WEB APPENDIX

Systematic Review Protocol

(July 2012)

Is Socioeconomic Status Associated With Biologic Aging, as Measured by Telomere Length?

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A. Background

Throughout the world there are socially-derived inequalities in health(1). Not only do the poorest members of society suffer the worst health, but there is also a social gradient, whereby each step up the social ladder is associated with improved health. However, the pathways and mechanisms by which socioeconomic status (SES) 'gets under the skin' are less well understood. One possible pathway is through a process referred to as 'biological ageing'. Here, lower SES individuals would suffer greater degeneration of both physical functioning and the ability of the body to meet its physiological demands, compared to higher SES individuals of the same chronological age (2-4). This biological ageing works via the accumulation of damage to macromolecules (DNA, RNA, proteins, lipids) (5), with this damage driven by exposure to physical, mental and behavioural insults. Importantly, all of these insults are more prevalent with lower SES.(6) Understanding the relationship between SES and biological ageing is important to aid our understanding of not only how social circumstances get under the skin to increase rates of early morbidity and mortality, but also so that we can attempt to minimise these detrimental effects and promote the need for a narrowing of the social inequality gap that presides currently.

Telomeres are nucleoprotein structures (proteins associated with DNA) present at the ends of chromosomes that erode over time through various processes of genetic damage and cell proliferation. This gradual shortening of telomeres has made telomere length a potential measure of an individual's biological age.(7) If socioeconomic disadvantage does lead to greater cellular damage and more rapid biological ageing, this should be reflected in shorter telomeres.(2)

The evidence for an association between SES and telomere length has thus far been mixed. This myriad of results includes disadvantaged SES being associated with

shorter telomeres, (8-9) disadvantaged SES being associated with longer telomeres (10) and SES not being associated with telomere length.(11-13) Therefore, there is a need to quantitatively assess this relationship. To our knowledge, this is the first such systematic review with meta-analysis in this field.

B. Review Aims

To systematically review and quantitatively assess the evidence (using meta-analysis) for the association between SES and telomere length.

Our objectives, in terms of the PICOS statement, were as follows:

Population:	Adult men and women (18+)
Intervention:	N/A
Comparator:	Socioeconomic Status
Outcome:	Telomere length differences between high and low socioeconomic status groups
Study design:	Longitudinal, cross-sectional and repeat-cross sectional studies. Population/community-based studies. Population/community-based studies sampling from specific occupation, hospital admission or disease state groups. Case-control studies.

C. Search strategy

Author abbreviations: Tony Robertson (TR), G David Batty (DB), Geoff Der (GD), Candida Fenton (CF), Paul Shiels (PS) and Michaela Benzeval (MB).

Date of Search: 24/10/11

Authors involved: CF and TR

1. ISI Web of Knowledge (http//:wok.mimas.ac.uk all years), Embase (www.embase.com 1980-2011) and Medline (http://www.ncbi.nlm.nih.gov 1948-2011) will be searched.
2. For telomere, these terms included: telomere; telomere binding-proteins; cell aging; cell ageing; biological aging; biological ageing; cellular aging; cellular ageing; nucleoprotein structure. For socioeconomic status, these terms included: socio-economic; socioeconomic; education; income; area deprivation; neighbourhood; neighborhood; employment; housing; financial difficulties; car ownership; class; poverty; social; status; income; tenure.
3. All publications identified by electronic searches were stored in EndNote.
4. All authors contacted experts in the field
5. A cited-reference search of all articles included in the systematic review following exclusion/inclusion (see section D below) was carried out (followed by identical exclusion/inclusion review as before).
6. Reference sections of identified and relevant articles were scrutinized.

D. Selection criteria

Inclusion criteria

1. A full report in a peer-reviewed journal (excludes interviews, book reviews meeting summaries and conference presentations/abstracts).
2. Published in English.
3. Abstract available.
4. A human study population (not animal or plant).
5. Community, not laboratory-based.

6. An empirical article (excludes reviews and cohort profiles).

Exclusion criteria

1. No evidence of telomere length.
2. No evidence of SES measures.
3. No evidence of telomere-SES analyses with telomere measured at a single point in time.
4. SES-telomere analysis, but no results presented. This includes where SES was used as a covariate, but no results presented or significance reported.
5. Telomere length measured in childhood (18+).

Selection process

1. Articles were assessed to confirm they meet the inclusion criteria by TR and MB independently.
2. Results were combined and compared. For those that did not match TR and MB discussed and when a consensus was reached, the articles were included/excluded accordingly. Where a consensus was not reached a third author (GD) was available for their opinion and the majority view to be taken. This was not necessary.
3. TR identified any duplicate articles and these were verified by MB.
4. Articles that remained were scrutinised by TR and MB independently, with articles excluded if any of the above exclusion criteria were met.
5. Results were combined and compared. For those that did not match TR and MB discussed and where a consensus was reached, the articles were included/excluded accordingly. If a consensus was not reached a third author

(GD) was available for their opinion and the majority view to be taken. This was not necessary.

E. Study quality assessment

1. Checklist defined by TR and MB (Table 1).
2. TR and MB independently assessed each article and assigned a score for each criterion using the data extracted (see section F). Any discrepancies were discussion and a final score agreed. All authors also checked during the draft paper stage using the extracted data.
3. Any disagreements on scores assigned could be discussed by all authors until a consensus was reached, although this was not necessary.

F. Data extraction

1. Data required for the systematic review agreed by all authors:

Information on study participants (sample size, age range, sex, study design), telomere measure (technique and measurement units), SES dimensions, main results and adjustments in analysis.

2. TR extracted the data for each article according to the above features of each article and entered the data in a Microsoft Word table.
3. MB verified.
4. All authors checked data extraction had been completed properly during draft paper stage.

G. Synthesis

1. Extracted data were assessed for their suitability for quantitative analysis using meta-analysis by TR, MB and GD in order to perform a high-low SES comparison and a linear trend comparison (using a Relative Index of Inequality), with data required:

   Mean telomere length (sex and age adjusted) for each category, error measurement (SD/SE/CI) and sample size.

2. Inclusion criteria:

   i) Telomere was analyzed as a continuous measure.

   ii) SES measures were available as ordinal categories.

   iii) Results were available as mean telomere length, SD and the sample size for each SES category.

3. Where full results that meet the above criteria were not presented in the articles, authors were contacted by TR and requests made for the necessary summary statistics.
4. Quality scores were adjusted for the meta-analysis based on the complete data provided.
5. If more than one article presented identical analysis, the earliest-published article was used.
6. If telomere was measured more than once, baseline telomere length was used/sought.
7. TR summarised the available data according to three categories for the most consistent SES measures across studies:

   Childhood SES, Contemporaneous SES and Education

8. For contemporaneous and childhood SES where social class (own/parental) was not available, income was used. Where income was available, employment status was used. For education, where attainment was not available, years of full-time education were used.
9. Separate meta-analyses were run for childhood SES, contemporaneous SES and education, using both the low-high and the RII comparison (as a sensitivity measure).
10. Comprehensive Meta-Analysis (CMA, version 2.2.064, Biostat, New Jersey, USA) was used for all analyses and for the production of forest plots / publication bias plots.
11. Heterogeneity between studies was considered by estimating a random-effects model, with the inverse variation method used to weight studies' effect sizes. Meta-regression against quality score was used where heterogeneity identified. The sensitivity analyses below was also used to ascertain if the heterogeneity identified in any meta-analysis was linked to any subgroups or individual articles by calculating the same heterogeneity statistics for each sensitivity analysis.
12. The robustness of the results were checked in six ways:
    i. By applying a fixed-effects model.
    ii. By limiting articles to those where adjustments were made for only age, sex and assay plate (i.e. excluding those with a range of possible mediators).
    iii. By removing articles that did not adjust for age/sex (where applicable).
    iv. By removing poorer quality (lower and intermediate ranking) articles.
    v. By repeating the meta-analyses with each article removed.

vi. By re-running the meta-analyses using a continuous measure of SES (to allow for more gradated associations between SES and telomere length).

