

## B2: Evidence on sedentary behaviour for adults (18 to under 65 years of age)

### Guiding Questions

- B2. What is the association between **sedentary behaviour** and health-related outcomes?
- Is there a dose response association (total volume, frequency, **duration**, and intensity of interruptions)?
  - Does the association vary by type and domain of sedentary behaviour?
  - Does physical activity modify the effect of sedentary behaviour on mortality?

### Inclusion Criteria

**Population:** Adults 18 years of age and older

**Exposure:** Greater volume, decreased frequency, duration or intensity of interruption of sedentary behaviour

**Comparison:** Lesser volume, increased frequency, duration or intensity of interruption of sedentary behaviour

| Outcomes                                                            | Importance |
|---------------------------------------------------------------------|------------|
| All-cause and cause-specific mortality                              | Critical   |
| Incidence of cardiovascular disease                                 | Critical   |
| Incidence of cancer (site-specific)                                 | Critical   |
| Incidence of Type 2 Diabetes                                        | Critical   |
| Adiposity/Prevention of weight gain/Body composition                | Critical   |
| Mental health outcomes (e.g. depressive symptoms, anxiety symptoms) | Important  |
| Cognitive outcomes (e.g. dementia, cognition)                       | Important  |
| Physical function (e.g., physical strength, fitness)                | Important  |
| Musculoskeletal health (e.g., pain)                                 | Important  |
| Sleep duration and quality                                          | Important  |
| Health-related quality of life                                      | Important  |

### Included Evidence

Twenty-two studies (published from 2017 to 2019) were initially identified that examined the association between sedentary behaviour and health-related outcomes among adults (1-22). Five review were subsequently excluded from further evaluation given the study design or exposures that were out-of-scope. **Table 3.1** presents the reviews that were excluded and their reason for exclusion.

**Table 3.1. Excluded Systematic Reviews, with Reasons for Exclusion**

| Author, Year           | Reason for Exclusion | Rationale                                                                                  |
|------------------------|----------------------|--------------------------------------------------------------------------------------------|
| Al Tunaiji 2019 (2)    | Exposure             | Examines relationship between lack of MVPA and CVD incidence                               |
| Baumeister 2019 (4)    | Exposure             | Examines relationship between PA and liver cancer                                          |
| Chastin 2017 (7)       | Exposure             | Examines relationship between light-intensity PA and health outcomes                       |
| Friedenreich 2019 (11) | Design               | Modelling study; underlying risk estimates not based on full systematic review methodology |
| Fuzeki 2017 (12)       | Design               | Analysis of NHANES data only                                                               |

**Table 3.2** presents the ratings for each remaining review according to all the AMSTAR 2 main domains. In general, the included reviews were of moderate credibility. One review was rated as having high credibility, 9 were rated as having moderate credibility, 3 were rated as having low credibility, and the remaining 4 were rated as having critically low credibility. Given concerns regarding the comprehensiveness and the validity of the results presented in reviews rated as having critically low credibility, they were not incorporated into the final Evidence Profiles. One exception was made where we included the review by Mañas (18) for physical function outcomes, given that it was the only review reporting these outcomes.

**Table 3.3** lists the 17 reviews that were included by outcome. No reviews were identified that reported the association between sedentary behaviour and the following outcomes: mental health symptoms or diagnoses, cognition, musculoskeletal health (including pain), sleep duration or quality, or health-related quality-of-life.

Evidence Profiles for these outcomes, therefore, are not included in this report. Extracted data for each included review is presented in **Appendix A**.

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Table 3.2. Credibility Ratings (based on AMSTAR 2 (23))

| Author, Year           | PICO <sup>1</sup> | Apriori Methods <sup>2</sup> | Study Design Selection <sup>3</sup> | Lit Search Strategy <sup>4</sup> | Study Selection <sup>5</sup> | Data Extraction <sup>6</sup> | Excluded Studies <sup>7</sup> | Included Studies <sup>8</sup> | RoB Assessment <sup>9</sup> | Funding Sources <sup>10</sup> | Statistical Methods <sup>11</sup> | Impact of RoB <sup>12</sup> | RoB Results <sup>13</sup> | Heterogeneity <sup>14</sup> | Publication Bias <sup>15</sup> | COI <sup>16</sup> | Overall Rating <sup>17</sup> |
|------------------------|-------------------|------------------------------|-------------------------------------|----------------------------------|------------------------------|------------------------------|-------------------------------|-------------------------------|-----------------------------|-------------------------------|-----------------------------------|-----------------------------|---------------------------|-----------------------------|--------------------------------|-------------------|------------------------------|
| Ahmad 2017 (1)         | Y                 | PY                           | N                                   | PY                               | Y                            | Y                            | Y                             | PY                            | PY                          | N                             | N/A                               | N/A                         | Y                         | Y                           | N/A                            | N                 | Moderate                     |
| Bailey 2019 (3)        | Y                 | PY                           | N                                   | PY                               | Y                            | Y                            | PY                            | PY                            | PY                          | N                             | Y                                 | Y                           | Y                         | Y                           | Y                              | Y                 | Moderate                     |
| Berger 2019 (5)        | Y                 | PY                           | N                                   | PY                               | Y                            | Y                            | PY                            | Y                             | Y                           | N                             | Y                                 | Y                           | Y                         | Y                           | Y                              | Y                 | Moderate                     |
| Chan 2019 (6)          | Y                 | PY                           | N                                   | PY                               | N                            | Y                            | Y                             | Y                             | Y                           | N                             | Y                                 | Y                           | Y                         | Y                           | Y                              | Y                 | Moderate                     |
| del Pozo-Cruz 2018 (8) | Y                 | PY                           | N                                   | PY                               | Y                            | N                            | PY                            | PY                            | Y                           | N                             | Y                                 | Y                           | Y                         | Y                           | Y                              | Y                 | Moderate                     |
| Ekelund 2018 (9)       | Y                 | Y                            | N                                   | PY                               | N                            | Y                            | PY                            | Y                             | PY                          | N                             | Y                                 | Y                           | Y                         | Y                           | Y                              | Y                 | Moderate                     |
| Ekelund 2019 (10)      | Y                 | PY                           | N                                   | PY                               | N                            | Y                            | PY                            | Y                             | Y                           | N                             | Y                                 | N                           | N                         | N                           | Y                              | Y                 | Moderate                     |
| Ku 2018 (13)           | Y                 | N                            | Y                                   | PY                               | N                            | Y                            | Y                             | Y                             | Y                           | N                             | Y                                 | Y                           | N                         | Y                           | Y                              | Y                 | Moderate                     |
| Ku 2019 (14)           | Y                 | N                            | Y                                   | PY                               | N                            | Y                            | Y                             | Y                             | Y                           | N                             | Y                                 | Y                           | N                         | Y                           | Y                              | Y                 | Moderate                     |
| Lee 2019 (15)          | N                 | N                            | N                                   | PY                               | N                            | N                            | PY                            | Y                             | Y                           | N                             | N                                 | N                           | N                         | Y                           | Y                              | Y                 | Critically Low               |
| Ma 2018 (16)           | N                 | N                            | N                                   | PY                               | Y                            | Y                            | N                             | N                             | N                           | N                             | N                                 | N                           | N                         | N                           | Y                              | N                 | Critically Low               |
| Mahmood 2017 (17)      | Y                 | PY                           | N                                   | PY                               | Y                            | Y                            | PY                            | Y                             | N                           | N                             | Y                                 | N                           | N                         | Y                           | Y                              | Y                 | Low                          |
| Mañas 2017 (18)        | Y                 | N                            | N                                   | PY                               | Y                            | N                            | PY                            | Y                             | N                           | N                             | N/A                               | N/A                         | N                         | N                           | N/A                            | Y                 | Critically Low               |
| Patterson 2018 (19)    | Y                 | N                            | N                                   | PY                               | N                            | Y                            | PY                            | Y                             | PY                          | N                             | Y                                 | Y                           | N                         | Y                           | Y                              | Y                 | Low                          |
| Shepard 2017 (20)      | Y                 | N                            | N                                   | N                                | N                            | N                            | N                             | Y                             | N                           | N                             | N/A                               | N/A                         | N                         | N                           | N/A                            | N                 | Critically Low               |
| Wang 2018 (21)         | Y                 | Y                            | Y                                   | Y                                | Y                            | Y                            | PY                            | Y                             | Y                           | N                             | Y                                 | Y                           | Y                         | Y                           | Y                              | Y                 | High                         |
| Xu 2019 (22)           | Y                 | PY                           | N                                   | N                                | N                            | N                            | N                             | Y                             | N                           | N                             | Y                                 | N                           | N                         | Y                           | N                              | Y                 | Low                          |

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Abbreviations: COI = conflict of interest; N = no; N/A = not applicable; PICO = population, intervention, comparator, outcome; PY = partial yes; RoB = risk of bias; Y = yes

- <sup>1</sup> Did the research questions and inclusion criteria for the review include the components of PICO?
- <sup>2</sup> Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
- <sup>3</sup> Did the review authors explain their selection of the study designs for inclusion in the review?
- <sup>4</sup> Did the review authors use a comprehensive literature search strategy?
- <sup>5</sup> Did the review authors perform study selection in duplicate?
- <sup>6</sup> Did the review authors perform data extraction in duplicate?
- <sup>7</sup> Did the review authors provide a list of excluded studies and justify the exclusions?
- <sup>8</sup> Did the review authors describe the included studies in adequate detail?
- <sup>9</sup> Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
- <sup>10</sup> Did the review authors report on the sources of funding for the studies included in the review?
- <sup>11</sup> If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?
- <sup>12</sup> If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
- <sup>13</sup> Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?
- <sup>14</sup> Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
- <sup>15</sup> If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
- <sup>16</sup> Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?
- <sup>17</sup> Shea et al. 2017. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.

Table 3.3. Included Systematic Reviews, by Author

| Author, Year                  | Outcomes       |                          |     |            |          |           |                        |                    |                   |                         |       |       | Last Search Date | AMSTAR 2       |
|-------------------------------|----------------|--------------------------|-----|------------|----------|-----------|------------------------|--------------------|-------------------|-------------------------|-------|-------|------------------|----------------|
|                               | ACM            | Cause-specific mortality | CVD | Cancer     | Diabetes | Adiposity | Mental health outcomes | Cognitive outcomes | Physical function | Musculo-skeletal health | Sleep | HRQOL |                  |                |
| Ahmad 2017 (1)                |                |                          | X   |            | X        | X         |                        |                    |                   |                         |       |       | Dec 2016         | Moderate       |
| Bailey 2019 (3)               |                |                          | X   |            | X        |           |                        |                    |                   |                         |       |       | Feb 2019         | Moderate       |
| Berger 2019 (5)               |                | Prostate                 |     | Prostate   |          |           |                        |                    |                   |                         |       |       | Jan 2019         | Moderate       |
| Chan 2019 (6)                 |                |                          |     | Breast     |          |           |                        |                    |                   |                         |       |       | Apr 2017         | Moderate       |
| del Pozo-Cruz 2018 (8)        | X              |                          | X   |            | X        | X         |                        |                    |                   |                         |       |       | Dec 2016         | Moderate       |
| Ekelund 2018 <sup>a</sup> (9) |                | CVD, Cancer              |     |            |          |           |                        |                    |                   |                         |       |       | Oct 2015         | Moderate       |
| Ekelund 2019 (10)             | X              |                          |     |            |          |           |                        |                    |                   |                         |       |       | Jul 2018         | Moderate       |
| Ku 2018 (13)                  | X              |                          |     |            |          |           |                        |                    |                   |                         |       |       | Jan 2018         | Moderate       |
| Ku 2019 (14)                  | X              |                          |     |            |          |           |                        |                    |                   |                         |       |       | Mar 2019         | Moderate       |
| Lee 2019 (15)                 |                |                          |     | Ovarian    |          |           |                        |                    |                   |                         |       |       | Dec 2017         | Critically Low |
| Ma 2018 (16)                  |                |                          |     | Colorectal |          |           |                        |                    |                   |                         |       |       | Feb 2017         | Critically Low |
| Mahmood 2017 (17)             |                |                          |     | Colorectal |          |           |                        |                    |                   |                         |       |       | Dec 2015         | Low            |
| Mañas 2017 (18)               | X <sup>b</sup> |                          |     |            |          |           |                        |                    | X                 |                         |       |       | Oct 2016         | Critically Low |
| Patterson 2018 (19)           | X              | CVD, Cancer              |     |            | X        |           |                        |                    |                   |                         |       |       | Sep 2016         | Low            |
| Shepard 2017 (20)             |                |                          |     | Bladder    |          |           |                        |                    |                   |                         |       |       | Jun 2016         | Critically Low |
| Wang 2018 (21)                |                |                          |     | Colorectal |          |           |                        |                    |                   |                         |       |       | Sep 2018         | High           |
| Xu 2019 <sup>c</sup> (22)     | X              |                          |     |            |          |           |                        |                    |                   |                         |       |       | May 2018         | Low            |

