**Title: Obesity accelerates Leukocyte Telomere length (LTL) shortening in apparently healthy adults: A meta-analysis**

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**Supplementary Material**

**Sup. Table 1. PRISMA Checklist [1]**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Section/topic** | **#** | | | **Checklist item** | **Reported on page #** |
| **TITLE** | | | | |  |
| Title | 1 | | | Identify the report as a systematic review, meta-analysis, or both. | Page 1; line 1-3 |
| **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. | Page 2; lines 1-28 |
| **INTRODUCTION** | | | | |  |
| Rationale | 3 | | | Describe the rationale for the review in the context of what is already known. | Page 3 |
| Objectives | 4 | | | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | Page 4; lines 22-24 |
| **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. | | | Page 4 lines 1-4 |
| 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. | | | Page 4; lines 13-21 |
| 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. | | | Page 4; lines 13-21 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | | | Page 4, line 17-28 |
| 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). | | | Supplementary material Table 2 |
| 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. | | | Page 5; lines 6-15 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | | | Page 5; lines 6-15 |
| 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. | | | Page 5; lines 6-15 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | | | Page 5; lines 16-25 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis. | | | Page 6; lines 1-13 |
| 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). | | Page 6; lines 1-13 |
| Additional analyses | 16 | | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | | Page 6; lines 1-13 |
| **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. | | Page 6, line 16-25  Page 7, line 1-19 |
| 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. | | Page 6, line 16-25  Page 7, line 1-19  Table 1, 2 |
| 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). | | Table 3, 4 |
| 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. | | Figure 1, Figure 2  Page 7, line 20-26  Page 8, line 1-10 |
| Synthesis of results | 21 | | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | | Figures 1, 2, 3 |
| Risk of bias across studies | 22 | | Present results of any assessment of risk of bias across studies (see Item 15). | | Sup. Figure 1 |
| Additional analysis | 23 | | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | | Table 3, 4 |
| **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). | | Page 8; lines 12-26 |
| 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). | | Page 9; lines 26.  Page 10, line 1 |
| Conclusions | 26 | | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | | Page 9, line 25-26  Page 10, lines 1-6 |
| **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. | | Page 10; line 6 |

**Sup. Table 2**. Search strategies and the number of records according to different electronic database

|  |  |  |
| --- | --- | --- |
| **Search strategy** | **Database** | **Num. of records** |
| ((telomerase [Title/Abstract]) OR (telomerase[MeSH Terms])) OR (telomere length[Title/Abstract])) OR (telomere length[MeSH Terms])) OR (Telomere)) OR (Telomere[MeSH Terms])) AND ((((((((((((((((((Body Mass Index[Title/Abstract]) OR (Body Mass Index[MeSH Terms])) OR (obesity[Title/Abstract])) OR (obesity[MeSH Terms])) OR (abdominal obesity[Title/Abstract])) OR (abdominal obesity[MeSH Terms])) OR (BMI[Title/Abstract])) OR (waist circumference[Title/Abstract])) OR (WC[Title/Abstract])) OR (waist to hip ratio[Title/Abstract])) OR (WHR[Title/Abstract])) OR (overweight[Title/Abstract])) OR (waist to hip ratio[Title/Abstract])) OR (WHR[Title/Abstract])) OR (overweight[Title/Abstract])) OR (fat mass[Title/Abstract])) OR (adiposity[Title/Abstract])) OR (adipose tissue[Title/Abstract])) | PubMed | 1310 |
| Scopus | 1798 |
| ProQuest | 2205 |
| Embase | 1494 |

**Sup. Table 3.** Agency for Healthcare Research and Quality (AHRQ) checklist to assess quality of the included studies

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ARHQ Methodology Checklist items for Cross-Sectional study** | **Linghui D et al [2]** | **Zgheib NK et al [3]** | **Milte CM et al [4]** | **Mazidi M [5]** | **Batsis JA[6]** | **Xhao H [7]** | **Mwasongwe, S et al [8]** | **Min KB et al [9]** | **Mazidi M et al [10]** |
| 1) Define the source of information (survey, record review) | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 2) List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 3) Indicate time period used for identifying patients | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 4) Indicate whether or not subjects were consecutive if not population-based | ⊕ | U | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | U |
| 5) Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants | U | U | U | U | U | U | U | U | U |
| 6) Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements) | U | U | U | U | U | U | U | U | U |
| 7) Explain any patient exclusions from analysis | U | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 8) Describe how confounding was assessed and/or controlled. | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 9) If applicable, explain how missing data were handled in the analysis | U | U | ⊕ | U | U | ⊕ | ⊕ | ⊕ | U |
| 10) Summarize patient response rates and completeness of data collection | U | U | ⊕ | U | U | ⊕ | ⊕ | ⊕ | U |
| 11) Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained | U | U | ⊕ | ⊕ | U | ⊕ | ⊕ | U | U |
| **Final score** | **5** | **5** | **9** | **7** | **6** | **9** | **9** | **8** | **5** |

L, low risk of bias; H, high risk of bias; U, unclear risk of bias.

**Sup. Table 3.** Cont’d.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ARHQ Methodology Checklist items for Cross-Sectional study** | **Jullin B et al [11]** | **Müezzinler A et al [12]** | **Ciu Y et al [13]** | **Strandberg TE et al [14]** | **Fitzpatrick et al AL[15]** | **Cassidy AD et al [16]** | **Hardikar SH et al [17]** | **Zalli A et al [18]** | **Chen S et al [19]** | **Liu J et al [20]** |
| 1) Define the source of information (survey, record review) | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 2) List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications | ⊕ | ⊕ | U | ⊕ | ⊕ | ⊕ | U | U | ⊕ | ⊕ |
| 3) Indicate time period used for identifying patients | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 4) Indicate whether or not subjects were consecutive if not population-based | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 5) Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants | ⊕ | U | U | U | ⊕ | U | ⊕ | U | ⊕ | ⊕ |
| 6) Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements) | ⊕ | ⊕ | U | ⊕ | U | ⊕ | ⊕ | U | ⊕ | ⊕ |
| 7) Explain any patient exclusions from analysis | ⊕ | ⊕ | U | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 8) Describe how confounding was assessed and/or controlled. | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ | ⊕ |
| 9) If applicable, explain how missing data were handled in the analysis | ⊕ | ⊕ | U | U | ⊕ | ⊕ | U | U | U | ⊕ |
| 10) Summarize patient response rates and completeness of data collection | ⊕ | U | ⊕ | ⊕ | U | ⊕ | ⊕ | U | ⊕ | ⊕ |
| 11) Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained | ⊕ | ⊕ | U | ⊕ | ⊕ | ⊕ | ⊕ | U | U | ⊕ |
| **Final score** | **11** | **9** | **5** | **9** | **9** | **10** | **9** | **6** | **9** | **11** |

**(A)**

**C:\Users\farhangi\Desktop\funnel-BMI.tif**

**(B)**

**C:\Users\farhangi\Desktop\funnel-TLT.tif**

**Sup. Figure 1.**Begg's funnel plot (with pseudo 95% CIs) of the WMD versus the se (WMD) for the comparison of BMIin those with the highest versus lowest relative telomere length (rTLT) [P egger= 0.131; P begg =0.131](A) and for the comparison of relative telomere length (rTLT) in obese versus non-obese individuals[P egger= 0.44; P begg =0.41] (B)

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