10. Publication bias was considered using the Begg and Mazumdar rank correlation test, as well as using a funnel plot in which the standardized mean differences are plotted against the sample sizes.(14-15)

I. Search Diary

Medline 25.10.11

Ovid MEDLINE(R) 1948 to October Week 2 2011

1. exp Telomere-Binding Proteins/ or exp Telomere/ or telomere.mp.

13906

2. Cell Aging.mp. or exp Cell Aging/

12871

3. biological aging.ti. or biological aging.ab. or biological ageing.ti. or biological ageing.ab. or Cellular aging.ti. or Cellular aging.ab. or Cellular ageing.ti. or Cellular ageing.ab. or Nucleoprotein structure*.ti. or Nucleoprotein structure*.ab.

1652

4. Social Class.mp. or exp Social Class/

31591

5. Socioeconomic Factors.mp. or exp Socioeconomic Factors/

298068

6. exp Employment, Supported/ or exp Employment/ or Employment.mp.

68363

7. Educational Status.mp. or exp Educational Status/

34621

8. exp Income/ or Income.mp. or exp Employee Retirement Income Security Act/

81867

9. Housing.mp. or exp Housing/ or exp Public Housing/ or exp Housing for the Elderly/

32333

10. exp Poverty Areas/ or exp Poverty/ or Poverty.mp.

32659

11. socio-economic.ti. or socio-economic.ab. or socioeconomic.ti. or socioeconomic.ab. or Education*.ti. or Education*.ab. or Income.ti. or Income.ab. or Area deprivation.ti. or Area deprivation.ab. or Social status.ti. or Social status.ab. or neighborhood.ti. or neighborhood.ab. or neighbourhood.ti. or neighbourhood.ab. or Employment.ti. or Employment.ab. or Housing.ti. or Housing.ab. or Financial difficulties.ti. or Financial difficulties.ab. or Car ownership.ti. or Car ownership.ab. or social class.ti. or social class.ab. or poverty.ti. or poverty.ab. or social.ti. or social.ab. or income.ti. or income.ab. or housing tenure.ti. or housing tenure.ab.

582121

12. 1 or 2 or 3

26423

13. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11

774067

14. 12 and 13

128

Embase 24.10.11

Embase 1980 to 2011 Week 42 via Ovid

1. exp telomere binding protein/ or exp telomere/ or telomere.mp.

16205

2. Cell Aging.mp. or exp cell aging/

8188

3. biological aging.ti. or biological aging.ab. or biological ageing.ti. or biological ageing.ab. or Cellular aging.ti. or Cellular aging.ab. or Cellular ageing.ti. or Cellular ageing.ab. or Nucleoprotein structure*.ti. or Nucleoprotein structure*.ab.

1800

4. Social Class.mp. or exp social class/

25284

5. Socioeconomic Factors.mp. or exp socioeconomics/

139169

6. exp temporary employment/ or exp employment discrimination/ or exp parttime employment/ or exp employment/ or exp employment status/ or employment.mp. or exp "employment of women"/ or exp self employment/

60684

7. educational status.mp. or exp educational status/

25629

8. exp lowest income group/ or income.mp. or exp income/

82931

9. Poverty.mp. or exp poverty/

28938

10. socio-economic.ti. or socio-economic.ab. or socioeconomic.ti. or socioeconomic.ab. or Education*.ti. or Education*.ab. or Income.ti. or Income.ab. or Area deprivation.ti. or Area deprivation.ab. or Social status.ti. or Social status.ab. or neighborhood.ti. or neighborhood.ab. or neighbourhood.ti. or neighbourhood.ab. or Employment.ti. or Employment.ab. or Housing.ti. or Housing.ab. or Financial difficulties.ti. or Financial difficulties.ab. or Car ownership.ti. or Car ownership.ab. or social class.ti. or social class.ab. or poverty.ti. or poverty.ab. or social.ti. or social.ab. or income.ti. or income.ab. or housing tenure.ti. or housing tenure.ab.

681281

11. work schedule.mp. or exp work schedule/

5530

12. exp housing/

13112

13. 1 or 2 or 3

24169

14. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12

803305

15. 13 and 14

162

ISI Web of Knowledge 24.10.11

All years

1. Topic=(Telomere*) OR Topic=("Cell Aging") OR Topic=("Cell Ageing") OR Topic=("biological aging") OR Topic=("biological ageing") OR Topic=("Cellular aging") OR Topic=("Cellular ageing") OR Topic=("Nucleoprotein structure*")

Timespan=All Years

Search language=English Lemmatization=Off

75,244

2. Topic=("Social Class") OR Topic=(Socioeconomic) OR Topic=("Socio-economic") OR Topic=(Employment) OR Topic=("Educational Status") OR Topic=(Income) OR Topic=("Housing tenure") OR Topic=(Poverty) OR Topic=(Education) OR Topic=(Income) OR Topic=("Area deprivation") OR Topic=("Social status") OR Topic=(neighborhood) OR Topic=(neighbourhood) OR Topic=(Employment) OR Topic=("Financial difficulties") OR Topic=("Car ownership") OR Topic=("social class") OR Topic=(poverty) OR Topic=(social) OR Topic=(income)

Timespan=All Years

Search language=English Lemmatization=Off

4,134,334

3. #2 AND #1

Timespan=All Years

Search language=English Lemmatization=Off

256

I. Tables

Table 1. Strengths and Limitations Criteria for Review Quality Score

STRENGTHS	LIMITATIONS
A. Community/population-based study (+1) - Sampled from the population of the geographic/demographic area of interest.	**A. Other study** - Includes case-control studies and those sampling population groups based on occupation, hospital admissions or disease state.
A. Representative sample (+1) - Generalisable to the wider population of the geographic/demographic area of interest (i.e. sex, age, ethnic-specific groups).	**A. Non-representative sample** - A subset of the population that does not reflect the members of the wider population of the geographic/demographic area of interest. This includes exclusions based on disease state/health, socioeconomic group, behaviours or socio-demographic factors (e.g. marital and parenting status).
B. More than one SES dimension (+1) - More than one SES dimension tested for their respective associations with telomere length, including reporting of the significance of the association.	**B. Only one SES dimension** - One SES dimension used and tested for its association with telomere length, including reporting of the significance of the association.
B. Hierarchical, graded SES categories (+1) - Ordinal categories or continuous SES measure	**B. Binary SES variables** - Dichotomized SES measure, either formed from the original question (eg yes/no) or reduced to a binary measure from a multiple-category ordinal measure (eg 6-category Registrar General social class based on occupation reduced to manual/non-manual)
B. SES-telomere results adjusted for age and/or sex (where applicable) (+1) - Adjusting for the potential confounding effects of age and sex in the model of the association between SES and telomere length. Where age/sex have been tested and found non-significant (P>0.05), this is regarded as equivalent to statistical adjustment of the model. Studies that only include one sex and/or a fixed year age group are exempt and will receive a '+1'. This is irrespective of adjustment for other variables.	**B. No adjustment for age and/or sex in SES-telomere analysis (where applicable)** - Not adjusting for the potential confounding effects of age and sex in the model of the association between SES and telomere length, unless it has been clearly stated that neither variable is a confounder of the association of interest. This is irrespective of adjustment for other variables
C. SES-telomere results presented in the form of beta-coefficients/means with SD/SE/CI and *P* value (+1) - SES-telomere results presented in the form of beta-coefficients/means for telomere length by SES group with SD/SE/CI for at least one SES dimension. P-values are acceptable when included with the other summary statistics listed previous	**C. Incomplete results presented for SES-telomere analysis** - SES-telomere results missing beta-coefficients/means with SD/SE/CI. P-values are not acceptable unless included with the other summary statistics listed previous