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<sup>a</sup> Secondary data analysis of 2016 review

<sup>b</sup> Not included for this outcome given better quality reviews reporting this outcome

<sup>c</sup> Individual participant data meta-analysis

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## B.2. Sedentary Behaviour

**Table B.2.a. All-cause and cause-specific mortality: Association between sedentary behaviour and all-cause mortality among adults (in alphabetical order by author)**[See the Supplementary materials](#) for description of evidence and conclusions of US PAGAC (24) by outcome

| Systematic review evidence        | No. of studies/<br>Study design               | Quality Assessment      |                       |                         |                        |       | Description of evidence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Certainty             |
|-----------------------------------|-----------------------------------------------|-------------------------|-----------------------|-------------------------|------------------------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
|                                   |                                               |                         |                       |                         |                        |       | Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                       |
| Review credibility                | No. of participants                           | Risk of bias            | Inconsistency         | Indirectness†           | Imprecision            | Other |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                       |
| Berger 2019 (5)<br><br>Moderate   | 3 prospective cohort studies<br><br>N=277,763 | Serious risk of bias    | Serious inconsistency | Serious indirectness    | No serious imprecision | None  | Most studies used self-report sedentary behaviour (one study combined self-report and job title assignment). Mean follow-up was not reported. No significant association was found between high versus low ST and risk of <b>prostate cancer-related mortality</b> (RR = 1.14 [95% CI 0.94 to 1.38], 3 studies).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | VERY LOW <sup>a</sup> |
| del Pozo-Cruz (8)<br><br>Moderate | 3 prospective cohort studies<br><br>N=12,108  | No serious risk of bias | NA <sup>b</sup>       | No serious indirectness | NA <sup>b</sup>        | None  | Included adults aged mean age ranged 49 to 61 years; mean follow-up time not reported. All studies used accelerometers to measure ST with <100 cpm (from the vertical axis of the accelerometer) used to define ST.<br><br>The review reported that all 3 studies found that replacing 30 minutes of ST with LIPA or MVPA was associated with significantly lower risk of <b>all-cause mortality</b> . One study found that replacing ST with LIPA also had a significant beneficial association with risks of <b>CVD-</b> and <b>cancer-related mortality</b> and that “MPVA had an even better significant association with risks of mortality from <b>any cause</b> and <b>CVD</b> .” “Hazards ratios ranged from 0.80 to 0.87 for LIPA and from 0.19 to 0.51 for MVPA”, no data given by study including variance for effect estimates. | LOW <sup>c</sup>      |

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| Systematic review evidence<br><br>Review credibility | No. of studies/<br>Study design<br><br>No. of participants | Quality Assessment      |                 |                         |                        |                                         | Description of evidence<br><br>Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Certainty         |
|------------------------------------------------------|------------------------------------------------------------|-------------------------|-----------------|-------------------------|------------------------|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
|                                                      |                                                            | Risk of bias            | Inconsistency   | Indirectness†           | Imprecision            | Other                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                   |
| Ekelund 2018 (9)<br><br>Moderate                     | 11 prospective cohort studies<br><br>N=888,327             | No serious risk of bias | NA <sup>d</sup> | No serious indirectness | No serious imprecision | Dose-response relationship <sup>e</sup> | <p>Secondary data analysis of 2016 review on the relationship between sitting time and all-cause mortality. Sitting time was categorized into four groups (0 to &lt;4 hrs/day, 4 to &lt; 6 hrs/day, 6-8 hrs/day, and &gt;8 hrs/day) and TV-viewing time into four groups (&lt;1 hr/day, 1-2 hrs/day, 3-4 hrs/day, and &gt;5 hrs/day).</p> <p>Nine studies had data on the relationship between <b>sitting time</b> and <b>CVD mortality</b> (n=850,060; median follow-up 10.2 years). A significant dose-response relationship was found between sitting time and CVD mortality for the lowest quartile of PA (&lt;2.5 MET-hrs/week): the HR for for CVD mortality was 1.32 (p for trend &lt;0.001, 95% CI only reported in figure) for those who sat for more than 8 hrs/day compared with the reference group (&lt;4 hrs/day). There was no clear dose-response association in any of the other quartiles of PA, but significantly increased hazards were observed in those with sitting time &lt;8 hrs/day vs. &lt;4 hrs/day for those in the 2<sup>nd</sup> quartile (16 MET-hrs/week) (HR = 1.11 [95% CI, 1.03 to 1.20]) and 3<sup>rd</sup> quartile (30 MET-hrs/week) (HR = 1.14 [95% CI, 1.03 to 1.26]) of PA. There was no increased risk for CVD mortality in the most active quartile of PA (&gt;35.5 MET-hrs/week) in any category of sitting time.</p> | HIGH <sup>f</sup> |

|                            |              |                       |  |  |  |  | <div><table><caption>Approximate data from Figure 1 forest plot</caption><thead><tr><th>Physical Activity Quartile</th><th>Sitting Time</th><th>Hazard Ratio (95% CI)</th></tr></thead><tbody><tr><td rowspan="4">&lt;2.5 MET-h/week</td><td>&lt;4 h/d (Ref)</td><td>1.0</td></tr><tr><td>4-6 h/d</td><td>~1.1</td></tr><tr><td>6-8 h/d</td><td>~1.2</td></tr><tr><td>&gt;8 h/d</td><td>~1.59</td></tr><tr><td rowspan="4">16 MET-h/week</td><td>&lt;4 h/d (Ref)</td><td>1.0</td></tr><tr><td>4-6 h/d</td><td>~1.0</td></tr><tr><td>6-8 h/d</td><td>~1.0</td></tr><tr><td>&gt;8 h/d</td><td>~1.1</td></tr><tr><td rowspan="4">30 MET-h/week</td><td>&lt;4 h/d (Ref)</td><td>1.0</td></tr><tr><td>4-6 h/d</td><td>~1.1</td></tr><tr><td>6-8 h/d</td><td>~1.0</td></tr><tr><td>&gt;8 h/d</td><td>~1.1</td></tr><tr><td rowspan="4">&gt;35.5 MET-h/week</td><td>&lt;4 h/d (Ref)</td><td>1.0</td></tr><tr><td>4-6 h/d</td><td>~1.0</td></tr><tr><td>6-8 h/d</td><td>~1.0</td></tr><tr><td>&gt;8 h/d</td><td>~1.0</td></tr></tbody></table></div> <p><b>Figure 1</b> Meta-analysis of the stratified associations between sitting time (n=850 060; 25 703 deaths) and CVD mortality. The reference categories are the groups with &lt;4 hour/day of sitting or &lt;1 hour/day of TV-viewing for all quartiles of physical activity. Median upper boundary for Q1–Q3 and lower boundary for Q4 in MET-hour/week. The equivalent amount of time spent in moderate intensity activity are ≥5 min/day (Q1); 25–35 min/day (Q2); 50–65 min/day (Q3) and 60–75 min/day (Q4).</p> <p>Five studies had data on the relationship between <b>TV-viewing time</b> and <b>CVD mortality</b> (n=458,127, median follow-up 8.5 years). Patterns were similar with those seen for sitting time. In the ‘inactive’ group (lowest PA quartile, &lt;2.5 MET-hrs/week) the hazard of CVD mortality was 1.59 (95% CI only shown in figure) in those who watched TV for &gt;5 hrs/day compared with those who watched TV for &lt;1 hr/day) (p for trend &lt;0.001). For the other quartiles of PA, the hazard estimates were only significantly increased in the 2<sup>nd</sup> quartile (HR=1.28, 95% CI not reported) and 3<sup>rd</sup> quartile (HR=1.41, 95% CI not reported) of PA when comparing &gt;5 hrs/day of TV time vs. &lt;1 hr/day of TV time. There was no increased risk of CVD mortality in the most active quartile of PA for any level of TV viewing time.</p> <p>Eight studies (n=777,696, median follow-up 11.5 years) had data on the relationship between <b>sitting time</b> and <b>cancer mortality</b>. There was no clear dose response relationship between sitting time and cancer risk by level of PA. In both the lowest quartile of PA (&lt;2.5 MET-hrs/week) and the 2<sup>nd</sup> quartile of PA (16 MET-hrs/week), there was a</p> | Physical Activity Quartile | Sitting Time | Hazard Ratio (95% CI) | <2.5 MET-h/week | <4 h/d (Ref) | 1.0 | 4-6 h/d | ~1.1 | 6-8 h/d | ~1.2 | >8 h/d | ~1.59 | 16 MET-h/week | <4 h/d (Ref) | 1.0 | 4-6 h/d | ~1.0 | 6-8 h/d | ~1.0 | >8 h/d | ~1.1 | 30 MET-h/week | <4 h/d (Ref) | 1.0 | 4-6 h/d | ~1.1 | 6-8 h/d | ~1.0 | >8 h/d | ~1.1 | >35.5 MET-h/week | <4 h/d (Ref) | 1.0 | 4-6 h/d | ~1.0 | 6-8 h/d | ~1.0 | >8 h/d | ~1.0 |
|----------------------------|--------------|-----------------------|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|--------------|-----------------------|-----------------|--------------|-----|---------|------|---------|------|--------|-------|---------------|--------------|-----|---------|------|---------|------|--------|------|---------------|--------------|-----|---------|------|---------|------|--------|------|------------------|--------------|-----|---------|------|---------|------|--------|------|
| Physical Activity Quartile | Sitting Time | Hazard Ratio (95% CI) |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
| <2.5 MET-h/week            | <4 h/d (Ref) | 1.0                   |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | 4-6 h/d      | ~1.1                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | 6-8 h/d      | ~1.2                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | >8 h/d       | ~1.59                 |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
| 16 MET-h/week              | <4 h/d (Ref) | 1.0                   |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | 4-6 h/d      | ~1.0                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | 6-8 h/d      | ~1.0                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | >8 h/d       | ~1.1                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
| 30 MET-h/week              | <4 h/d (Ref) | 1.0                   |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | 4-6 h/d      | ~1.1                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | 6-8 h/d      | ~1.0                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | >8 h/d       | ~1.1                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
| >35.5 MET-h/week           | <4 h/d (Ref) | 1.0                   |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | 4-6 h/d      | ~1.0                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | 6-8 h/d      | ~1.0                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |
|                            | >8 h/d       | ~1.0                  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |              |                       |                 |              |     |         |      |         |      |        |       |               |              |     |         |      |         |      |        |      |               |              |     |         |      |         |      |        |      |                  |              |     |         |      |         |      |        |      |

