR	stored	reported	raw	case-control	1 / 0 / 0 / 0 / 0
(79)	Fels Longitudinal Study	257	116	104	196	54	7	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(80, 81)	Ecran	188	38	150	121	41	26	PBMC	Real Time PCR		measured	raw	cohort	0 / 0 / 0 / 1 / 0
(82, 83)	Heart Scan Study	434	206	228	169	259	0	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(84, 85)	Boiler workers	104	104	0	97	7	0	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0.85 / 0.09 / 0.02 / 0.03
(86, 87)	Mayo	2886	1470	1416	2001	709	176	Leucocytes	Real Time PCR		measured	raw	case-control	0.98 / 0 / 0.01 / 0.01 / 0
(88, 89, 102, 105-108)	HBCS	1962	911	1051	703	1259	0	Leucocytes	Real Time PCR		measured	raw	cohort	1 / 0 / 0 / 0 / 0
(90-92)	PREVEND	7991	3994	3997	6094	1897	0	Leucocytes	Real Time PCR		measured	summary	cohort	0.96 / 0.01 /0.02 / 0 / 0.01
(93, 94, 103, 104)	Strong Heart Family Study	3256	1315	1941	2834	340	82	Leucocytes	Real Time PCR		measured	summary	cohort	0 / 0 / 0 / 0 / 1
(95)	PREDIMED-NAVARRA	521	236	285	81	401	38	Leucocytes	Real Time PCR	stored	measured	summary	RCT	1 / 0 / 0 / 0 / 0
(96)	NHANES	7349	3542	3807	5034	1564	751	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0.52 / 0.18 / 0 / 0.30 / 0

(97)	SWHS	2912	0	2912	1812	1100	0	Leucocytes	Real Time PCR		measured	summary	cohort	0 / 0 / 1 / 0 / 0
(98)	DHS white	1073	493	580	821	245	7	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(98)	DHS black	1667	606	1061	1348	317	17	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0 / 1 / 0 / 0 / 0
(98)	DHS hispanic	464	194	270	412	51	1	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0 / 0 / 0 / 1 / 0
(99)	DALS	734	401	333	268	366	100	Leucocytes	Real Time PCR	stored	measured	summary	case-control	0.96 / 0 / 0 / 0.03 / 0
(102, 110)	FinnTwin study	2096	1101	995	1589	385	122	Leucocytes	Real Time PCR		measured	summary	cohort	1 / 0 / 0 / 0 / 0
(109)	Former Athletes Study	586	586	0	1	376	209	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(101)	USKCS whole blood	765	442	323	395	320	50	Leucocytes	Real Time PCR	stored	measured	summary	case-control	0.61 / 0.39 / 0 / 0 / 0
(101)	USKCS buffy coat	126	70	56	87	36	3	Leucocytes	Real Time PCR	stored	measured	summary	case-control	0.66 / 0.34 / 0 / 0 / 0
(100)	Erasmus Rucphen Study	2449	1082	1367	1900	499	50	Leucocytes	Real Time PCR	stored	measured	summary	case-control	1 / 0 / 0 / 0 / 0
	Rotterdam Study	2231	944	1287	556	1272	404	Leucocytes	Real Time PCR	stored	measured	summary	case-control	1 / 0 / 0 / 0 / 0
(100)	KORA F3	3113	1509	1604	1768	1051	294	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(100)	KORA F4	3014	1457	1557	1824	943	247	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(134)	CAVASIC	315	315		155	160	0	Leucocytes	Real Time PCR	stored	measured	summary	case-control	1 / 0 / 0 / 0 / 0
(100, 135)	SAPHIR	1681	1055	626	1586	95	0	Leucocytes	Real Time PCR	stored	measured	summary	cohort	1 / 0 / 0 / 0 / 0
(112)	Cebu Longitudinal Health and Nutrition Survey (CLHNS)	3467	893	2574	3380	87	0	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0 / 0 / 1 / 0 / 0
(113)	Nutrition and Exercise for Women (NEW) Study	437	0	437	304	131	2	Leucocytes	Real Time PCR	stored	measured	raw	cohort	0.85 / 0.08 / 0.02 / 0.03 / 0.02
(114)	NESDO	495	173	322	17	354	124	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0.95 / 0.01 / 0.04 / 0 / 0
(115)	NESDA	2936	986	1950	2749	187	0	Leucocytes	Real Time PCR	stored	measured	summary	cohort	0.97 / 0.02 / 0.01 / 0 / 0

Table 2 Summary of the beta estimates (regression coefficients) from the meta-analysis of the association between BMI and telomere length as outcome