J. References

1. Marmot M, Friel S, Bell R, et al. Closing the gap in a generation: health equity through action on the social determinants of health. *The Lancet.* 2008; 372(9650):1661-1669.
2. Adams JM, White M. Biological ageing: a fundamental, biological link between socio-economic status and health? *Eur J Public Health.* 2004; 14(3):331-334.
3. Bond J, Coleman PG, Peace S eds. *Ageing in society: An Introduction to social gerontology*. 2nd ed. London: Sage; 1993.
4. Strehler BL ed *Time, cells, and aging*. Academic Press; 1977.
5. Rattan SI. Theories of biological aging: genes, proteins, and free radicals. *Free Radic Res.* 2006; 40(12):1230-1238.
6. Adler NE, Stewart J. Health disparities across the lifespan: meaning, methods, and mechanisms. *Ann N Y Acad Sci.* 2010; 1186(1):5-23.
7. Shiels PG. Improving Precision in Investigating Aging: Why Telomeres Can Cause Problems. *J Gerontol A Biol Sci Med Sci.* 2010; 65(8):789-791.
8. Cherkas LF, Aviv A, Valdes AM, et al. The effects of social status on biological aging as measured by white-blood-cell telomere length. *Aging Cell.* 2006; 5(5):361-365.
9. Cherkas LF, Hunkin JL, Kato BS, et al. The association between physical activity in leisure time and leukocyte telomere length. *Arch Intern Med.* 2008; 168(2):154-158.
10. Woo J, Suen EWC, Leung JCS, et al. Older men with higher self-rated socioeconomic status have shorter telomeres. *Age Ageing.* 2009; 38(5):553-558.
11. Adams J, Martin-Ruiz C, Pearce MS, et al. No association between socio-economic status and white blood cell telomere length. *Aging Cell.* 2007; 6(1):125-128.
12. Harris SE, Martin-Ruiz C, von Zglinicki T, et al. Telomere length and aging biomarkers in 70-year-olds: the Lothian Birth Cohort 1936. *Neurobiol Aging.* Advance access: October 25, 2011. (DOI:10.1016/j.neurobiolaging.2010.11.013).
13. Risques RA, Arbeev KG, Yashin AI, et al. Leukocyte telomere length is associated with disability in older US population. *J Am Geriatr Soc.* 2010; 58(7):1289-1298.
14. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics.* 1994; 50(4):1088-1101.
15. Rothstein H, Sutton AJ, Borenstein M eds. *Publication bias in meta-analysis : prevention, assessment and adjustments*. Chichester, England: Wiley; 2005.

Section/topic	#	Checklist item	Reported on page #
		TITLE	
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
		ABSTRACT	
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2 (unstructured as per journal style)
		INTRODUCTION	
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
		METHODS	
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4-5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8-9 33
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-9

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8-9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9-10; 29
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9-12; 34-37; Suppl data
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12-16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	12-16 30-33
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	12-16; 30-33
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	12-16; Suppl data
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12-16
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17-22
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17-22
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17-22
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Title page

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Web Table 1. In-Depth Summary of Studies Reporting on the Socioeconomic Status (SES) – Telomere Length Association Identified via Systematic Review

Article	Sample	Telomere measure	SES dimensions	Adjustments	Main results	Strengths (and Quality Score)	Limitations
Adams et al (2007)	- Newcastle Thousand Families Study (UK) - Birth cohort (1947) - Population-based - Both sexes - Telomere sample size = 318 (198 women) - Aged 50.	- qPCR - Units = base pairs (bp).	**- Occupation-based social class (Registrar General, RGSC, 6-category):** - at birth - at age 25 - at age 50 - change ages 0-25 - change ages 0-50 - change ages 25-50 - number of times in non-manual social class (0-3) **- Equivalised net household income at age 50 (£).**	- Sex - Smoking - Alcohol intake - Antioxidant intake - Body Mass Index (BMI) - Paternal age at birth.	In sex-specific and sex-combined analyses, none of the social class variables were associated with telomere length before and after adjustments. Income was positively associated with telomere length in women (β=139.59, CI=20.00 to 303.88), but not men. This association was attenuated (and not significant at the 95% level) by adjustment for lifestyle factors (β=152.53, CI=-27.45 to 337.21).	- Population-based (+1) - Representative sample (+1) - 2 SES dimensions (+1) - Hierarchical, graded SES categories used (+1) - Sex stratified with & without confounders (+1) - SES-telomere results presented as regression coefficients with CI (+1) **Total = 6.**	
Batty et al (2009)	- West of Scotland Coronary Prevention Study (WOSCOPS) (UK) - Case-controls study within population based intervention for coronary heart disease (CHD) risk - Men only - Telomere sample size = 1542 (484 cases) - Aged 45-64.	- qPCR - Units = not given - Log-transformed.	- Height (continuous) (used as a proxy for early life social position) - Carstairs score of area deprivation (continuous) - Employment status (unemployed, employed, retired or invalid) - Educational attainment (4-category).	- Age - Smoking status - Alcohol intake - BMI - Existing illness - Statin treatment - Case/Control status.	Height, Carstairs and education were not associated with telomere length (unadjusted and adjusted) For employment, unemployed men had shorter telomeres than employed men before (β=-0.117, CI=-0.189 to -0.046, *P* = 0.001) and after adjustments (β=-0.099, CI=-0.171 to -0.027, *P* = 0.007).	- 4 SES dimensions (+1) - Hierarchical, graded SES variables (+1) - Adjusted for age and other confounders (+1) - SES-telomere results presented as regression coefficients with CI (+1) **Total = 4.**	- Case-control study - Non-representative sample (high CHD risk)
a) Chan et al (2010) and	- Survey of elderly people living in Hong Kong (China) - Population-based - Both sexes - Aged 65+. a) Telomere sample size = 2006 (1030 women)	- qPCR - Units = kilo base pairs (kb).	a) – Education attainment (primary vs. secondary school) b) – Subjective social status ladder (10 point scale, split into 3 categories): 1. community ladder (top rung = most desirable)	a) n/a b) – Age	a) Unadjusted ANOVAs showed no association between education and telomere length in men (*P* = 0.608) or women (*P* = 0.573). b) Age-adjusted ANCOVAs revealed that those men	- Population-based (+1) - Representative sample (+1) a) - Means, SD, and p-values reported (+1) **Total (a) = 3** b)	a) - 1 SES dimension - Binary SES variable - No adjustment for age b)
b) Woo et al	b) Telomere sample						