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|--|--|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
|  |  |  |  |  |  | <p>significantly higher risk of cancer mortality in the highest sitting category (&gt;8 hrs/day) vs. lowest (&lt;4 hrs/day) (HR=1.21 [95% CI, 1.14 to 1.29] for the lowest PA quartile and HR=1.08 [95% CI, 1.00 to 1.15] for the 2<sup>nd</sup> PA quartile).</p> <p>Figure 3 Meta-analysis of the stratified associations between sitting time (n=777696; 30851 deaths) and cancer mortality. The reference categories are the groups with &lt;4 hour/day of sitting or &lt;1 hour/day of TV viewing for all quartiles of physical activity. Median upper boundary for Q1–Q3 and lower boundary for Q4 in MET-hour/week. The equivalent amount of time spent in moderate intensity activity are &lt;5 min/day (Q1); 25–35 min/day (Q2); 50–65 min/day (Q3) and 60–75 min/day (Q4).</p> <p>Five studies (n=458,091 median follow-up=8.5 years) had data on the relationship between <b>TV-viewing time</b> and <b>cancer mortality</b>. There was no significantly increased risk of cancer mortality by TV time among those in the inactive or most active PA quartiles, but there was a significantly increased hazards in the 2<sup>nd</sup> PA quartile (HR=1.18 [95% CI, 1.04 to 1.34] and 3<sup>rd</sup> PA quartile (HR=1.29 [95% CI, 1.10 to 1.51]) when comparing TV viewing time of &gt;5 hrs/day vs. &lt;1 hr/day.</p> |  |
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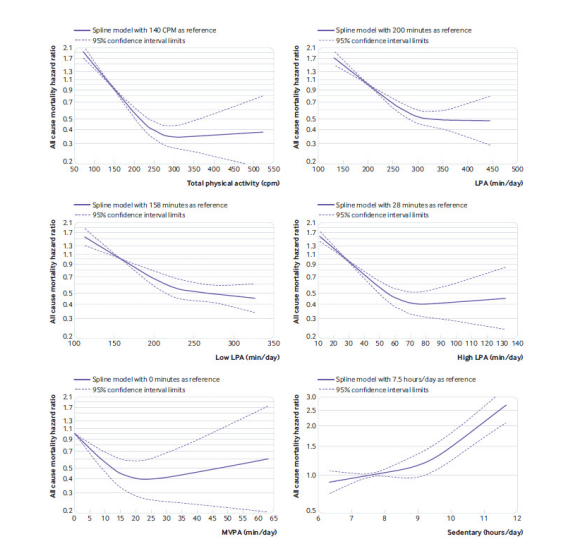
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| Systematic review evidence    | No. of studies/<br>Study design                                                     | Quality Assessment                |                                   |                                   |                        |                            | Description of evidence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Certainty |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
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|                               |                                                                                     | Risk of bias                      | Inconsistency                     | Indirectness†                     | Imprecision            | Other                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| Review credibility            | No. of participants                                                                 |                                   |                                   |                                   |                        |                            | Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| Ekelund 2019 (10)             | 8 prospective cohort studies                                                        | No serious risk of bias           | No serious inconsistency          | No serious indirectness           | No serious imprecision | Dose-response relationship | <p>Harmonized meta-analysis from eight prospective cohort studies, including data from 3 large surveillance systems and 2 from unpublished data. Mean age in studies was 63 years with median follow-up of 5.8 years (range 3 to 14.5 years). All 8 studies used accelerometers to measure ST (sedentary <math>\leq 100</math> cpm). Data was categorized into quartiles with the least active quartile as the referent.</p> <p>Increasing time spent in sedentary behaviour was significantly associated with <b>all-cause mortality</b>. Hazard ratios for increasing quarters of ST were 1.28 (95% CI, 1.09 to 1.51) for the 2<sup>nd</sup> quartile, 1.71 (95% CI, 1.36 to 2.15) for the 3<sup>rd</sup> quartile, and 2.63 (95% CI, 1.94 to 3.56) for the highest quartile of ST, after adjustment for potential confounders including time spent in MVPA (table below).</p> <table><caption>Table 2   Meta-analysis for associations between total physical activity, intensities of physical activity or sedentary time by quarters and all cause mortality</caption><thead><tr><th rowspan="2">Variables</th><th colspan="4">Hazard ratios (95% CI) for all cause mortality*; No. of participants; No. of deaths</th></tr><tr><th>First quarter (least active)</th><th>Second quarter</th><th>Third quarter</th><th>Fourth quarter (most active)</th></tr></thead><tbody><tr><td>Model B†</td><td></td><td></td><td></td><td></td></tr><tr><td>Total physical activity (cpm)</td><td>1 (ref) (n=9096, 1187)</td><td>0.48 (0.43 to 0.54) (n=9105, 483)</td><td>0.34 (0.26 to 0.45) (n=9096, 265)</td><td>0.27 (0.23 to 0.32) (n=9086, 214)</td></tr><tr><td>Physical activity intensity:</td><td></td><td></td><td></td><td></td></tr><tr><td>Light (min/d)</td><td>1 (ref) (n=9073, 1089)</td><td>0.60 (0.54 to 0.68) (n=9101, 511)</td><td>0.44 (0.38 to 0.51) (n=9090, 320)</td><td>0.38 (0.28 to 0.51) (n=9119, 229)</td></tr><tr><td>Low light (min/d)</td><td>1 (ref) (n=9066, 1010)</td><td>0.66 (0.56 to 0.77) (n=9106, 518)</td><td>0.47 (0.38 to 0.58) (n=9112, 353)</td><td>0.42 (0.34 to 0.52) (n=9099, 268)</td></tr><tr><td>High light (min/d)</td><td>1 (ref) (n=9054, 1159)</td><td>0.55 (0.49 to 0.63) (n=9120, 483)</td><td>0.38 (0.30 to 0.48) (n=9088, 278)</td><td>0.37 (0.32 to 0.44) (n=9113, 229)</td></tr><tr><td>Moderate to vigorous (min/d)</td><td>1 (ref) (n=9052, 1159)</td><td>0.64 (0.55 to 0.74) (n=9113, 468)</td><td>0.55 (0.40 to 0.74) (n=9113, 355)</td><td>0.52 (0.43 to 0.63) (n=9105, 217)</td></tr><tr><td>Sedentary (min/d)</td><td>1 (ref) (n=9102, 327)</td><td>1.28 (1.09 to 1.51) (n=9105, 417)</td><td>1.71 (1.36 to 2.15) (n=9096, 562)</td><td>2.63 (1.94 to 3.56) (n=9080, 843)</td></tr></tbody></table> <p>cpm=counts per minute.<br/>Model A: adjusted for sex (when applicable), age, and wear time (n=36852, 2304 deaths). Model B: adjusted for sex (when applicable), age, body mass index, socioeconomic position, and wear time (n=36383, 2149 deaths). Model C: additionally adjusted for covariates listed in table 1 (n=35932, 2047 deaths).<br/>*Bayes regression.<br/>†Moderate to vigorous physical activity and sedentary time are mutually adjusted.</p> <p>Differences in min/day between the referent (least sedentary) and 2<sup>nd</sup> quarter were broadly equal to 70 min/day of sedentary time.</p> <p>The dose-response relationship between ST and mortality increased gradually from about 7.5 to 9 hrs/day and were more pronounced at &gt;9.5 hrs/day (see figure below).</p> | Variables | Hazard ratios (95% CI) for all cause mortality*; No. of participants; No. of deaths |  |  |  | First quarter (least active) | Second quarter | Third quarter | Fourth quarter (most active) | Model B† |  |  |  |  | Total physical activity (cpm) | 1 (ref) (n=9096, 1187) | 0.48 (0.43 to 0.54) (n=9105, 483) | 0.34 (0.26 to 0.45) (n=9096, 265) | 0.27 (0.23 to 0.32) (n=9086, 214) | Physical activity intensity: |  |  |  |  | Light (min/d) | 1 (ref) (n=9073, 1089) | 0.60 (0.54 to 0.68) (n=9101, 511) | 0.44 (0.38 to 0.51) (n=9090, 320) | 0.38 (0.28 to 0.51) (n=9119, 229) | Low light (min/d) | 1 (ref) (n=9066, 1010) | 0.66 (0.56 to 0.77) (n=9106, 518) | 0.47 (0.38 to 0.58) (n=9112, 353) | 0.42 (0.34 to 0.52) (n=9099, 268) | High light (min/d) | 1 (ref) (n=9054, 1159) | 0.55 (0.49 to 0.63) (n=9120, 483) | 0.38 (0.30 to 0.48) (n=9088, 278) | 0.37 (0.32 to 0.44) (n=9113, 229) | Moderate to vigorous (min/d) | 1 (ref) (n=9052, 1159) | 0.64 (0.55 to 0.74) (n=9113, 468) | 0.55 (0.40 to 0.74) (n=9113, 355) | 0.52 (0.43 to 0.63) (n=9105, 217) | Sedentary (min/d) | 1 (ref) (n=9102, 327) | 1.28 (1.09 to 1.51) (n=9105, 417) | 1.71 (1.36 to 2.15) (n=9096, 562) | 2.63 (1.94 to 3.56) (n=9080, 843) | HIGH <sup>§</sup> |
| Variables                     | Hazard ratios (95% CI) for all cause mortality*; No. of participants; No. of deaths |                                   |                                   |                                   |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
|                               | First quarter (least active)                                                        | Second quarter                    | Third quarter                     | Fourth quarter (most active)      |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| Model B†                      |                                                                                     |                                   |                                   |                                   |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| Total physical activity (cpm) | 1 (ref) (n=9096, 1187)                                                              | 0.48 (0.43 to 0.54) (n=9105, 483) | 0.34 (0.26 to 0.45) (n=9096, 265) | 0.27 (0.23 to 0.32) (n=9086, 214) |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| Physical activity intensity:  |                                                                                     |                                   |                                   |                                   |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| Light (min/d)                 | 1 (ref) (n=9073, 1089)                                                              | 0.60 (0.54 to 0.68) (n=9101, 511) | 0.44 (0.38 to 0.51) (n=9090, 320) | 0.38 (0.28 to 0.51) (n=9119, 229) |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| Low light (min/d)             | 1 (ref) (n=9066, 1010)                                                              | 0.66 (0.56 to 0.77) (n=9106, 518) | 0.47 (0.38 to 0.58) (n=9112, 353) | 0.42 (0.34 to 0.52) (n=9099, 268) |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| High light (min/d)            | 1 (ref) (n=9054, 1159)                                                              | 0.55 (0.49 to 0.63) (n=9120, 483) | 0.38 (0.30 to 0.48) (n=9088, 278) | 0.37 (0.32 to 0.44) (n=9113, 229) |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| Moderate to vigorous (min/d)  | 1 (ref) (n=9052, 1159)                                                              | 0.64 (0.55 to 0.74) (n=9113, 468) | 0.55 (0.40 to 0.74) (n=9113, 355) | 0.52 (0.43 to 0.63) (n=9105, 217) |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |
| Sedentary (min/d)             | 1 (ref) (n=9102, 327)                                                               | 1.28 (1.09 to 1.51) (n=9105, 417) | 1.71 (1.36 to 2.15) (n=9096, 562) | 2.63 (1.94 to 3.56) (n=9080, 843) |                        |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |           |                                                                                     |  |  |  |                              |                |               |                              |          |  |  |  |  |                               |                        |                                   |                                   |                                   |                              |  |  |  |  |               |                        |                                   |                                   |                                   |                   |                        |                                   |                                   |                                   |                    |                        |                                   |                                   |                                   |                              |                        |                                   |                                   |                                   |                   |                       |                                   |                                   |                                   |                   |

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|------------------------------|-----------------------------------------------------------|----------------------------------|--------------------------|-------------------------|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
|                              |                                                           |                                  |                          |                         |                           |  <p>Fig 2   Dose-response associations between total physical activity (top left), light intensity physical activity (LPA) (top right), low LPA (middle left), high LPA (middle right), moderate-to-vigorous physical activity (MVPA) (bottom left), and sedentary time (bottom right), data from REGARDS (Reasons for Geographic and Racial Differences in Stroke)<sup>22</sup> and FHS (Women's Health Study)<sup>23</sup> are only included for MVPA and all cause mortality. Modelling performed using restricted cubic splines with knots at 25th, 50th, and 75th centiles of exposure specific distribution from medians of quarters (least to most active). The exposure reference is set as the median of the medians in the reference group (least active) (see supplementary table 3). Knot locations are available in supplementary table 6. cpm=counts per minute</p>                                                                           |                  |
| Ku 2018 (13)<br><br>Moderate | 19<br>prospective<br>cohort<br>studies<br><br>N=1,250,482 | No<br>serious<br>risk of<br>bias | Serious<br>inconsistency | Serious<br>indirectness | No serious<br>imprecision | <p>Potential overlap in 6 of 7 studies of device-based measures</p> <p>Analysis of the relationship between sedentary time and <b>all-cause mortality</b> in adults. Mean follow-up was 7.8 years (range 2.8 to 15.7 years). Mean age of participants ranged from 40 to 64 years. 12/19 included subjective measures of sedentary time and 7/19 used objective device-based measures. Cut-off points for categories of sedentary time were inconsistent across studies.</p> <p>A linear dose-response relationship was found between daily sedentary time and risk (log-linear) of <b>all-cause mortality</b>. A significant relationship was found when limited to both subjective measures (regression coefficient = 0.03 [SE, 0.01], p&lt;0.01) and device-based measures (regression coefficient = 0.09 [SE, 0.03], p&lt;0.01). The regression line and upper and lower 95% CI bounds showed that increased hazards of all-cause death became significant when total sedentary time exceeded approximately 7.5 hrs/day (7 hrs/day when</p> | LOW <sup>h</sup> |