Table 2a: absolute telomere length (bp)

	All together (total population, adjusted for age)					"Young" population (age ≥18 and ≤ 60 years)					"Middle " population (60 < age ≤ 75 years)					"Old" population (age > 75 years)				
	N[1]	estimate	95%C.I.		I^2 (%)	N	estimate	95%C.I.		I^2 (%)	N	estimate	95%C.I.		I^2 (%)	N	estimate	95%C.I.		I^2
Both sexes (Men and Women)[2]																				
Overall	26	**-4.14**	**-5.69**	**-2.59**	7.1	20	**-8.09**	**-10.26**	**-5.92**	15.3	19	**-2.59**	**-4.95**	**-0.23**	0.0	15	**-6.15**	**-11.05**	**-1.25**	11.5
White	20	**-4.77**	**-6.45**	**-3.01**	8.1	14	**-9.61**	**-11.44**	**-7.78**	0.0	14	**-3.19**	**-5.68**	**-0.71**	0.0	13	**-6.97**	**-12.29**	**-1.64**	15.4
African American	2	0.86	-4.75	6.46	0.0	2	0.960	-5.51	7.43	1.2	2	4.36	-7.25 15.97		0.0	1	74.70	-76.02 225.42		
Hispanic	0					0					0					0				
Asian	1	65.85	-216.58 348.27			1	104.99	-197.96 407.94			0					0				
Native American	0					0					0					0				
Design cohort	22	**-3.98**	**-5.77**	**-2.18**	20.3	16	**-7.88**	**-10.34**	**-5.42**	31.0	16	**-2.64**	**-5.00**	**-0.27**	0.0	13	**-5.07**	**-9.19**	**-0.95**	0.0
Design control	4	-5.76	-24.03 12.51		0.0	4	-7.62	-30.52	15.28	0.0	4	38.33	-50.49 127.15		**61.8**	2	**-60.24**	**-100.90**	**-19.58**	0.0
Men																				
Overall	24	**-4.22**	**-7.40**	**-1.04**	34.7	18	**-8.38**	**-12.87**	**-3.90**	42.3	17	-3.04	-7.57	1.50	9.9	14	-3.69	-9.05	1.67	0.0

White	19	**-4.89**	**-8.41**	**-1.37**	37.2	13	**-9.92**	**-14.77**	**-5.06**	43.4	13	-4.17	-9.14	0.80	11.2	12	-4.49	-10.11	1.13	0.0
African American	2	-3.83	-14.33	6.68	0.0	2	-4.38	-16.46	7.71	7.0	2	3.09	-20.84	27.02	0.0	1	-101.30	-885.68	683.08	
Hispanic	0					0					0					0				
Asian	1	-257.79	-541.64	26.07		1	-298.12	-639.90	43.66		0					0				
Native American	0					0					0					0				
Design cohort	22	**-4.18**	**-7.32**	**-1.32**	34.7	16	**-8.33**	**-12.79**	**-3.88**	43.9	16	-2.88	-7.69	1.94	15.0	13	-3.49	-8.86	1.89	0.0
Design control	2	-90.56	-323.80	142.70	**66.7**	2	-101.31	-366.67	164.05	**63.4**	1	5.29	-46.23	56.81		1	-48.41	-128.05	31.23	
Women																				
Overall	21	**-4.74**	**-6.44**	**-3.04**	0.0	19	**-9.12**	**-11.31**	**-6.94**	0.0	16	-2.35	-5.29	0.59	0.0	10	-6.41	-12.84	0.03	0.0
White	15	**-4.91**	**-6.70**	**-3.12**	0.0	13	**-9.92**	**-12.24**	**-7.60**	0.0	11	-2.60	-5.65	0.45	0.0	8	-7.67	-16.88	1.54	18.7
African American	2	-0.86	-7.54	5.82	0.0	2	-0.80	-8.56	6.97	0.0	2	3.68	-10.21	17.57	0.0	1	-14.80	-67.52	37.92	
Hispanic	0					0					0					0				
Asian	1	187.65	-272.75	648.04		1	246.73	-181.77	675.23		0					0				

Native American	0					0					0					0			
Design cohort	17	**-4.74**	**-6.44**	**-3.04**	0.0	15	**-9.13**	**-11.33**	**-6.94**	0.0	13	-2.38	-5.32	0.57	0.0	9	-7.02	-14.81 0.77	7.7
Design control	4	-5.11	-29.19 18.97		0.0	4	-7.36	-36.67	21.96	0.0	4	37.35	-60.90 135.60		**65.0**	1	-23.41	-168.15 121.33	