(2009)	size = 1936		2. Hong Kong Ladder (top rung = most money, education & respected jobs).		who rated themselves as lowest on the community ladder rungs had the longest telomeres (rungs1-4 mean TL=9.2±0.14), followed by those in the middle (rungs 5-6 mean TL=8.82±0.08) and then those self-rated as highest (rungs 7-10 mean TL=8.68±0.08) (*P* = 0.005). The same pattern was seen in women, but not as strong (*P* = 0.116). Age-adjusted models revealed that those that men who rated themselves as lowest on the Hong Kong ladder rungs had the longest telomeres (rungs 1-4 mean TL=8.91±0.08), followed by those in the middle (rungs 5-6 mean TL=8.80±0.08) and then those self-rated as highest (rungs 7-10 mean TL=8.52±0.15) (*P* = 0.056). The same pattern was seen in women, but not as strong (*P* = 0.221).	- Hierarchical, graded SES variable used (+1) - Adjusted for age, sex-stratified (+1) - Means, SE and p-values reported (+1) **Total (b) = 5**	- 1 SES dimension
a) Cherkas et al (2006) and	- St Thomas' (Twins UK) Adult Twin Registry (UK) - Population-based a) - Telomere sample size = 1552. Income sample = 898. - Aged 18-75	- Southern blot - Units = kb.	a) - Occupational-based social class (NS-SEC) (manual vs. non-manual) - Household income (£). - Educational attainment (12-point scale ranging from no qualification to university degree)	a) - Age - BMI - Smoking - Exercise - Parents' ages	a) Linear trend in age adjusted telomere with higher social class associated with longer telomeres (*P* <0.024). Dichotomized, non-manual (grades I-IIINM) had longer age-adjusted telomeres compared to manual grades (*P* < 0.01). This difference remained even after adjustment (*P* < 0.047). Household income (p-value not given) and education (p<0.25) were not associated with age-adjusted telomere length.	- Population-based (+1) a) - Representative sample (+1) - 3 SES dimensions (+1) - Hierarchical, graded SES variable used - Adjusted for age and other confounders (+1) - Means and SE (from figure) (+1)presented for social class (+1) **Total (a) = 6**	
b) Cherkas et al (2008)	b) - Telomere sample size = 2401 - Aged 18-81.		b) - Occupational-based social class (NS-SEC) (manual or non-manual).	b) - Age	b) Being a manual worker was associated with having shorter, age-adjusted, telomeres (*P* = 0.02).	**Total (b) = 1.**	b) - Non-representative sample (gender balance) - 1 SES dimension - Binary SES variable - No adjustment for sex - Only *P* value presented.
Epel et al (2006)	- The mothers of sick children (California, USA) - Case-control - Women only	- qPCR - Units = rel. T/S - Split into high and low groups.	- Education (years).	- n/a.	Education was not associated with telomere length (*P* > 0.05).	- Continuous SES dimension (+1) **Total = 1.**	- Case-control study - Non-representative sample - 1 SES dimension - No adjustments

	- Telomere sample size = 62 (40 cases, 22 controls) - Aged 20-50.						- No effect sizes or error reported.
Epel et al (2009)	- MacArthur Study of Successful Aging (Boston sample, USA) - Population-based with high functioning - Both sexes - Telomere sample size = 235 (120 women) at baseline, 134 (68 women) at follow-up - Aged 70-79 (baseline)	- qPCR - Units = bp - Telomere measured twice, 2.5 years apart.	- Education (years)	- n/a	Mean years of education did not differ between short and long telomere groups at baseline (10.6 and 10.4 years, respectively; ns). Education was also not associated with the percentage change in telomere length after 2.5 years (Spearman's r = -0.01, ns).	- Population-based (+1) - Continuous SES dimension (+1) **Total = 2.**	- Non-representative sample - 1 SES dimension - No adjustments - No errors given.
Fernandez-Egea et al (2009)	- Psychotic patients at 1st contact and healthy controls matched for BMI, smoking and demographics (Hospital Clinic of Barcelona, Spain) - Both sexes - Telomere sample size = 82 (41 cases) - Aged 18-64.	- Southern blot - Units = kb.	- Hollingshead-Redlich Scale of SES).	- n/a.	SES was not associated with telomere length ($P > 0.15$).	- Hierarchical, graded SES dimension (+1) **Total = 1.**	- Case-control study - Non-representative sample - 1 SES dimension - No adjustments - No effect sizes or error reported.
Geronimus et al (2010)	- Study of Women's Health Across the Nation (SWAN) (USA) - Multi-site, cohort study population-based - Non-menopausal, middle-aged women only, equal Black and White samples - Telomere sample size = 232 - Aged 49-55.	- qPCR - Units = bp.	- Poverty (< $20,000 vs. ≥$20,000).	- n/a	Being in poverty 7 years previous was associated with shorter telomeres (correlation = -0.095).	- Population-based (+1) **Total = 1.**	- Non-representative sample (+1) - 1 SES dimension - Binary SES variable - No adjustments - SE or p-values not reported.
Harris et al (2006)	- Lothian Birth Cohort 1921 (UK) - Population-based - Both sexes - Telomere sample size = 182 - Aged 79.	- qPCR - Units = kb.	- Occupation-based social class (RGSC, 6-category)	- n/a.	Telomere length was not associated with social class ($P > 0.05$).	- Population-based (+1) - Representative sample (+1) - Hierarchical, graded SES variable (+1) - Adjustments not required (sex not	- 1 SES dimension

						associated) (+1) - Means & SD (+1) **Total = 5.**	
Harris et al (2010)	- Lothian Birth Cohort 1936 (UK) - Population-based - Both sexes - Telomere sample size = 1048 - Aged 68-70.	- qPCR - Units = kb. - Log-transformed.	- Occupation-based social class (Registrar General, RGSC, 6-category) - Education (years).	- Age - Sex - qPCR batch/plate number.	Social class was not associated with telomere length in men (β=0.012 *P* = 0.79) or women (β=-0.023 *P* = 0.61), or the combined analysis (β=-0.004 *P* = 0.91). Education was not associated with telomere length in men (β=-0.041 *P* = 0.34) or women (β=0.007 *P* = 0.87), or the combined analysis (β=-0.018 *P* = 0.57).	- Population-based (+1) - Representative sample (+1) - 2 SES dimensions (+1) - Hierarchical, graded SES variables (+1) - Age and sex adjusted; also sex stratified (+1) - Mean and SD (+1) **Total = 6.**	
Honig et al (2006)	- Washington Heights-Inwood Columbia Aging Project (USA) - Case-control (dementia study) - Both sexes - Telomere sample size = 257 (166 women) - Aged 66-103.	- qPCR - units = rel. T/S.	- Education (years, dichotomized into less than or more than/ equal to 8 years).	- Age	Telomere length did not differ between those with more than 8 years of education (0.486 ± 0.236(SD) compared to those with less than 8 years (0.490 ± 0.199) (P>0.05)	- Means, SD and P-values (+1) **Total = 1.**	- Case-control study - Non-representative study - 1 SES dimension - Binary SES - No adjustment for sex..
Hou et al (2009)	- Gastric cancer population (Warsaw, Poland) - Case-control; controls from general population employed in this analysis - Both sexes - Telomere sample size (controls) = 416 - Aged 21-79.	- qPCR - Units = rel. T/S.	- Educational attainment (low, medium, high - not defined)	- Age - Sex - Smoking	In controls (N=416) telomeres were longest in those with 'high' education (mean TL=1.39 CI=1.33 to 1.45), followed by 'medium' (mean TL=1.34 CI=1.28 to 1.39) and then 'low' (mean TL=1.30 CI=1.25 to 1.36) (*P* = 0.05).	- Population-based (although case-control, controls only used for SES-telomere analysis) (+1) - Representative sample (controls) - Hierarchical, graded SES categories (+1) - Age and sex adjusted with other confounders (+1) - Means, SD and p-values (+1) **Total = 5.**	- 1 SES dimension
Houben et al (2011)	- The Zutphen Elderly Study (Netherlands) - Population-based, cohort study - Men only - Telomere sample size = 144.	- qPCR - Units = kbp (grouped into tertiles).	- Educational attainment (higher vocational education, college or university vs. not)	- n/a	Tertiles of telomere length did not differ in the proportions of those having achieved a higher level of educational attainment (P_{trend} = 0.48).	- Population-based (+1) - Representative sample (+1) **Total = 2.**	- 1 SES dimension - Binary SES - No adjustment for age - Means reported or SES by telomere length group (and not telomere length by