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|  |  |  |  |  |  |  |                                                                                                                                                                                                      |  |
|--|--|--|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
|  |  |  |  |  |  |  | looking at only subjective measures and 9 hrs/day when looking only at objective measures). Studies with longer follow-ups had weaker associations between daily sedentary time and mortality risks. |  |
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| Systematic review evidence<br><br>Review credibility | No. of studies/<br>Study design<br><br>No. of participants | Quality Assessment      |                          |                         |                        |                                      | Description of evidence<br><br>Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Certainty             |
|------------------------------------------------------|------------------------------------------------------------|-------------------------|--------------------------|-------------------------|------------------------|--------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
|                                                      |                                                            | Risk of bias            | Inconsistency            | Indirectness†           | Imprecision            | Other                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                       |
| Ku 2019 (14)<br><br>Moderate                         | 11 prospective cohort studies<br><br>N=36,341              | No serious risk of bias | No serious inconsistency | No serious indirectness | No serious imprecision | Potential overlap in 3 of 11 studies | <p>Analysis of the relationship between sedentary time and all-cause mortality in older adults (<math>\geq 65</math> years). Mean follow-up was 7.8 years (range 2.3 to 14.2 years). Mean age of participants ranged from 67 to 79 years. All studies used accelerometers to measure ST; 6 studies defined ST as <math>&lt;100</math> counts/min, 2 studies defined ST as <math>&lt;200</math> counts/min, 1 used <math>&lt;50</math> counts/min, and 2 studies did not report the cut point used to define ST.</p> <p>There was no significant dose-response association between ST and <b>all-cause mortality</b> among older adults (regression coefficient = 0.04 [SE, 0.03], <math>p=0.15</math>). Removing 3 studies that did not adjust for accelerometer wear time resulted in a significant dose response relationship between ST and all-cause mortality (regression coefficient = 0.08 [SE, 0.03], <math>p=0.02</math>). Within this model, the regression line and upper and lower 95% CI bounds showed that increased hazards of (log-transformed) all-cause death became significant when total sedentary time exceeded approximately 9 hrs/day.</p> | MODERATE <sup>e</sup> |
| Patterson 2018 (19)<br><br>Low                       | 34 prospective cohort studies<br><br>N=1,331,468           | No serious risk of bias | No serious inconsistency | Serious indirectness    | No serious imprecision | None                                 | <p>Mean follow-up was 8.9 years (range, 2 to 31 years). Most studies assessed sedentary behaviour via self-report, 3 included objective measurement via accelerometer. Categories used by the study authors to define levels of sedentary behaviour varied considerably across studies.</p> <p>For <b>total sitting time</b>, the PA-adjusted relationship was not significantly linear for <b>all-cause mortality</b> or <b>CVD mortality</b>. In PA-adjusted analysis, the RR was 1.01 (95% CI 1.00 to 1.01) for each additional hr/day below 8 hrs/day and 1.04 (95% CI, 1.03 to 1.05) for each hr/day above 8 hr/day for <b>all-cause mortality</b>. For <b>CVD mortality</b> the adjusted RR per 1 hr/day was 1.01 (95% CI, 0.99 to 1.02) when total exposure was <math>\leq 6</math> hrs/day and RR=1.04 (95% CI, 1.03 to 1.04) when <math>&gt;6</math> hrs/day. For <b>cancer mortality</b>, the adjusted RR was 1.01 (95% CI, 1.00 to 1.02) with no evidence of non-linearity.</p>                                                                                                                                                                         | MODERATE <sup>e</sup> |

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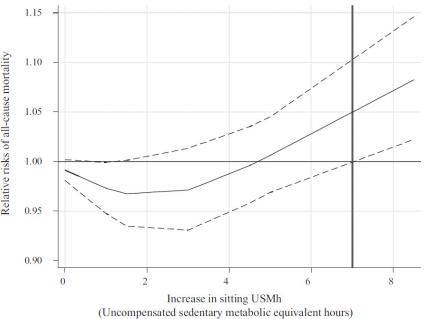
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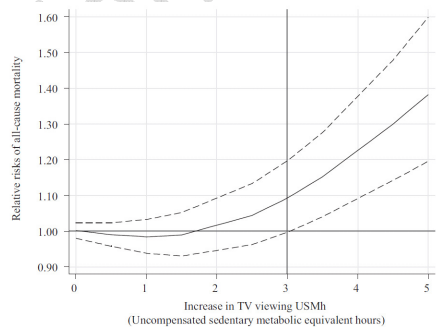
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| Systematic review evidence           | No. of studies/<br>Study design               | Quality Assessment |                 |                 |                 |                                                                                                                                      | Description of evidence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Certainty        |
|--------------------------------------|-----------------------------------------------|--------------------|-----------------|-----------------|-----------------|--------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
|                                      |                                               | Risk of bias       | Inconsistency   | Indirectness†   | Imprecision     | Other                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                  |
| Review credibility                   | No. of participants                           |                    |                 |                 |                 |                                                                                                                                      | Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |
| Xu 2019 <sup>j</sup> (22)<br><br>Low | 7 prospective cohort studies<br><br>N=284,161 | NA <sup>d</sup>    | NA <sup>d</sup> | NA <sup>d</sup> | NA <sup>d</sup> | <p>Dose-response relationship</p> <p>Does not include all available and eligible cohort studies</p> <p>Does not account for LIPA</p> | <p>Examination of the relationship between sedentary activity and all-cause mortality according to PA level using individual participant level data. All measures of ST and PA were self-reported. Mean follow-up ranged from 6.6 to 13.7 years. Sedentary activity was defined by a measure that takes into account both time spent in specific activities and the intensity of those activities by computing a “net uncompensated sedentary behaviour metabolic equivalent hours” (USMh) (where USMh = [MET x hr on SB] – [MET x hr on MVPA]).</p> <p>Data from 5 cohort studies (n=258,688) were pooled to examine the relationship between <b>sitting</b> and <b>all-cause mortality</b>. The predicted dose-response RRs of sitting were 0.97 (95% CI, 0.95 to 1.00) at 1 USMh, 0.97 (95% CI, 0.93 to 1.01) at 3 USMh, 1.01 (95% CI, 0.97 to 1.05) at 5 USMh, 1.05 (95% CI, 1.00 to 1.10) at 7 USMh, and 1.08 (95% CI, 1.02 to 1.15) at 8.5 USMh. The threshold for risk started to 7 USMh, and on average, between 0 and the maximum of 8.5 USMh of 8.5 hrs, the increase in mortality was 1% (RR=1.01 [95% CI, 1.00 to 1.02]).</p>  <p>Fig 1. Increase in sitting (USMh) and risk of all-cause mortality. The solid line is the nonlinear prediction of the risk and the dotted lines indicate the 95% confidence interval. The threshold is 7 USMh. USMh indicates the uncompensated sedentary metabolic equivalent hours. For example, for people with no reported physical activity at all, the threshold (7 USMh/d) is reached after sitting 7 hours/d. If there was a 4-MET activity for 30 minutes/d, then this threshold (7 USMh/d) would only be reached after 9 hours of sitting per day.</p> | LOW <sup>k</sup> |

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|  |  |  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |
|--|--|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
|  |  |  |  |  |  |  | <p>Data from 4 cohort studies (n=156,593) were pooled to examine the relationship between <b>TV viewing</b> and <b>all-cause mortality</b>. The predicted dose-specific RRs of TV viewing were 0.98 (95% CI, 0.94 to 1.03) at 1 USMh, 1.09 (95% CI, 1.00 to 1.20) at 3 USMh, and 1.38 (95% CI, 1.20 to 1.60) at 5 USMh. The threshold for risk started at 3 USMh and the average increase in risk of death between 0 and the maximum value of 5 USMh was an increase of 7% (RR 1.07 [95% CI, 1.04 to 1.10]).</p>  <p><b>Fig. 2.</b> Increases in TV viewing (USMh) and risk of all-cause mortality. The solid line is the nonlinear prediction of the risk and the dotted lines indicate the 95% confidence interval. The threshold is 3 USMh/d. USMh indicates the uncompensated sedentary metabolic equivalent hours. For example, for people with no reported physical activity at all, the threshold (3 USMh/d) is reached after watching TV 3 hours/d. If there was a 4-MET activity for 30 minutes/d, then this threshold (3 USMh/d) would only be reached after 4 hours of TV viewing per day.</p> |  |
|--|--|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|

Abbreviations: CI = confidence interval; cpm = counts per minute; CVD = cardiovascular disease; HR = hazard ratio; hrs = hours; min = minutes; LIPA = light intensity physical activity; MET = metabolic equivalents of task; MVPA = moderate-to-vigorous intensity physical activity; NA = not assessed; PA = physical activity; RR = risk ratio; SE = standard error; ST = sedentary time; USMh = net uncompensated sedentary behaviour metabolic equivalent hours

\*Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

<sup>a</sup> Certainty of evidence not upgraded given serious risk of bias of most studies (generally lack of adjustment for potential confounding variables) and downgraded due to serious inconsistency in direction of effects and high statistical heterogeneity

<sup>b</sup> Unable to assess given data presented in article and supplemental material (i.e., qualitative results only, no effect estimates or measures of variance)

<sup>c</sup> Certainty of evidence not upgraded given unknown consistency and precision of effects

<sup>d</sup> Not able to assess given data presented in article and supplemental materials

<sup>e</sup> For the relationship between sitting time and CVD mortality and TV-viewing time and CVD mortality only. No dose response relationship was found according to level of PA for cancer mortality.

<sup>f</sup> Certainty of evidence upgraded given no serious limitations of included evidence and indication of dose-response relationship

<sup>g</sup> Certainty of evidence upgraded given no serious limitations in the body of evidence, individual participant-level data meta-analysis, and evidence of a dose response relationship

<sup>h</sup> Certainty of evidence not upgraded given serious inconsistency in pooled effects and serious indirectness given the variability in measurement and cut points defining sedentary time

<sup>i</sup> Certainty of evidence upgraded given no major study limitations. The potential overlap in study populations was not judged as being significant enough to warrant downgrading.

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<sup>j</sup> Individual participant data meta-analysis

<sup>k</sup> Certainty of evidence not upgraded here given lack of detail about individual studies; however, all data comes from existing systematic reviews that serve as the basis for several secondary data analysis presented in this evidence profile. Main limitation is that it does not include all available and eligible cohort studies that could have contributed to this analysis.