[1]N= number of studies; [2]Adjusted for sex; Bold: p< 0.05 or I^2>50%

Table 2b relative telomere length (T/S ratio)

	All together (total population, adjusted for age)					"Young" population (age ≥18 and ≤ 60 years)					"Middle " population (60 < age ≤ 75 years)					"Old" population (age > 75 years)				
	N[1]	estimate	95%C.I.		I^2 (%)	N	estimate	95%C.I.		I^2 (%)	N	estimate	95%C.I.		I^2 (%)	N	estimate	95%C.I.		I^2 (%)
Both sexes (Men and Women)[2]																				
Overall	46	**-1.50**	**-2.12**	**-0.88**	41.1	43	**-2.30**	**-3.75**	**-0.84**	**83.7**	43	**-0.95**	**-1.68**	**-0.21**	0.0	24	0.31	-1.56	2.17	10.7
white	35	**-1.85**	**-2.49**	**-1.22**	15.7	32	**-2.36**	**-4.55**	**-1.725**	**86.9**	32	**-1.59**	**-2.46**	**-0.71**	0.0	18	-0.08	-2.36	2.21	9.4
African American	2	5.66	-6.60	17.92	**80.0**	2	5.21	-5.67	16.08	**68.7**	2	0.08	-6.20	6.36	0.0	1	-0.74	-12.62	11.14	
Hispanic	3	2.53	-5.18	10.25	17.7	3	-0.42	-4.19	3.34	0.0	3	2.31	-2.35	6.97	0.0	2	27.29	-40.32	94.61	**77.7**
Asian	2	-0.09	-2.85	2.67	52.4	2	**-5.00**	**-5.77**	**-3.22**	0.0	2	2.18	-2.90	7.27	0.0	0				
Native American	1	**-2.64**	**-3.60**	**-1.68**		1	**-4.14**	**-5.28**	**-3.00**		1	2.23	-1.00	5.46		1	4.68	-2.35	11.71	
Design cohort	36	**-1.58**	**-2.25**	**-0.91**	38.8	33	**-2.56**	**-4.36**	**-0.79**	**86.8**	35	**-1.16**	**-1.95**	**-0.37**	0.0	18	0.04	-2.04	2.13	13.2
Design control	9	-0.32	-2.31	1.67	26.2	9	-0.39	-2.39	1.61	0.0	7	-1.18	-4.56	2.19	34.2	5	-0.60	-6.95	5.75	12.5
Men																				
Overall	42	**-1.64**	**-2.40**	**-0.53**	34.3	39	**-2.37**	**-3.95**	**-0.79**	59.4	37	-0.71	-2.22	0.80	21.6	23	-4.26	-10.54	2.03	**74.0**
white	32	**-1.83**	**-2.98**	**-0.67**	30.6	29	**-2.76**	**-4.88**	**-0.64**	60.5	29	-0.99	-3.00	1.02	34.7	18	-8.56	-17.77	0.65	**79.4**

African American	2	-1.16	-10.39 12.69		38.6	2	2.39	-11.17 15.96		39.5	2	-2.29	-13.36 8.78		0.0	1	-0.39	-22.18 21.41		
Hispanic	3	-2.12	-6.54	2.31	0.0	3	-2.99	-8.61	2.62	0.0	3	0.45	-8.17	9.06	0.0	1	2.04	-9.98 14.06		
Asian	1	3.53	-0.05	7.11		1	3.03	-0.59	6.65		0					0				
Native American	1	**-2.31**	**-3.72**	**-0.90**		1	**-3.96**	**-5.57**	**-2.36**		1	0.61	-6.04	7.26		1	5.93	-5.39 17.25		
Design cohort	32	**-1.72**	**-2.69**	**-0.75**	24.9	29	**-2.95**	**-4.88**	**-1.03**	**64.0**	29	-0.89	-2.21	0.44	2.1	17	-0.36	-4.90	4.16	38.1
Design control	9	-0.37	-3.95	3.20	40.5	9	1.76	-1.22	4.74	0.0	7	-1.19	-8.40	6.10	**64.1**	5	-32.84	-68.99 3.32		**92.6**
Women																				
Overall	41	**-1.49**	**-2.18**	**-0.80**	33.5	39	**-3.06**	**-4.12**	**-2.01**	**53.9**	40	**-1.26**	**-2.18**	**-0.35**	0.0	23	0.56	-1.89	3.00	13.7
white	30	**-1.72**	**-2.45**	**-1.00**	8.1	28	**-3.12**	**-4.54**	**-1.69**	**51.8**	29	**-2.30**	**-3.38**	**-1.21**	0.0	17	-0.13	-2.93	3.20	14.3
African American	2	6.10	-5.70 17.91		**71.3**	2	4.67	-3.87 13.21		39.9	2	1.43	-6.29	9.14	0.8	1	-1.66	-15.20 11.89		
Hispanic	3	7.25	-6.05 20.55		39.3	3	1.14	-4.74	7.02	2.4	3	3.03	-2.53	8.59	0.0	2	28.54	-36.12 93.20		**75.4**
Asian	2	-0.22	-2.43	1.95	33.8	2	**-5.68**	**-7.04**	**-4.31**	0.0	2	2.18	-2.90	7.27	0.0	0				
Native American	1	**-2.92**	**-4.11**	**-1.73**		1	**-4.42**	**-5.81**	**-3.03**		1	3.54	0.11	6.98		1	4.67	-3.14 12.48		
Design cohort	34	**-1.44**	**-2.21**	**-0.67**	34.7	32	**-3.12**	**-4.37**	**-1.87**	**59.5**	33	**-1.67**	**-2.65**	**-0.68**	0.0	17	0.13	-2.56	2.84	14.9
Design control	6	-0.92	-2.98	1.13	0.0	6	-1.94	-4.68	0.79	0.0	6	-1.17	-4.59	2.26	0.0	5	0.34	-9.01	9.68	24.8