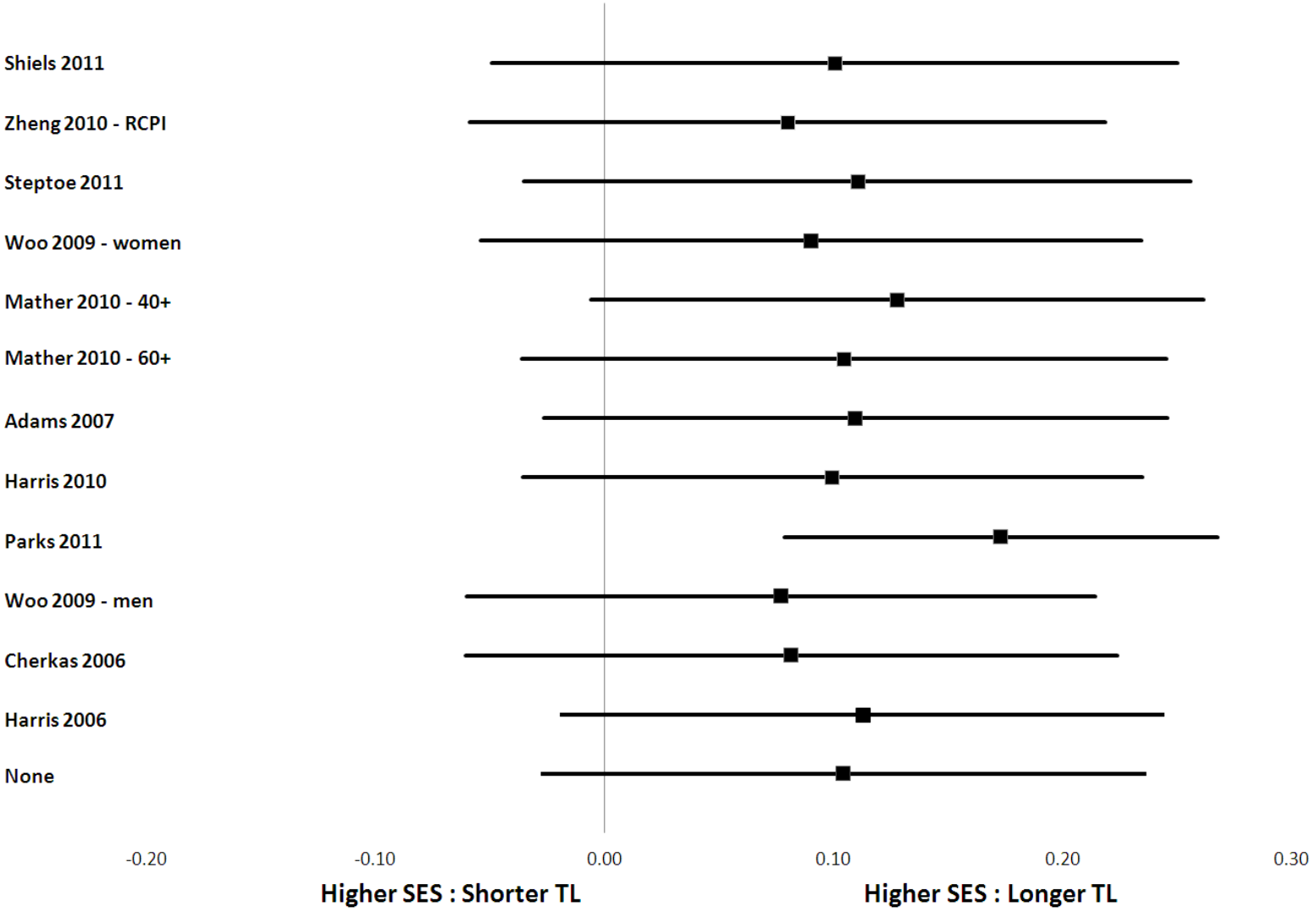
	- Aged 73-91.						SES group)
Kananen et al (2010)	- Health 2000 study (Finland) - Case-control (anxiety disorders) - Both sexes - Telomere sample size = 974 - Aged 30-87.	- qPCR - Units = rel. T/S - Log-transformed and, adjusted for batch, outliers removed and standardized.	- Educational attainment, 3 category – not defined. - Employment status (employed unemployed retired or other) - List of childhood adversities, including financial difficulties and parental unemployment (yes/no).	- Age - Sex - Hospital district - Marital status	In fully adjusted models, education and employment status were not associated with telomere length ($P > 0.05$). Parental unemployment was associated with shorter telomeres (β=-0.157±0.059(SE), P=0.008); there was no association with childhood financial difficulties	- 4 SES dimensions (+1) - Hierarchical, graded SES variables (+1) - Adjusted for age and sex and other confounders (+1) - Regression coefficient, SE and p-values reported for parental unemployment, **Total = 4.**	- Case-control study - Non-representative sample
Lee et al (2011)	- Fels Longitudinal Study (USA) - Population-based - Both sexes - Telomere sample size = 245 - Aged = 8-90.	- qPCR - Units = rel. T/S	- Educational attainment (college/university degree – yes/no)for adults (n=245)	- Age	Higher educational attainment was not associated with longer telomeres (β=0.04, P>0.05).	- Population-based (+1) - Representative sample (+1) **Total = 2.**	- 1 SES - Binary SES variable - Not adjusted for sex - No error or significance values reported.
a) Mather et al (2010)	- Personality and Total Health (PATH) Through Life Project (Canberra & Queanbeyan , Australia) - Population-based, tri-cohort study 20+, 40+, 60+ - Both sexes - Telomere sample size = 351 (40+ cohort) & 295 (60+ cohort). 20+ cohort not included. - Aged 44-49 64-70.	- qPCR - Units = rel. T/S - Log-transformed.	- Occupation-based social class (Australian Standard Classification of Occupations, 3-category: professional, white collar or blue collar) - Education (years).	- n/a	* Results from supplementary documents* 40+ cohort: Social class was not associated with telomere length, for both men (P = 0.234) and women (P = 0.219). No results for education were reported. 60+ cohort: Social class was not associated with telomere length, for both men (P = 0.721) and women (P = 0.897). No results for education were reported.	- Population-based (+1) - Representative sample (+1) - Hierarchical, graded SES variable (+1) - Narrow age cohorts (age and sex not significant as shown by testing) (+1) **Total = 4.**	- 1 SES dimension (education available but not used) - No effect sizes or errors reported.
Mirabello et al (2009)	- PLCO Cancer Screening Trial (USA) - Case-control - Men only - Telomere sample size = 1661 (612 cases) - Aged 55-74.	- qPCR - Units = rel. T/S.	- Education (years of high school and/or college).	- Age - Smoking (packs/year)	A greater number of years spent in higher education was not associated with age and smoking adjusted telomere length (Spearman's r = 0.034, P = 0.171).	- Continuous SES dimension (+1) - Adjusted for age and other confounders(+1) **Total = 2.**	- Case-control - Non-representative sample - 1 SES dimension - No errors.