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**Table B.2.b. CVD incidence: Association between sedentary behaviour and CVD incidence among adults (in alphabetical order by author)**See the [Supplementary materials](#) for description of evidence and conclusions of US PAGAC (24) by outcome

| Systematic review evidence<br><br>Review credibility | No. of studies/<br>Study design<br><br>No. of participants | Quality Assessment      |                          |                           |                        |       | Description of evidence<br><br>Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Certainty             |
|------------------------------------------------------|------------------------------------------------------------|-------------------------|--------------------------|---------------------------|------------------------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
|                                                      |                                                            | Risk of bias            | Inconsistency            | Indirectness <sup>†</sup> | Imprecision            | Other |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                       |
| Ahmad 2017 (1)<br><br>Moderate                       | 1 case-control study<br><br>N=655                          | No serious risk of bias | No serious inconsistency | Serious indirectness      | Serious imprecision    | None  | One case-control study found a significantly higher risk of MI among those self-reporting $\geq 215$ min/day of ST vs. $< 70$ min/day of ST (RR=1.58 [95% CI, 1.05 to 2.36]). There was no difference in MI risk among those reporting $> 130$ -214 min/day of ST vs. $< 70$ min/day (RR = 0.96 [95% CI, 0.64 and 1.44]).                                                                                                                                                                                                                                                                                                                                                                                                                   | VERY LOW <sup>a</sup> |
| Bailey 2019 (3)<br><br>Moderate                      | 5 prospective cohort studies<br><br>N=224,414              | No serious risk of bias | No serious inconsistency | Serious indirectness      | No serious imprecision | None  | Mean age of sample ranged from 44 to 64 years and mean follow-up ranged from 2.7 to 13 years. All studies used a single-item self-report measure of total daily sitting time; cutpoints for categories of sitting time were not consistent across studies (range for highest sitting category was $\geq 7.1$ hrs to 16 hrs/day and range for the lowest sitting category was $< 4$ hrs to $< 8$ hrs/day). All studies but one adjusted for physical activity.<br><br>Higher total daily sitting time was associated with significantly increased risk of CVD when not adjusted for PA levels (HR = 1.29 [95% CI, 1.27 to 1.30]; the risk was attenuated but remained significant with adjustment for PA (HR = 1.14 [95% CI, 1.04 to 1.23]). | MODERATE <sup>b</sup> |

Abbreviations: CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratio; hrs = hours; MI = myocardial infarction; min = minutes; PA = physical activity; RR = risk ratio

<sup>†</sup>Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review<sup>a</sup> Certainty of evidence downgraded given serious indirectness in measures of sedentary behavior and serious imprecision in measures of effects<sup>b</sup> Certainty of evidence upgraded given no significant study limitations

**Table B.2.c. Cancer incidence: Association between sedentary behaviour and cancer incidence among adults (in alphabetical order by author)**  
[See the Supplementary materials](#) for description of evidence and conclusions of US PAGAC (24) by outcome

| Systematic review evidence<br><br>Review credibility | No. of studies/<br>Study design<br><br>No. of participants                                   | Quality Assessment   |                          |                      |                        |       | Description of evidence<br><br>Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Certainty             |
|------------------------------------------------------|----------------------------------------------------------------------------------------------|----------------------|--------------------------|----------------------|------------------------|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
|                                                      |                                                                                              | Risk of bias         | Inconsistency            | Indirectness†        | Imprecision            | Other |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                       |
| Berger 2019 (5)<br><br>Moderate                      | 12 prospective cohort studies<br><br>N=671,852                                               | Serious risk of bias | Serious inconsistency    | Serious indirectness | No serious imprecision | None  | Most studies used self-report sedentary behaviour (one study combined self-report and job title assignment). Mean follow-up time was not reported. There was no association between high versus low ST and risk of incident <b>prostate cancer</b> (RR = 1.07 [95% CI 0.99 and 1.16], 11 studies).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | VERY LOW <sup>a</sup> |
| Chan 2019 (6)<br><br>Moderate                        | 6 prospective cohort studies<br><br>N=285,295                                                | Serious risk of bias | Serious inconsistency    | Serious indirectness | Serious imprecision    | None  | Increased total sitting time was not associated with <b>premenopausal breast cancer</b> (RR = 1.04 [95% CI, 0.83 to 1.32], 2 studies, n=1,290) but was associated with <b>postmenopausal breast cancer</b> (RR = 1.20 [95% CI, 1.00 to 1.44], 4 studies, n=4,704). No significant associations were found between sitting watching TV or sitting at work and either pre- or post-menopausal breast cancer.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | VERY LOW <sup>b</sup> |
| Mahmood 2017 (17)<br><br>Low                         | 4 prospective cohort studies<br><br>N=1,709,572<br><br>4 case-control studies<br><br>N=2,463 | NR                   | No serious inconsistency | Serious indirectness | No serious imprecision | None  | Six studies investigated occupational sedentary behaviour and two studies assessed recreational sedentary behaviour. Sedentary behaviour ascertained based on job title or measured via self-report.<br><br>The pooled RR for the highest vs. lowest category of occupational sitting time for <b>colon cancer</b> was 1.44 (95% CI, 1.28 to 1.62). No significant association was found between occupational sitting time and <b>rectal cancer</b> (RR = 1.02 [95% CI, 0.82 to 1.28]). Two studies evaluated the association between self-reported recreational TV time (hrs/day): 1 study found that watching TV for more than 9 hrs/day (compared with less than 3 hrs/day) was associated with significantly increased risk of <b>colon cancer</b> in men (RR = 1.56 [95% CI 1.11 to 1.20]) and women (RR = 1.45 [95% CI, 0.99 and 2.13]) and the other found an association between TV time ≥2 hrs/day vs. <1.14 hrs/day and <b>colon cancer</b> in both men and women (RR = 2.22 [95% CI, 1.23 to 4.17]). | LOW <sup>c</sup>      |
| Wang 2018 (21)<br><br>High                           | 3 cross-sectional studies                                                                    | Serious risk of bias | No serious inconsistency | Serious indirectness | No serious imprecision | None  | All 3 studies used self-reported measures of SB; one study included overall SB, two studies reported recreational SB (including one limited to TV viewing only), and one study also included transport-related SB.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | VERY LOW <sup>d</sup> |

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|  | N=56,412 |  |  |  |  |  | <p>Categorization of SB was highly variable between studies Age ranged from 40 to 74 years in all 3 studies.</p> <p>None of the 3 studies reported statistically significant associations between time spent in SB and <b>any colorectal neoplasia</b> or <b>advanced colorectal neoplasia</b>; however, the pooled result suggested a significant increased risk of advanced colorectal neoplasia with higher levels of SB (RR = 1.24 [95% CI, 1.04 to 1.49], 3 studies).</p> |  |
|--|----------|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|

Abbreviations: CI = confidence interval; hrs = hours; NR = not reported; RR = risk ratio; SB = sedentary behaviour; TV = television

\*Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

<sup>a</sup> Certainty of evidence not upgraded given serious risk of bias of most studies (generally lack of adjustment for potential confounding variables) and due to serious inconsistency in direction of effects and high statistical heterogeneity

<sup>b</sup> Certainty of evidence not upgraded given serious risk of bias of most studies (generally lack of adjustment for potential confounding variables) and due to serious inconsistency and imprecision in direction and magnitude of effects

<sup>c</sup> Certainty of evidence not upgraded given lack of risk-of-bias assessment of individual studies and indirectness in measures of sedentary behaviour

<sup>d</sup> Certainty of evidence downgraded given serious risk of bias of all included studies and serious indirectness in measures of sedentary behaviour

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**Table B.2.d. Type 2 diabetes incidence: Association between sedentary behaviour and Type 2 diabetes incidence among adults (in alphabetical order by author)**

[See the Supplementary materials](#) for description of evidence and conclusions of US PAGAC (24) by outcome

| Systematic review evidence<br><br>Review credibility | No. of studies/<br>Study design<br><br>No. of participants                  | Quality Assessment      |                          |                      |                        |       | Description of evidence<br><br>Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Certainty             |
|------------------------------------------------------|-----------------------------------------------------------------------------|-------------------------|--------------------------|----------------------|------------------------|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
|                                                      |                                                                             | Risk of bias            | Inconsistency            | Indirectness†        | Imprecision            | Other |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                       |
| Ahmad 2017 (1)<br><br>Moderate                       | 1 prospective cohort,<br>1 case-control, 2 cross-sectional<br><br>N=158,964 | No serious risk of bias | No serious inconsistency | Serious indirectness | Serious imprecision    | None  | All four studies suggested that greater <b>sedentary time</b> is associated with higher prevalence of diabetes. The one prospective cohort study (n=1,376) found an 84% increased risk for developing diabetes in the highest quartile of TV and sitting time. One cross-sectional study (n=617) found that the odds of diabetes was 43% (OR = 1.43 [95% CI, 0.72 to 2.82]) greater in those sitting ≥185 min/day vs. <185 min/day and were over four times greater (OR = 4.23 [95% CI 2.13 to 8.41]) in those watching ≥85 min/day or TV compared to those with <85 min/day. One cross-sectional (n=156,316) and one case-control study (n=655) reported higher proportions of diabetes among those watching TV almost every day (vs. those watching TV once a week or less) and those in sedentary activities longer than 215 min/day (vs. ≤70 min/day), respectively. | VERY LOW <sup>a</sup> |
| Bailey 2019 (3)<br><br>Moderate                      | 5 prospective cohort studies<br><br>N=4,575                                 | No serious risk of bias | No serious inconsistency | Serious indirectness | No serious imprecision | None  | Mean age of sample ranged from 44 to 64 years and mean follow-up ranged from 2.7 to 13 years. All studies used a single-item self-report measure of total daily sitting time; cutpoints for categories of sitting time were not consistent across studies (range for highest sitting category was ≥7.1 hrs to 16 hrs/day and range for the lowest sitting category was <4 hrs to <8 hrs/day). All studies but one adjusted for physical activity.<br><br>Higher <b>total daily sitting time</b> was associated with significantly increased risk of diabetes when not adjusted for PA levels (HR = 1.13 [95% CI, 1.04 to 1.22] and with adjustment for PA (HR = 1.11 [95% CI, 1.01 to 1.19]).                                                                                                                                                                            | MODERATE <sup>b</sup> |
| Patterson 2018 (19)<br><br>Low                       | 11 prospective cohort studies                                               | No serious risk of bias | No serious inconsistency | Serious indirectness | No serious imprecision | None  | Mean follow-up was 8.9 years (range, 2 to 31 years). Most studies assessed sedentary behaviour via self-report, 3 included objective measurement via accelerometer. Categories used by the study authors                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | MODERATE <sup>b</sup> |

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|  | N=400,292 |  |  |  |  |  | <p>to define levels of sedentary behaviour varied considerably across studies.</p> <p>Increased <b>total sitting time</b> and <b>TV viewing</b> (linear RR for a 1 hr/day increase in sedentary behaviour) was associated with an increased risk of diabetes (total sitting time: RR=1.10 [95% CI, 1.00 to 1.01], 4 studies and TV viewing time: RR=1.09 [95% CI, 1.07 to 1.12], 6 studies) after adjustment for level of PA, but there was no evidence of a significant linear association.</p> |  |
|--|-----------|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|

Abbreviations: CI = confidence interval; hrs = hours; min = minutes; NR = not reported; OR = odds ratio; PA = physical activity; RR = risk ratio; ST = sedentary time; TV = television

\*Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

<sup>a</sup> Certainty of evidence downgraded given serious indirectness in measures of sedentary behaviour and serious imprecision in measures of effects

<sup>b</sup> Certainty of evidence upgraded given no significant study limitations

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**Table B.2.e. Adiposity: Association between sedentary behaviour and measures of adiposity among adults (in alphabetical order by author)**See the [Supplementary materials](#) for description of evidence and conclusions of US PAGAC (24) by outcome

| Systematic review evidence<br><br>Review credibility | No. of studies/<br>Study design<br><br>No. of participants                       | Quality Assessment   |                          |                         |                     |       | Description of evidence<br><br>Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Certainty             |
|------------------------------------------------------|----------------------------------------------------------------------------------|----------------------|--------------------------|-------------------------|---------------------|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
|                                                      |                                                                                  | Risk of bias         | Inconsistency            | Indirectness†           | Imprecision         | Other |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                       |
| Ahmad 2017 (1)<br><br>Moderate                       | 1 prospective cohort, 1 case-control, 13 cross-sectional studies<br><br>N=13,395 | Serious risk of bias | No serious inconsistency | NA <sup>a</sup>         | NA <sup>a</sup>     | None  | 13/15 studies reported that higher amounts of ST were significantly associated with <b>BMI</b> ; 2/15 reported no significant association. Data by study not presented.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | VERY LOW <sup>b</sup> |
| del Pozo-Cruz (8)<br><br>Moderate                    | 6 cross-sectional studies<br><br>N=4,774                                         | Serious risk of bias | Serious inconsistency    | No serious indirectness | Serious imprecision | None  | All studies used accelerometers to measure ST; cut points for defining ST varied across studies, with <100 cpm when only data from the vertical axis of the accelerometer were used or <200 cpm when data from the vector axis of the accelerometer were used. Reallocation of 30 minutes of ST with LIPA was significantly associated with lower <b>waist circumference</b> (regression coefficient = -0.57 [95% CI, -0.86 to -0.27], 5 studies) but not <b>BMI</b> (regression coefficient = -0.010 [95% CI -0.385 to 0.365], 6 studies). Reallocation of 30 minutes of ST with MVPA was significantly associated with <b>waist circumference</b> (regression coefficient = -2.955 [95% CI, -3.878 to -2.032], 5 studies) and <b>BMI</b> (regression coefficient = -0.921 [95% CI, -1.31 to -0.531], 6 studies). After removing one study that was contributing to the statistical heterogeneity of the pooled analysis, the result was no longer statistically significant for the relationship between replacing ST with MVPA and BMI. | VERY LOW <sup>c</sup> |