[1]N= number of studies; [2]Adjusted for sex; Bold: p< 0.05 or I^2>50%

LEGEND OF FIGURES

Figure 1

Inclusion flow chart

Figure 2

Forest plot of the beta estimates (regression coefficients) from the meta-analysis of the association between BMI and absolute telomere length (bp) (A) or relative telomere length (T/S ratio) (B) as outcome in the total population

Figure 2a: absolute telomere length (bp)

Figure 2b: relative telomere length (T/S ratio)

Figue 3

Forest plot of the beta estimates (regression coefficients) from the meta-analysis of the association between BMI and absolute telomere length (bp) or relative telomere length (T/S ratio) (B) as outcome in the "young" population (age ≥18 and ≤ 60 years)

Figure 2a: absolute telomere length (bp)

Figure 2b: relative telomere length (T/S ratio)

Figure 1 Inclusion flow chart

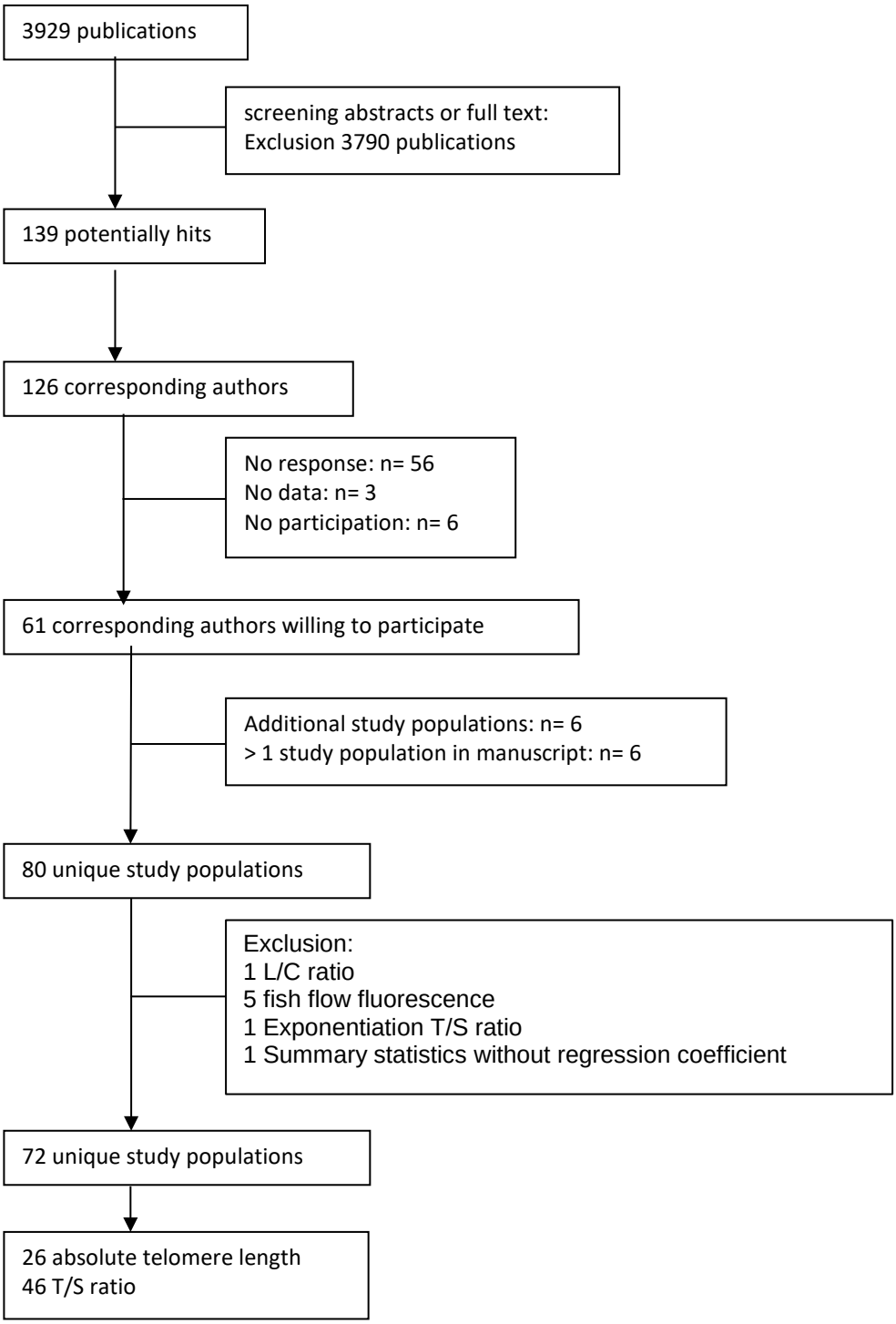


Figure 2 Forest plot of the beta estimates (regression coefficients) from the meta-analysis of the association between BMI and absolute telomere length (bp) (A) or relative telomere length (T/S ratio) (B) as outcome in the total population

Figure 2a: absolute telomere length (bp)