a) Nettleton et al (2008) and	- Multi-Ethnic Study of Atherosclerosis (MESA) (multi-site, USA) - Population-based, free of CVD at baseline - 2 cities and 3 ethnic groups - Both sexes - Aged 45-84.	- qPCR - Units = relative T/S ratio (rel.T/S)				- Population-based (+1)	- Not-representative sample
	a) – Telomere sample size, = 840 (434 women)	a) rel. T/S converted into quartiles	a) - Household income ($, dichotomized into less than $25,000 vs. more than/equal to $25,000) - Education (years, dichotomized into less than high school vs. high school or above).	a) - Age	a) The proportion of respondents with a higher income did not differ between telomere length quartiles (P_{trend} = 0.89). The proportion of respondents with a higher education decreased with increasing telomere length quartiles (P_{trend} = 0.04).	a) - 2 SES variables (+1) **Total (a) = 2.**	a) - Binary SES - Not adjusted for sex - No errors as percentages only used.
b) Diez Roux et al (2009)	b) - Telomere sample size = 981.		b) - Household income ($) - Education (years)	b) - Age - Sex - Ethnicity	b) In mutually adjusted models higher household income (per $10,000 increase) was not associated with longer telomeres (β=0.002±0.002(SE) *P* = 0.2762). More years of education were associated with shorter telomeres (β=-0.004±0.001(SE) *P* = 0.0056).	b) - 2 SES variables (+1) - Continuous SES dimension (+1) - Adjusted for age and sex and other confounders(+1) - Regression coefficients, SE & *P* values (+1) **Total (b) = 5.**	
Nordfjall et al (2008)	- MONICA (Northern Sweden) - Population-based - Both sexes - Telomere sample size = 440 (139 cases) - Aged 25-74.	- qPCR - Units = rel. T/S.	- Educational attainment, (10 categories analysed as higher than primary school vs. > primary school).	- Age	Telomere length was reported as not being associated with education (*P* > 0.05) (results not shown)	- Population-based (+1) - Representative sample (+1) - Adjusted for age, sexes analysed separately (+1) **Total = 3.**	- 1 SES dimension - Binary SES variable - No effect sizes or errors.
O'Donovan et al (2011)	- Post-traumatic stress disorder study (USA) - Case-control - Both sexes - Telomere sample size = 90 - Aged 21-49.	- qPCR - Units = bp.	- Education (years)	- Age	Education was reported as not associated with telomere length (P>0.05) (results not shown).	- Continuous SES dimension (+1) **Total = 1.**	- Case-control study - Non-representative sample - 1 SES dimension - No adjustment for sex - Effects sizes or errors not reported.
Parks et al (2011)	- Sister Study (USA) - Sisters of women	- qPCR - Units = bp.	– Employment status (employed vs.	- Age	Shorter telomeres in employed women (5559bp CI=5456 to 5663) versus not employed women	- Adjusted for age (+1) - Means & CI (+1)	- Hospital/sick sibling sample

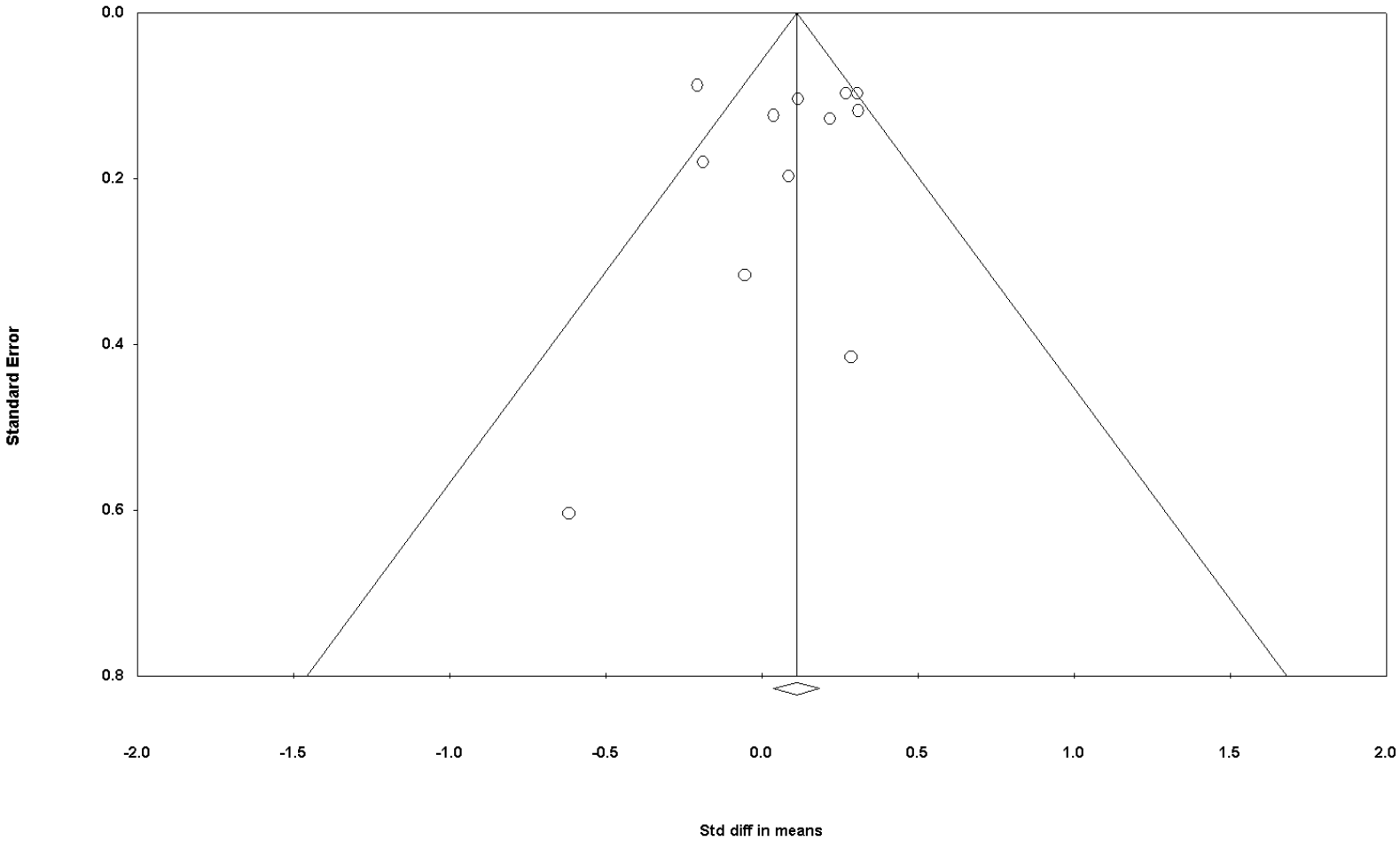
	with breast cancer, but without breast cancer themselves, oversampled those with high stress, smokers and non-white - Telomere sample size = 647 - Aged 35-74.		not employed).		(5785bp CI=5629 to 5942)	**Total = 2.**	- Non-representative sample (over-representative of stress, non-whites and smokers) - 1 SES dimension - Binary SES variable
Risques et al (2010)	-National Long Term Care Survey (NLTCS) (USA) - Study of U.S. Medicare recipients, oversampled for people with disabilities - Both sexes - Telomere sample size = 638 - Aged 65-89.	- qPCR - Units = rel. T/S.	- Educational attainment (< high school vs. ≥ high school).	- n/a.	There was a "weak trend" for higher educational attainment (mean TL0.663±0.13) to be associated with longer telomeres compared to lower educational attainment (mean TL=0.644±0.14) (P = 0.11)	- Population-based (+1) - Means & SE (+1) **Total = 2.**	- Non-representative sample - 1 SES dimension - Binary SES variable - No adjustments
Shiels et al (2011)	- Psychological, social, and biological determinants of ill health (pSoBid) study (Glasgow, UK) - Population-based sampled from highest and lowest quintiles of area deprivation - Both sexes - Telomere sample size = 382 (181 women) - Aged 35-64.	- qPCR - Units rel. T/S - Log-transformed.	- Occupational-based social class (RGSC) (manual vs. non-manual) - Household income (<£25,000 vs. ≥ £25,000) - Education (years, dichotomized to bottom vs top 50%) - Housing tenure (owner/occupier or tenant).	- Age - Sex - Deprivation group (sampling unit)	Social class, income, education and housing tenure were not associated with telomere length (P>0.05). However, lower income (P = 0.024) and renting one's home (P = 0.038) were associated with steeper age-related differences in telomere length. Social class was not associated with age-related differences in telomere (P = 0.437) while education was weakly associated (P = 0.062).	- Population-based (+1) - 4 SES dimensions (+1) - Age & sex adjusted (+1) **Total = 3.**	- Non-representative sample - Binary SES variables - No effect sizes or errors.
Steptoe et al (2011)	- Whitehall II (UK) - Study of London-based civil servants - Occupation-based - Both sexes - Telomere sample size = 434 - Aged 53-76.	- qPCR - Units = rel. T/S.	- Educational attainment (no qualifications, O levels, A/S level or degree). - Occupational grade (lower, intermediate or higher British civil service grade) - Income (<£20,000, £20-40,000 or >£40,000).	- Age - Sex - Current paid employment - Systolic blood pressure - Glycated haemoglobin (diabetes marker) - HDL-cholesterol	Higher educational attainment was significantly associated with longer telomeres (P = 0.040). Occupation and income were not associated with telomere length (P = 0.51 and P = 0.71, respectively).	- 3 SES dimensions (+1) - Hierarchical, graded SES variables (+1) - Age & sex adjusted - Means & SE (+1) **Total = 5.**	- Occupation-specific sample (civil servants) - Non-representative sample
Surtees et al (2011)	- European Prospective	- qPCR - Units = delta Ct	- Parental unemployment prior	- Age - PCR plate	Age-adjusted telomere lengths were not different between those classed as manual vs. non-manual (β =	- Population-based (+1) - 2 SES dimensions (+1)	- Non-representative sample

	Investigation into Cancer (EPIC)-Norfolk Population Study (UK) - Population-based, prospective cohort study - Free of cancer at baseline, with all measurements of SES/telomere length at baseline - Both sexes (women only for this article) - Telomere sample size = 4,441 (women only) - Aged 41-80.		to age 17 (yes vs. no). -Own occupational-based social class (RGSC) (manual vs. non-manual)		0.014, CI = -0.008 to 0.036). Parental unemployment was not associated with age (β = 0.013, CI = -0.025 to 0.051) adjusted telomere length .	- Age and plate adjusted (only one sex) (+1) - Regression coefficients & CI (+1) **Total = 4.**	- Binary SES variables
Wolkowitz et al (2011)	- Major depressive disorder study (USA) - Case-control study - Both sexes - Telomere sample size = 35 (17 controls) - Aged 24-48.	- qPCR - Units = bp.	- Subjective social status (MacArthur ladders) - Income (annual household, $) - Education (years)	- Age - Sex	No results presented for subjective social status or education. Income not associated with telomere length (r=0.13, *P*>0.05).	- Continuous SES dimension (+1) - Age and sex adjusted (+1) **Total = 2.**	- Case-control study - Non-representative sample - 1 SES dimension - No error terms reported.
Yaffe et al (2009)	- Health Ageing and Body Composition (Health ABC) Study (Memphis & Pittsburgh, USA) - Prospective, cohort study - Population-based sampled from Medicare eligible people, no difficulties ADLs, no cancer no plans to move for 3 years - Both sexes - Telomere sample size = 2734 - Aged 70-79.	- qPCR - Units = rel. T/S - Split into tertiles.	- Educational attainment (<high school vs. ≥ high school).	- n/a	Those in the long telomere tertile group had a higher percentage of high school graduates (78.3%) versus the medium (72.9%) and short (74.3%) telomere groups (*P* = 0.02).	- Population-based (+1) **Total = 1.**	- Non-representative sample - 1 SES dimension - Binary SES variable - No adjustment for sex - Only percentages and p-value to be presented.
Zheng et al (2010) (2 studies)	a) - Roswell Park Cancer Institute (RPCI) - Breast Cancer Study (USA) - Breast cancer patients	a) - qPCR - Units = kb.	a) - Educational attainment (≤high school vs. high school & 4-years of college) - Household Income (<$50,000 vs.	a)- n/a	a) RCPI income not associated with telomere length in controls, but was in cases (*P* < 0.01). No results for education were reported.	a) **Total (a) = 0.**	a) - Case-control studies - Non-representative sample - 1 SES dimension (education measured but not used) - Binary SES