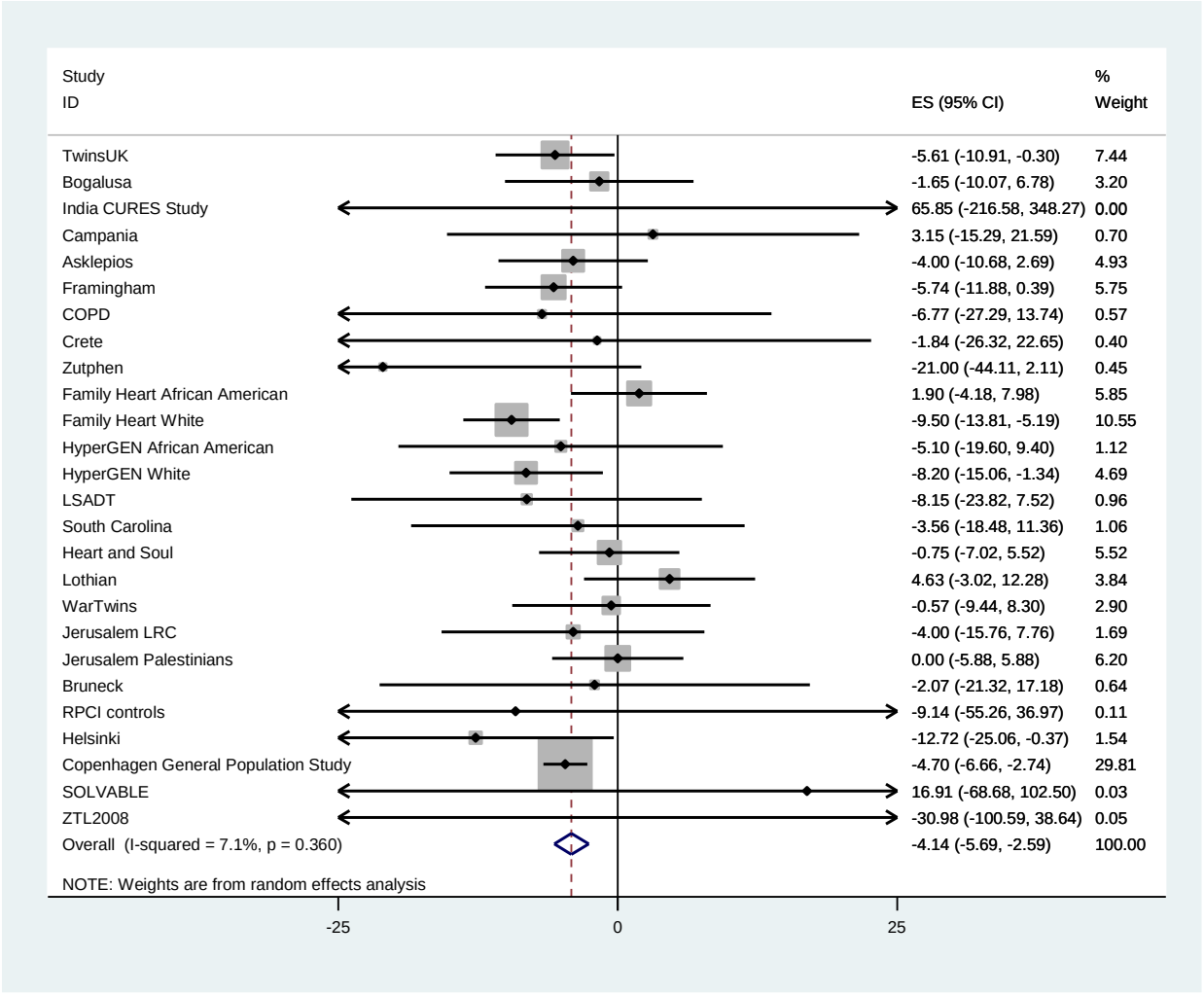


Figure 2b: relative telomere length (T/S ratio)

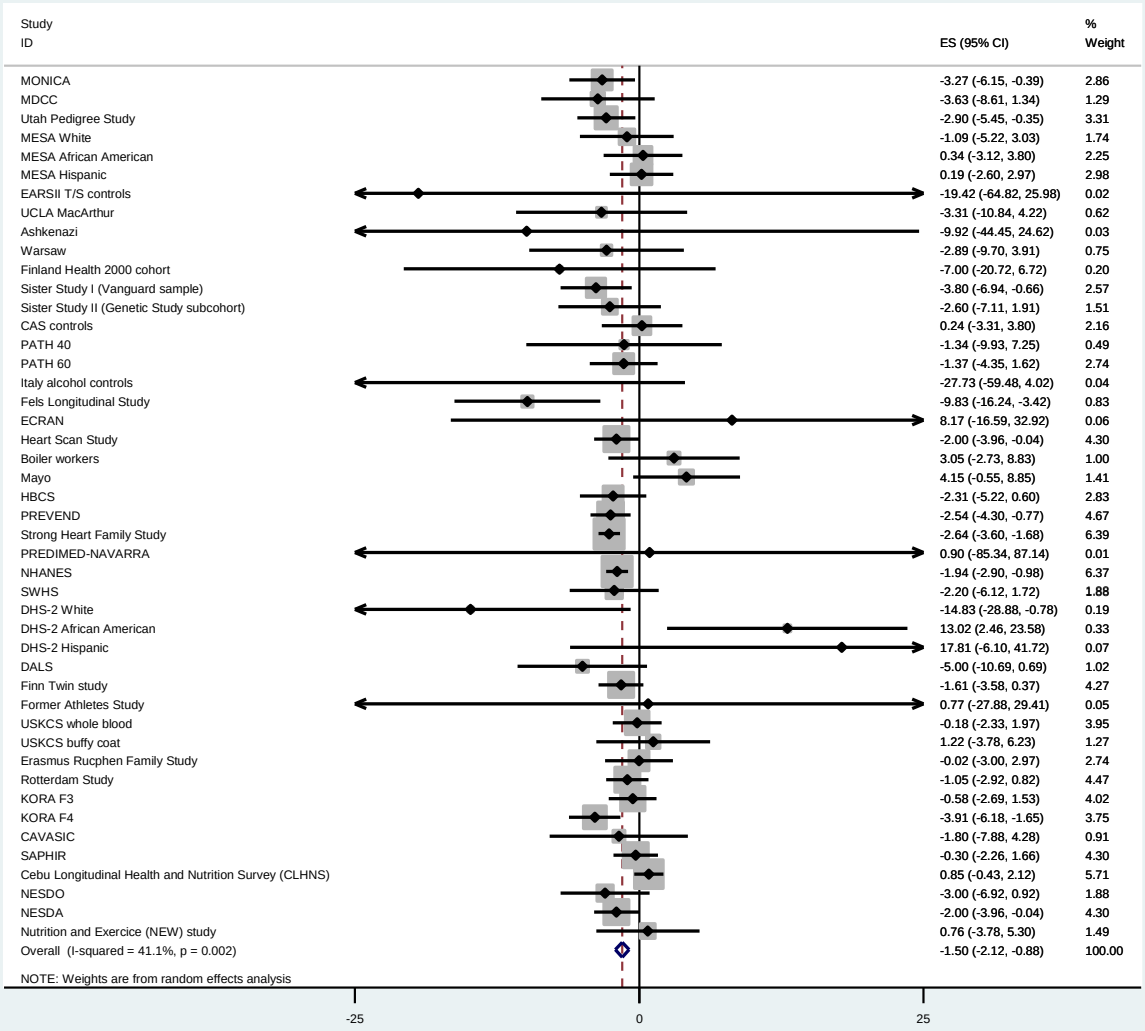


Fig 3 Forest plot of the beta estimates (regression coefficients) from the meta-analysis of the association between BMI and absolute telomere length (bp) or relative telomere length (T/S ratio) (B) as outcome in the "young" population (age ≥18 and ≤ 60 years)