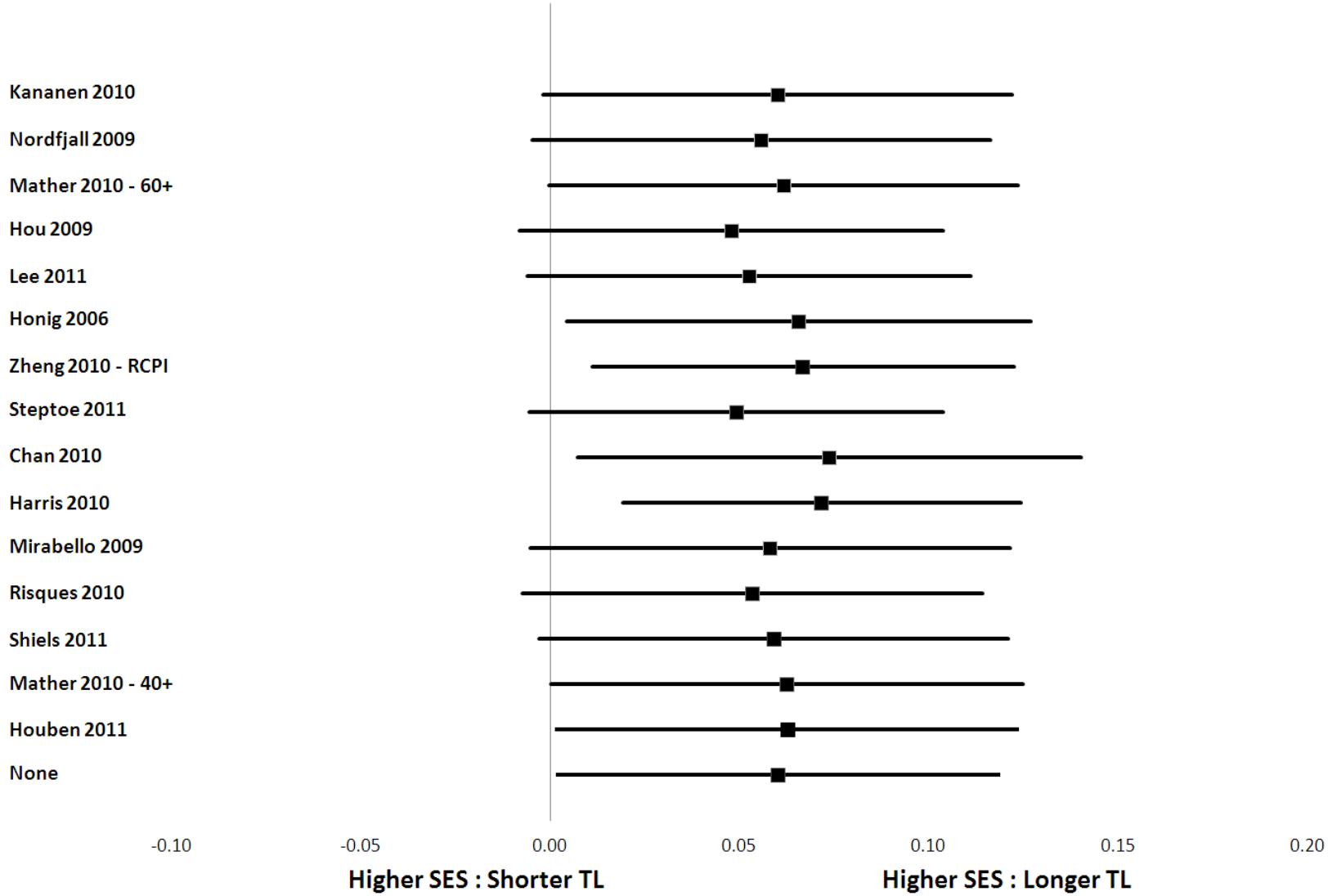
- Case-control - Women only - Telomere sample size = 328 - Aged 43-69		≥$50,000)				variables - No adjustments - No effect sizes or errors.
b) Lombardi Comprehensive Cancer Center (LCCC) - Breast Cancer Study (USA) - Breast cancer patients - Case-control - Women only - Telomere sample size = 299 - Aged 42-63.	b) - Fluorescence in situ hybridization (FISH) - Units = fluorescent intensity units (FIU)	b) - Educational attainment (≤high school high school & 4-years of college or high school plus >4 years of college) - Household income (<$100,000 vs. ≥$100,000).	b)- n/a	b) LCCC income not associated with telomere length in controls or cases ($P > 0.05$). No results for education were reported.	b) **Total (b) = 0.**	b) - Case-control studies - Non-representative sample - 1 SES dimension (education measured but not used) - Binary SES variables - No adjustments - No effect sizes or errors.



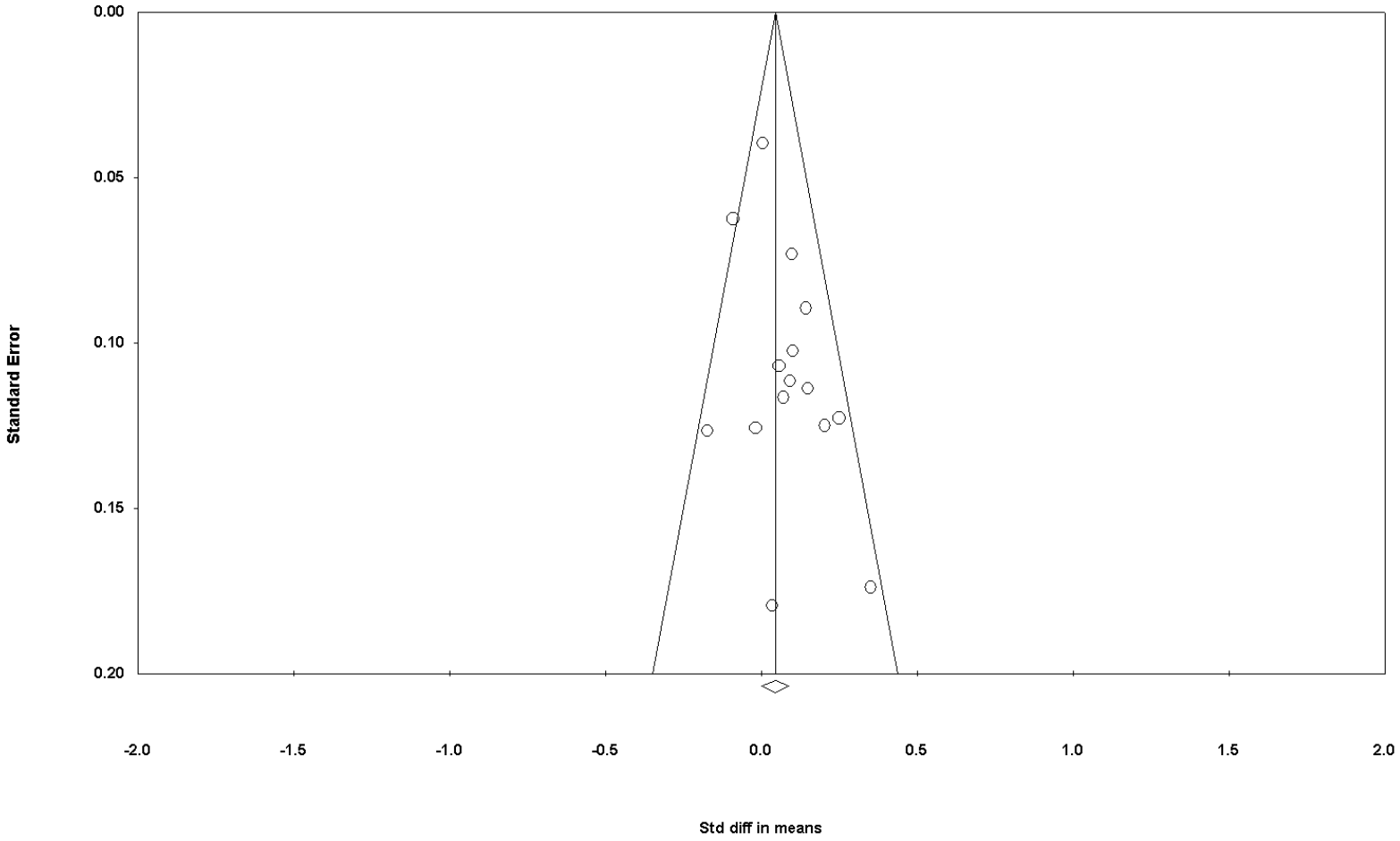
Web Figure 1. Random Effects Meta-Analysis Results for the Standardized Mean Difference Between Low & High Contemporaneous SES Following Systematic Removal of each Study



Web Figure 2. Funnel Plot of High-Low Contemporaneous SES comparisons for telomere length. Std diff in means = Standardized Mean Difference. Circles = individual studies. Diamond = All studies combined



Web Figure 3. Random Effects Meta-Analysis Results for the Standardized Mean Difference Between Low & High Education Following Systematic Removal of each Study



Web Figure 4. Funnel Plot of High-Low Education comparisons for telomere length. Std diff in means = Standardized Mean Difference. Circles = individual studies. Diamond = All studies combined