Figure 3a: absolute telomere length (bp)

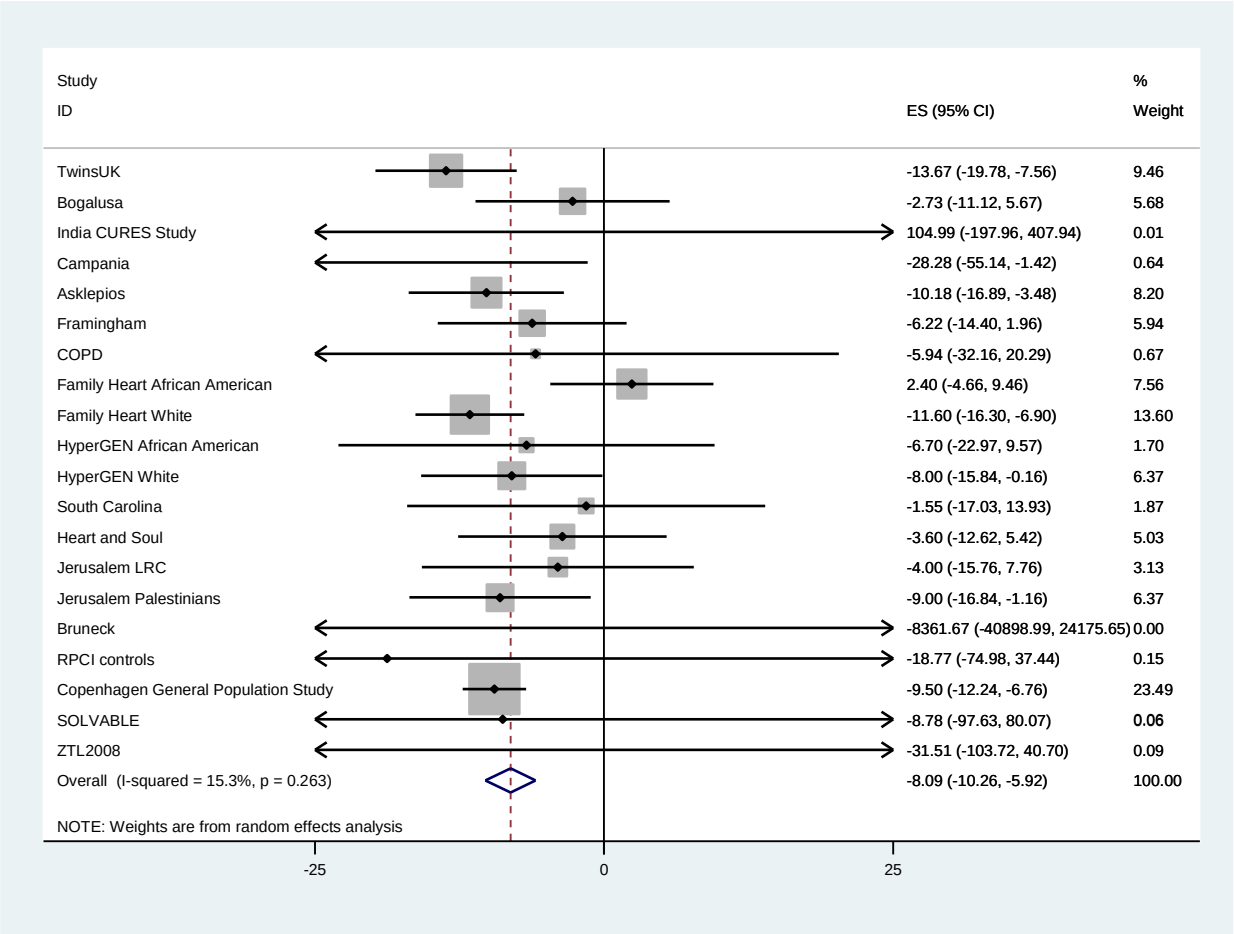
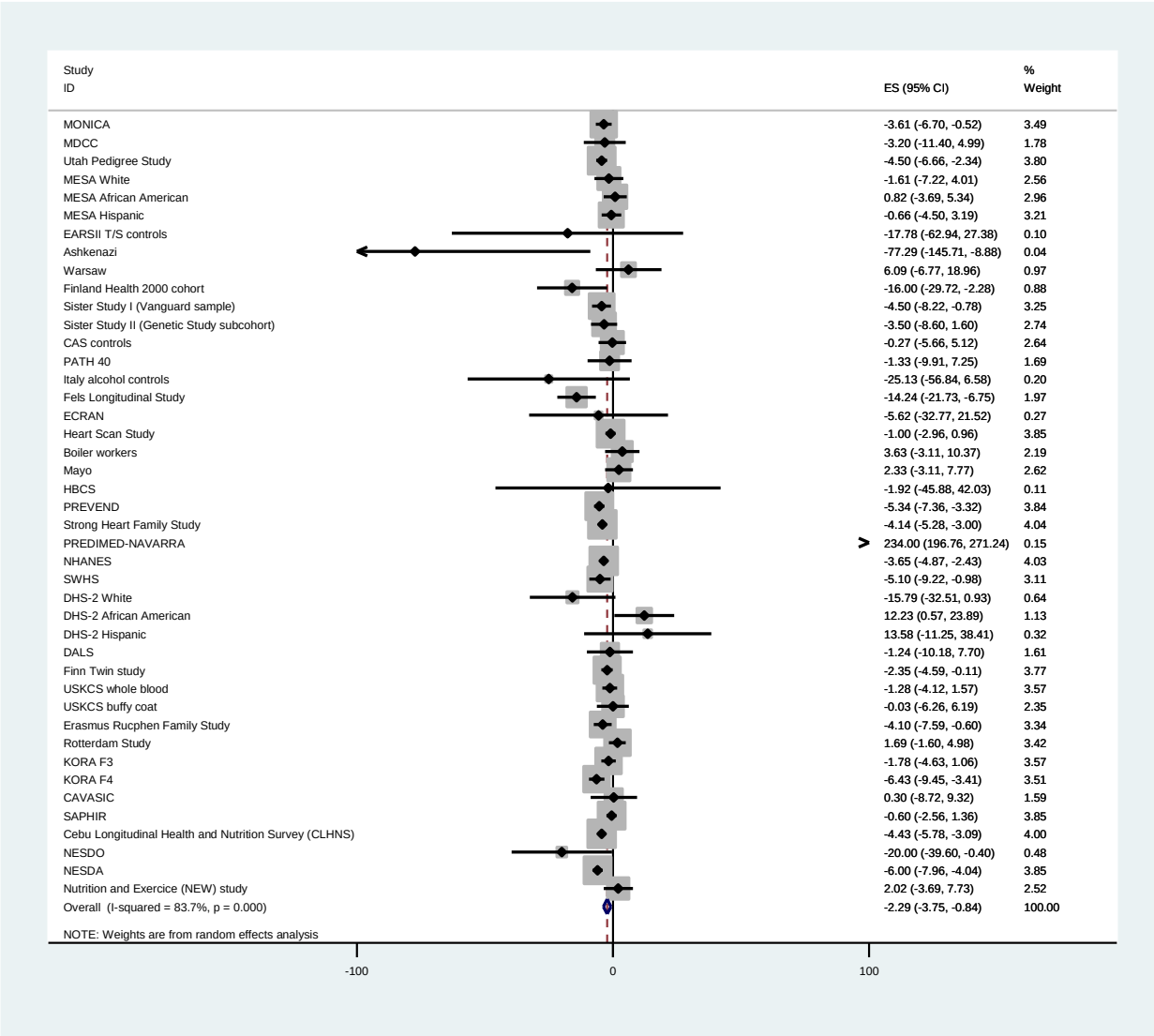


Figure 3b: relative telomere length (T/S ratio)



ELECTRONIC SUPPLAMENTARY MATERIAL

Online resource 1

Electronic supplemental material

Contains additional information about search, assessing heterogeneity (Meta-regression and sources of heterogeneity), sensitivity analyses and the study protocol for participating PIs

Online resource 2

Electronic Figure 1a Absolute telomere length

All forest plots of the beta estimates (regression coefficients) from the meta-analysis of the association between BMI and absolute telomere length (bp) as outcome stratified by age, sex, ethnicity and study design.

Online resource 3

Electronic Figure 1b Relative telomere length.

All forest plots of the beta estimates (regression coefficients) from the meta-analysis of the association between BMI and relative telomere length (T/S ratio) as outcome stratified by age, sex, ethnicity and study design.