Abbreviations: BMI = body mass index; CI = confidence interval; hrs = hours; min = minutes; NA = not assessed; OR = odds ratio; RR = risk ratio; ST = sedentary time; TV = television

†Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

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<sup>a</sup> Certainty of evidence downgraded given serious indirectness in measures of sedentary behaviour and serious imprecision in measures of effects

<sup>b</sup> Certainty of evidence downgraded given serious risk of bias; majority of evidence from cross-sectional studies

<sup>c</sup> Certainty of evidence downgraded given serious risk of bias of all included studies and serious inconsistency and imprecision in measures of effects between studies and outcomes

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**Table B.2.f. Physical function: Association between sedentary behaviour and measures of physical function among adults (in alphabetical order by author)**

[See the Supplementary materials](#) for description of evidence and conclusions of US PAGAC (24) by outcome

| Systematic review evidence<br><br>Review credibility | No. of studies/<br>Study design<br><br>No. of participants            | Quality Assessment |                     |                      |                     |       | Description of evidence<br><br>Summary of findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Certainty             |
|------------------------------------------------------|-----------------------------------------------------------------------|--------------------|---------------------|----------------------|---------------------|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
|                                                      |                                                                       | Risk of bias       | Inconsistency       | Indirectness†        | Imprecision         | Other |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                       |
| Mañas 2017 (18)<br><br>Critically Low <sup>a</sup>   | 7 cross-sectional studies, 1 RCT, and 1 pre-post study<br><br>N=2,933 | NR                 | Serious consistency | Serious indirectness | Serious imprecision | None  | Included studies evaluated the relationship between objectively measured sedentary time and measures of physical performance among older adults aged ≥60 years. Measures of physical performance varied widely between studies.<br><br>One RCT found that participants within a sedentary behaviour reduction group (reducing ST by 1-hr each day) had improved <b>SPPB scores</b> over 12 weeks (and no difference was seen among a PA group). One pre-post study found that older adults with overweight or obesity participating in a 8-week intervention to reduce sedentary time had a significant improvement in gait speed, but not chair stands or SPPB scores. Results were mixed in all 7 cross-sectional studies with some showing significant associations between ST and measures of <b>gait speed</b> and <b>SPPB</b> and others reporting no association on other measures of physical performance. | VERY LOW <sup>b</sup> |

Abbreviations: hrs = hours; NR = not reported; PA = physical activity; RCT = randomized clinical trial; SPPB = Short Physical Performance Battery; ST = sedentary time

†Serious indirectness indicates measurement of intermediate/indirect outcomes or heterogeneity in exposures and comparisons assessed; certainty of evidence was not always downgraded for indirectness if it was not judged to impact the certainty in the findings for the outcome evaluated in the review

<sup>a</sup> Review included despite Critically Low credibility rating because it was the only review identified that reported physical function outcomes

<sup>b</sup> Certainty of evidence not upgraded given serious limitations in included evidence and existing systematic review

## APPENDIX A. DATA EXTRACTIONS OF INCLUDED EVIDENCE (IN ALPHABETICAL ORDER BY AUTHOR)

|                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>SR/MA</b><br><b>Citation:</b> Ahmad S, Shanmugasagaram S, Walker KL, Prince SA. Examining sedentary time as a risk factor for cardiometabolic diseases and their markers in South Asian adults: a systematic review. Int J Public Health. 2017 May;62(4):503-515                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Purpose:</b> To systematically review the literature to determine whether sedentary time was associated with cardiometabolic diseases and their risk factors among South Asian adults.                                                                                           | <b>Abstract:</b><br><b>OBJECTIVES:</b><br>The objective was to systematically review the literature to determine whether sedentary time was associated with cardiometabolic diseases and their risk factors among South Asian adults.<br><b>METHODS:</b><br>Six electronic databases were searched to identify all studies that examined the association between sedentary time and cardiometabolic diseases (e.g., diabetes, cardiovascular disease) and their risk factors [e.g., body mass index (BMI), waist circumference (WC), lipids, blood pressure (BP), glucose] among South Asian adults. Two independent reviewers performed abstract/full-text screening, data abstraction, and quality assessments.<br><b>RESULTS:</b><br>Searching identified 1757 potential articles; 22 were used in the analysis. Greater sedentary time was associated with an increased likelihood of diabetes (n = 5), higher BMI (n = 13), WC (n = 3), BP (n = 2), and glucose (n = 4). Thirteen out of 22 studies were of higher quality.<br><b>CONCLUSION:</b><br>Results identified a trend whereby greater sedentary time was associated with an increased risk for diabetes, and several other cardiometabolic risk factors among South Asian adults. High quality studies are needed to identify whether risk factors are independent of physical activity levels to inform culturally-specific interventions for South Asians. |
| <b>Timeframe:</b> N/A                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Total # studies included:</b> 22 (one prospective study on incident diabetes)                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Other details (e.g. definitions used, exclusions etc)</b> studies in South East Asian adults included. Results from one prospective study indicating 84% higher risk for developing diabetes in top vs bottom quartile for sedentary time. No dose-response and no meta-analysis |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Outcomes addressed:</b> Type 2 diabetes and CVD risk factors                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |

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|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>SR</b><br><b>Citation:</b> Al Tunaiji H, Davis JC, Mansournia MA, Khan KM. Population attributable fraction of leading non-communicable cardiovascular diseases due to leisure-time physical inactivity: a systematic review. <i>BMJ Open Sport Exerc Med.</i> 2019 Apr 9;5(1):e000512. doi: 10.1136/bmjsem-2019-000512. eCollection 2019. PMID: 31191969. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <b>Purpose:</b> To summarize available estimations of the PAF of leisure-time physical inactivity in relation to coronary artery disease, hypertension and stroke.                                                                                                                                                                                            | <b>Abstract:</b> Objective: The aim of this systematic review was to investigate the methods used for estimating the population attributable fraction (PAF) to leisure-time physical inactivity (PI) of coronary artery diseases, hypertension and stroke in order to provide the best available estimate for PAF. Design: Systematic review. Data sources: Four electronic databases (MEDLINE/PubMed, EMBASE, SPORTDiscus, and Cumulative Index to Nursing and Allied Health Literature) were searched from inception to August 2018. Eligibility criteria for selecting studies: This review included prospective cohort studies, with men and women aged ≥18 years old, investigating the PAF attributable to leisure-time PI related to coronary artery diseases, hypertension and stroke. Results: The PAF estimates of the three studies included were 13% (3%–22%) for ‘stage-1 hypertension’ subtype incidence due to ‘non-regular exercise’; 25% (10.4%–35.8%) for ‘stage-2 hypertension’ subtype incidence due to ‘activity of daily living’ and ‘vigorous-intensity sports’; and 8.5% (1.7%–16.7%) for ‘total: fatal and non- fatal’ cardiovascular events of ‘incidence and mortality’ endpoints due to non-accumulation of 550 kcal/week (subsets not specified). Conclusions: The PAF estimate exhibited a protective dose–response relationship between hypertension and an increased amount of energy expenditure of leisure-time PI. In order to enhance accuracy of PAF estimates, the following steps are recommended: (1) to clearly define and state the working definition of leisure-time PI and dose using a reliable and valid objective measurement tool; (2) use a clear definition of outcome subtypes and endpoints using reliable and valid objective measures; and (3) estimate PAF using modelling techniques based on prospective data and ensuring to report 95% CI. |
| <b>Timeframe:</b> Inception to August 2018.                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <b>Total # studies included:</b> 3                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <b>Other details (e.g. definitions used, exclusions etc)</b> Exclusion criteria: no PAF estimate; no use of an exposure related to leisure-time PI; no prospective study design.                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <b>Outcomes addressed:</b> Coronary artery disease, hypertension and stroke.                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

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| <b>SR/MA</b>                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| <b>Citation:</b> Bailey DP, Hewson DJ, Champion RB, Sayegh SM. Sitting time and risk of cardiovascular disease and diabetes: a systematic review and meta-analysis. American journal of preventive medicine. 2019 Aug 1. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| <b>Purpose: Sitting time and CVD and Diabetes</b>                                                                                                                                                                        | <p><b>Abstract:</b> Context: Whether physical activity attenuates the association of total daily sitting time with cardiovascular disease and diabetes incidence is unclear. This systematic review and meta-analysis examined the association of total daily sitting time with cardiovascular disease and diabetes with and without adjustment for physical activity.</p> <p>Evidence acquisition: PubMed, Web of Science, BASE, MEDLINE, Academic Search Elite, and ScienceDirect were searched for prospective studies, published between January 1, 1989, and February 15, 2019, examining the association of total daily sitting time with cardiovascular disease or diabetes outcomes. Data extraction and study quality assessments were conducted by 2 independent reviewers. Pooled hazard ratios (HRs) were calculated using a fixed-effects model. The quality assessment and meta-analysis procedures were completed in 2018.</p> <p>Evidence synthesis: Nine studies with 448,285 participants were included. A higher total daily sitting time was associated with a significantly increased risk of cardiovascular disease (HR=1.29, 95% CI=1.27, 1.30, p&lt;0.001) and diabetes (HR=1.13, 95% CI=1.04, 1.22, p&lt;0.001) incidence when not adjusted for physical activity. The increased risk for diabetes was unaffected when adjusting for physical activity (HR=1.11, 95% CI=1.01, 1.19, p&lt;0.001). For cardiovascular disease, the increased risk was attenuated but remained significant (HR=1.14, 95% CI=1.04, 1.23, p&lt;0.001).</p> <p>Conclusions: Higher levels of total daily sitting time are associated with an increased risk of cardiovascular disease and diabetes, independent of physical activity. Reductions in total daily sitting may be recommended in public health guidelines. Am J Prev Med 2019;57(3):408–416. © 2019 American Journal</p> |
| <b>Timeframe: Jan 1989 to Feb 2019</b>                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| <b>Total # studies included: 9</b>                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| <b>Other details (e.g. definitions used, exclusions etc)</b>                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| <b>Outcomes addressed: Incidence of CVD Incidence of Diabetes</b>                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |

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| <b>SR/MA</b><br><b>Citation:</b> Berger FF, Leitzmann MF, Hillreiner A, Sedlmeier AM, Prokopidi-Danisch ME, Burger M, Jochem C. Sedentary Behaviour and Prostate Cancer: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. Cancer Prev Res (Phila). 2019 Oct;12(10):675-688. doi: 10.1158/1940-6207.CAPR-19-0271. Epub 2019 Jul 30. PMID: 31362941. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Purpose:</b> To examine sedentary behaviour and total, advanced, and fatal prostate cancer with particular attention paid to aggressive prostate cancer because obesity (a correlate of SB) is linked to advanced prostate cancer only.                                                                                                                             | <b>Abstract:</b> Prostate cancer is the second most common cancer in men worldwide, and sedentary behaviour is widespread, yet reviews and meta-analyses summarizing the role of sedentary behaviour as a potential risk factor for prostate cancer are scarce. We searched PubMed, Web of Science, and Cochrane databases for relevant articles up to January 2019. We pooled maximally adjusted risk estimates in a random effects model and performed meta-regression meta-analysis, assessed heterogeneity and publication bias using $I^2$ , funnel plots, Egger's and Begg's tests, and conducted sensitivity analyses and influence diagnostics. Data from 12 prospective cohort studies including a total of 30,810 prostate cancer cases were analyzed. We found no statistically significant association between high versus low sedentary behaviour and prostate cancer incidence (relative risk (RR)=1.07, 95% confidence interval (CI)=0.99-1.16, P=0.10). We noted that adjustment for body mass index (BMI) modified the relation of sedentary behaviour to prostate cancer, particularly aggressive cancer. Sedentary behaviour was related to a statistically significant increased risk of aggressive prostate cancer in analyses not adjusted for BMI (RR=1.21, 95% CI=1.03-1.43), whereas no association was apparent in BMI-adjusted analyses (RR=0.98, 95% CI=0.90-1.07), and the difference between those summary risk estimates was statistically significant (P(difference)=0.02). Sedentary behaviour is not independently associated with prostate cancer. However, prolonged sedentary behaviour may be related to increased risk of aggressive prostate cancer through a mechanism involving obesity. This finding represents a potentially important step towards considering sedentary behaviour as a modifiable behavioural risk factor for aggressive prostate cancer. |
| <b>Timeframe:</b> Inception to January 2019                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Total # studies included:</b> 12                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Other details (e.g. definitions used, exclusions etc)</b> Inclusion criteria included use of total daily sitting time or sedentary behaviours during occupation, leisure time, or transportation as exposure variables.                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Outcomes addressed:</b> Incidence of total prostate cancer and aggressive prostate cancer (the latter includes prostate cancer mortality)                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |

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| <b>SR/MA</b><br><b>Citation:</b> Chan DS, Abar L, Cariolou M, Nanu N, Greenwood DC, Bandera EV, McTiernan A, Norat T. World Cancer Research Fund International: Continuous Update Project—systematic literature review and meta-analysis of observational cohort studies on physical activity, sedentary behavior, adiposity, and weight change and breast cancer risk. <i>Cancer Causes &amp; Control</i> . 2019 Aug 30:1-8. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Purpose: Incidence of breast cancer</b>                                                                                                                                                                                                                                                                                                                                                                                    | <b>Abstract:</b><br><b>Purpose</b> The purpose of the present study was to systematically review the complex associations between energy balance related factors and breast cancer risk, for which previous evidence has suggested different associations in the life course of women and by hormone receptor (HR) status of the tumour.<br><b>Methods</b> Relevant publications on adulthood physical activity, sedentary behaviour, body mass index (BMI), waist and hip circumferences, waist-to-hip ratio, and weight change and pre- and postmenopausal breast cancer risk were identified in PubMed up to 30 April 2017. Random-effects meta-analyses were conducted to summarize the relative risks across studies.<br><b>Results</b> One hundred and twenty-six observational cohort studies comprising over 22,900 premenopausal and 103,000 postmenopausal breast cancer cases were meta-analyzed. Higher physical activity was inversely associated with both pre- and postmenopausal breast cancers, whereas increased sitting time was positively associated with postmenopausal breast cancer.<br>Although higher early adult BMI (ages 18–30 years) was inversely associated with pre- and postmenopausal breast cancers, adult weight gain and greater body adiposity increased breast cancer risk in postmenopausal women, and the increased risk was evident for HR+ but not HR– breast cancers, and among never but not current users of postmenopausal hormones. The evidence was less consistent in premenopausal women. There were no associations with adult weight gain, inverse associations with adult BMI (study baseline) and hip circumference, and non-significant associations with waist circumference and waist-to-hip ratio that were reverted to positive associations on average in studies accounting for BMI. No significant associations were observed for HR-defined premenopausal breast cancers.<br><b>Conclusion</b> Better understanding on the impact of these factors on pre- and postmenopausal breast cancers and their subtypes along the life course is needed. |
| <b>Timeframe: inception to Apr 2017</b>                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Total # studies included: 126</b>                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Other details (e.g. definitions used, exclusions etc) mixture of physical activity, sedentary, and diet studies</b>                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Outcomes addressed: Incidence of breast cancer</b>                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

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| <b>MA</b><br><b>Citation:</b> Del Pozo-Cruz J, García-Hermoso A, Alfonso-Rosa RM, Alvarez-Barbosa F, Owen N, Chastin S, Del Pozo-Cruz B. Replacing Sedentary Time: Meta-analysis of Objective-Assessment Studies. Am J Prev Med. 2018 Sep;55(3):395-402. doi: 10.1016/j.amepre.2018.04.042. PMID: 30122216. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Purpose:</b> To examine replacing time spent sedentary with physical activity in relation to cardiometabolic risk markers and all-cause mortality using device-based measurement.                                                                                                                        | <b>Abstract:</b> Context: The aim was to summarize estimates of the potential benefits for cardiometabolic risk markers and all-cause mortality of replacing time spent in sedentary behaviours with light-intensity physical activity or with moderate to vigorous physical activity, from studies using device-based measurement. Evidence acquisition: Four databases covering the period up to December 2016 were searched and analyzed (February 2017). Data were extracted by two independent reviewers. For the meta- analyses, the estimated regression coefficients (b) and 95% CIs were analyzed for BMI, waist circumference, and high-density lipoprotein cholesterol. Pooled relative rate and 95% CIs were calculated for fasting glucose, fasting insulin, and homeostatic model assessment-insulin resistance values.                                                                                                                                                                                                                                                                                                                                                          |
| <b>Timeframe:</b> Inception to December 2016.                                                                                                                                                                                                                                                               | Hazard ratios were extracted from studies of all-cause mortality risk.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Total # studies included:</b> 10                                                                                                                                                                                                                                                                         | Evidence synthesis: Ten studies (with 17,390 participants) met the inclusion criteria. Reallocation of 30 minutes of sedentary time to light-intensity physical activity was associated with reductions in waist circumference, fasting insulin, and all-cause mortality risk; and with an increase in high-density lipoprotein cholesterol. Reallocating 30 minutes of sedentary time to moderate to vigorous physical activity was associated with reductions in BMI, waist circumference, fasting glucose, fasting insulin, and all-cause mortality (not pooled) and with an increase in high-density lipoprotein cholesterol. Conclusions: Replacing sedentary time with either light-intensity physical activity or moderate to vigorous physical activity may be beneficial, but when sedentary time is replaced with moderate to vigorous physical activity, the predicted impacts are stronger and apparent for a broader range of risk markers. These findings point to potential benefits of replacing sedentary time with light-intensity physical activity, which may benefit those less able to tolerate or accommodate higher-intensity activities, including many older adults. |
| <b>Other details (e.g. definitions used, exclusions etc)</b> Inclusion criteria: reported objective measure of activity and sedentary behaviour; used isotemporal models of the effects of replacing sedentary behaviour with LIPA or MVPA on at least one cardiometabolic factor or mortality.             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Outcomes addressed:</b> BMI, waist circumference, fasting glucose, fasting insulin, high-density lipoprotein, and all-cause mortality.                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

**SR/MA**

**Citation:** Ekelund U, Tarp J, Steene-Johannessen J, Hansen BH, Jefferis B, Fagerland MW, Whincup P, Diaz KM, Hooker SP, Chernofsky A, Larson MG. Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. *bmj*. 2019 Aug 21;366:l4570. <https://doi.org/10.1136/bmj.l4570>

**Purpose:** to examine the association between accelerometer measured physical activity and sedentary time and all-cause mortality.

**Abstract:**

**Objective:** To examine the dose-response associations between accelerometer assessed total physical activity, different intensities of physical activity, and sedentary time and all cause mortality.

**Design:** Systematic review and harmonised meta-analysis.

**Data sources:** PubMed, PsycINFO, Embase, Web of Science, Sport Discus from inception to 31 July 2018.

**Eligibility criteria:** Prospective cohort studies assessing physical activity and sedentary time by accelerometry and associations with all cause mortality and reported effect estimates as hazard ratios, odds ratios, or relative risks with 95% confidence intervals.

**Data extraction and analysis:** Guidelines for meta-analyses and systematic reviews for observational studies and PRISMA guidelines were followed. Two authors independently screened the titles and abstracts. One author performed a full text review and another extracted the data. Two authors independently assessed the risk of bias. Individual level participant data were harmonised and analysed at study level. Data on physical activity were categorised by quarters at study level, and study specific associations with all cause mortality were analysed using Cox proportional hazards regression analyses. Study specific results were summarised using random effects meta-analysis.

**Main outcome measure:** All-cause mortality.

**Results:** 39 studies were retrieved for full text review; 10 were eligible for inclusion, three were excluded owing to harmonisation challenges (eg, wrist placement of the accelerometer), and one study did not participate. Two additional studies with unpublished mortality data were also included. Thus, individual level data from eight studies (n=36 383; mean age 62.6 years; 72.8% women), with median follow-up of 5.8 years (range 3.0-14.5 years) and 2149 (5.9%) deaths were analysed. Any physical activity, regardless of intensity, was associated with lower risk of mortality, with a non-linear dose-response. Hazards ratios for mortality were 1.00 (referent) in the first quarter (least active), 0.48 (95% confidence interval 0.43 to 0.54) in the second quarter, 0.34 (0.26 to 0.45) in the third quarter, and 0.27 (0.23 to 0.32) in the fourth quarter (most active). Corresponding hazards ratios for light physical activity were 1.00, 0.60 (0.54 to 0.68), 0.44 (0.38 to 0.51), and 0.38 (0.28 to 0.51), and for moderate-to-vigorous physical activity were 1.00, 0.64 (0.55 to 0.74), 0.55 (0.40 to 0.74), and 0.52 (0.43 to 0.61). For sedentary time, hazards ratios were 1.00 (referent; least sedentary), 1.28 (1.09 to 1.51), 1.71 (1.36 to 2.15), and 2.63 (1.94 to 3.56).

**Conclusion**

Higher levels of total physical activity, at any intensity, and less time spent sedentary, are associated with substantially reduced risk for premature mortality, with evidence of a non-linear dose-response pattern in middle aged and older adults.

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| <b>SR/MA</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Citation:</b> Ekelund U, Brown WJ, Steene-Johannessen J, Fagerland MW, Owen N, Powell KE, Bauman AE, Lee IM. Do the associations of sedentary behaviour with cardiovascular disease mortality and cancer mortality differ by physical activity level? A systematic review and harmonised meta-analysis of data from 850 060 participants. British Journal of Sports Medicine. 2019 Jul 1;53(14):886-94. <a href="https://doi.org/10.1136/bjsports-2017-098963">https://doi.org/10.1136/bjsports-2017-098963</a> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Purpose:</b> to examine whether these modifying effects of physical activity exist for relationships between sitting and cause-specific mortality                                                                                                                                                                                                                                                                                                                                                               | <b>Abstract:</b><br>Objective To examine whether the associations between sedentary behaviours (ie, daily sitting/TVviewing time) and mortality from cardiovascular disease (CVD) and cancer differ by different levels of physical activity (PA). Design Harmonised meta-analysis of prospective cohort studies. Data on exposure variables were harmonised according to a predefined protocol and categorised into four groups for sedentary behaviours and into quartiles of PA (MET-hour/week). Data sources PubMed, PsycINFO, Embase, Web of Science, Sport Discus and Scopus.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Timeframe:</b> inception to 10 Nov 2014                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Eligibility criteria for selecting studies Individual level data on both sedentary behaviours and PA and reported effect estimates for CVD or cancer mortality.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Total # studies included: 14 prospective cohort studies</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Results Nine studies (n=850 060; deaths=25 730) and eight studies (n=777 696; deaths=30 851) provided data on sitting time and CVD and cancer mortality, respectively. Five studies had data on TV-viewing time and CVD (n=458 127; deaths=13 230) and cancer (n=458 091; deaths=16 430) mortality. A dose-response association between sitting time (9%–32% higher risk; p for trend <0.001) and TV time (3%–59% higher risk; p for trend <0.001) with CVD mortality was observed in the 'inactive', lowest quartile of PA. Associations were less consistent in the second and third quartiles of PA, and there was no increased risk for CVD mortality with increasing sedentary behaviours in the most active quartile. Associations between sedentary behaviours and cancer mortality were generally weaker; 6%–21% higher risk with longer sitting time observed only in the lowest quartile of PA. Conclusion PA modifies the associations between sedentary behaviours and CVD and cancer mortality. These findings emphasise the importance of higher volumes of moderate and vigorous activity to reduce, or even eliminate these risks, especially for those who sit a lot in their daily lives. |
| <b>Other details (e.g. definitions used, exclusions etc)</b> In the end, only subjective measures were included. Sitting exposures distinguished sitting time or TV time.                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Outcomes addressed:</b> CVD mortality, cancer mortality                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |

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| <b>SR/MA</b><br><b>Citation:</b> Ku PW, Steptoe A, Liao Y, Hsueh MC, Chen LJ. A cut-off of daily sedentary time and all-cause mortality in adults: a meta-regression analysis involving more than 1 million participants. BMC medicine. 2018 Dec;16(1):74. <a href="https://doi.org/10.1186/s12916-018-1062-2">https://doi.org/10.1186/s12916-018-1062-2</a> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <b>Purpose:</b> to explore the cut-off duration associated with elevating the risk of all-cause mortality.                                                                                                                                                                                                                                                   | <b>Abstract:</b><br>Background: The appropriate limit to the amount of daily sedentary time (ST) required to minimize mortality is uncertain. This meta-analysis aimed to quantify the dose-response association between daily ST and all-cause mortality and to explore the cut-off point above which health is impaired in adults aged 18–64 years old. We also examined whether there are differences between studies using self-report ST and those with device-based ST.                                                              |
| <b>Timeframe:</b> inception to 31 Jan 2018                                                                                                                                                                                                                                                                                                                   | Methods: Prospective cohort studies providing effect estimates of daily ST (exposure) on all-cause mortality (outcome) were identified via MEDLINE, PubMed, Scopus, Web of Science, and Google Scholar databases until January 2018. Dose-response relationships between daily ST and all-cause mortality were examined using random-effects meta-regression models.                                                                                                                                                                       |
| <b>Total # studies included: 19 cohort studies</b>                                                                                                                                                                                                                                                                                                           | Results: Based on the pooled data for more than 1 million participants from 19 studies, the results showed a log-linear dose-response association between daily ST and all-cause mortality. Overall, more time spent in sedentary behaviours is associated with increased mortality risks. However, the method of measuring ST moderated the association between daily ST and mortality risk ( $p < 0.05$ ). The cut-off of daily ST in studies with self-report ST was 7 h/day in comparison with 9 h/day for those with device-based ST. |
| <b>Other details (e.g. definitions used, exclusions etc) included only with PA adjustment.</b>                                                                                                                                                                                                                                                               | Conclusions: Higher amounts of daily ST are log-linearly associated with increased risk of all-cause mortality in adults. On the basis of a limited number of studies using device-based measures, the findings suggest that it may be appropriate to encourage adults to engage in less sedentary behaviours, with fewer than 9 h a day being relevant for all-cause mortality                                                                                                                                                            |
| <b>Outcomes addressed:</b> all-cause mortality                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

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| <b>SR/MA</b>                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Citation:</b> Ku PW, Steptoe A, Liao Y, Hsueh MC, Chen LJ. A Threshold of Objectively-Assessed Daily Sedentary Time for All-Cause Mortality in Older Adults: A Meta-Regression of Prospective Cohort Studies. Journal of clinical medicine. 2019 Apr;8(4):564. <a href="https://doi.org/10.3390/jcm8040564">https://doi.org/10.3390/jcm8040564</a> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Purpose:</b> to explore the dose-response relationship between daily ST and all-cause mortality in older adults.                                                                                                                                                                                                                                   | <b>Abstract:</b><br>Background: This meta-analysis aimed to estimate the shape of the dose-response association between objectively-assessed daily sedentary time (ST) and all-cause mortality, and to explore whether there is a threshold of ST above which there is an increase in mortality risk in older adults.<br>Methods:<br>Searches for prospective cohort studies providing effect estimates of daily ST (exposure) on all-cause mortality (outcome) were undertaken in five databases up to 31 March 2019. A random-effects meta-regression model was conducted to quantify the dose-response relationship between daily ST and all-cause mortality. Sensitivity analyses were also performed to test the stability of the results.<br>Results: Our analysis of pooled data from 11 eligible studies did not reveal a consistent shape of association between ST and mortality. After excluding three studies with potential confounding bias, there was a log-linear dose-response relationship between daily ST and all-cause mortality. Overall, higher amounts of time spent in sedentary behaviours were associated with elevated mortality risks in older adults. Visual assessments of dose-response relationships based on meta-regression analyses indicated that increased mortality risks became significant when total ST exceeded approximately 9 h/day.<br>Conclusions: Based on a limited number of studies, this meta-analysis provides a starting point for considering a cut-off daily sedentary time, suggesting older adults spend less time in daily sitting. |
| <b>Timeframe:</b> inception to 31 March 2019                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Total # studies included:</b> 11 cohort studies                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Other details</b> (e.g. definitions used, exclusions etc) healthy aged 65 or above; included only with device-based measures.                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Outcomes addressed:</b> all-cause mortality                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

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| <b>SR/MA</b><br><b>Citation:</b><br>S. Mahmood; R. J. MacInnis; D. R. English; A. Karahalios; B. M. Lynch. Domain-specific physical activity and sedentary behaviour in relation to colon and rectal cancer risk: a systematic review and meta-analysis. Int J Epidemiol. 2017 Dec 1;46(6):1797-1813. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>Purpose:</b> to examine the associations between physical activity, sedentary behaviour and the risk of colon and rectal cancers separately for occupational, recreational, transport and household domains                                                                                        | <b>Abstract:</b><br>Background: Physical activity is associated with reduced risk of colorectal cancer, but most epidemiological studies have focused on occupational and recreational physical activity. The evidence for other domains of activity, and for sedentary behaviour, is limited. Methods: Medline, Embase and Web of Science were searched from inception to December 2015 for studies examining domain-specific physical activity or sedentary behaviour and the risk of colon and/or rectal cancer. We extracted maximally adjusted relative risks (RRs) except when RRs not adjusted for body mass index, were also presented. We used random-effects meta-analysis to compute pooled RRs comparing the highest versus the lowest level of exposure. We used meta-regression to assess sources of heterogeneity in estimates. Results: We identified 17 cohort and 21 case-control studies, of which 17 had occupational data, 23 had recreational data, three each had data on transport and household physical activity domains, and 6 studies had data on occupational sedentary behaviour. The pooled relative risks (RRs) for colon cancer were 0.74 (95% confidence interval (CI): 0.67, 0.82) for occupational activity, 0.80 (95% CI: 0.71, 0.89) for recreational activity, 0.66 (95% CI: 0.45, 0.98) for transport-related physical activity, 0.85 (95% CI: 0.71, 1.02) for household physical activity, and 1.44 (95% CI: 1.28, 1.62) for occupational sedentary behaviour. For rectal cancer, the pooled RRs were 0.88 (95% CI: 0.79, 0.98) for occupational activity, 0.87 (95% CI: 0.75, 1.01) for recreational activity, 0.88 (95% CI: 0.70, 1.12) for transport-related physical activity, 1.01 (95% CI: 0.80, 1.27) for household physical activity, and 1.02 (95% CI: 0.82, 1.28) for occupational sedentary behaviour. Conclusions: In addition to increasing occupational and recreational physical activity, promoting physical activity during transport and reducing sedentary behaviour in the workplace may also be useful colorectal cancer prevention strategies. |
| <b>Timeframe:</b> Inception to 31 December 2015                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>Total # studies included:</b> 38 (6 studies on occupational sedentary behaviours)                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>Other details (e.g. definitions used, exclusions etc)</b> Cohort and case-control studies included that specifically examined domain specific behaviours; Six studies of interest for sedentary behaviour; data reported as comparing the highest vs lowest category. No dose-response             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>Outcomes addressed:</b><br>Colorectal cancer                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

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| <b>SR &amp; MA</b><br><b>Citation:</b> Patterson R, McNamara E, Tainio M, de Sá TH, Smith AD, Sharp SJ, Edwards P, Woodcock J, Brage S, Wijndaele K. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. Eur J Epidemiol. 2018 Sep;33(9):811-829. doi: 10.1007/s10654-018-0380-1. Epub 2018 Mar 28. PMID: 29589226. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Purpose:</b> To examine the relation of sedentary behaviour to all-cause mortality, cardiovascular disease mortality and cancer mortality, and incident type 2 diabetes                                                                                                                                                                                                                                                         | <b>Abstract:</b> Purpose: To estimate the strength and shape of the dose–response relationship between sedentary behaviour and all-cause, cardiovascular disease (CVD) and cancer mortality, and incident type 2 diabetes (T2D), adjusted for physical activity (PA). Data Sources: Pubmed, Web of Knowledge, Medline, Embase, Cochrane Library and Google Scholar (through September-2016); reference lists. Study Selection: Prospective studies reporting associations between total daily sedentary time or TV viewing time, and C one outcome of interest. Data Extraction: Two independent reviewers extracted data, study quality was assessed; corresponding authors were approached where needed. Data Synthesis: Thirty-four studies (1,331,468 unique participants; good study quality) covering 8 exposure–outcome combinations were included. For total sedentary behaviour, the PA-adjusted relationship was non-linear for all-cause mortality (RR per 1 h/day: were 1.01 (1.00–1.01) B 8 h/day; 1.04 (1.03–1.05)[8 h/day of exposure), and for CVD mortality (1.01 (0.99–1.02) B 6 h/day; 1.04 (1.03–1.04)[6 h/day). The association was linear (1.01 (1.00–1.01)) with T2D and non-significant with cancer mortality. Stronger PA-adjusted associations were found for TV viewing (h/day); non-linear for all-cause mortality (1.03 (1.01–1.04) B 3.5 h/day; 1.06 (1.05–1.08)[3.5 h/day) and for CVD mortality (1.02 (0.99–1.04) B 4 h/day; 1.08 (1.05–1.12)[4 h/day). Associations with cancer mortality (1.03 (1.02–1.04)) and T2D were linear (1.09 (1.07–1.12)). Conclusions: Independent of PA, total sitting and TV viewing time are associated with greater risk for several major chronic disease outcomes. For all-cause and CVD mortality, a threshold of 6–8 h/day of total sitting and 3–4 h/day of TV viewing was identified, above which the risk is increased. |
| <b>Timeframe:</b> Inception to September 2016                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Total # studies included:</b> 34                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Other details (e.g. definitions used, exclusions etc)</b> Analyses of dose–response associations and for different types of sedentary behaviour. Also, dose–response curves with and without adjustment for PA were compared. In addition, PAFs were calculated.                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Outcomes addressed:</b> All-cause mortality, cardiovascular disease mortality, cancer mortality, and type 2 diabetes incidence.                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

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| <b>SR/MA</b><br><b>Citation:</b><br>J. Wang; L. Huang; Y. Gao; Y. Wang; S. Chen; J. Huang; W. Zheng; P. Bao; Y. Gong; Y. Zhang; M. Wang; M. C. S. Wong. Physically active individuals have a 23% lower risk of any colorectal neoplasia and a 27% lower risk of advanced colorectal neoplasia than their non-active counterparts: systematic review and meta-analysis of observational studies. Br J Sports Med Epub ahead of print: [please include Day Month Year]. doi:10.1136/bjsports-2018-100350 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>Purpose:</b> Examine the associations between physical activity (PA), sedentary behaviour (SB) and risk of colorectal neoplasia (CN).                                                                                                                                                                                                                                                                                                                                                               | <b>Abstract:</b><br>BACKGROUND: Few studies have examined the associations between physical activity (PA), sedentary behaviour (SB) and risk of colorectal neoplasia (CN). METHODS: We systematically searched Medline, Embase, PsylInfo, Cochrane and other sources from their inception to 30 September 2018 for cohort, case-control and cross-sectional studies that evaluated these associations in asymptomatic, average-risk subjects. Random-effect models were used to estimate relative risks (RRs) of any-type CN, advanced CN, and non-advanced CN, respectively, in individuals with the highest versus the lowest level of PA and SB. Dose-response analyses and subgroup analyses were conducted. The I(2) statistic was used to examine heterogeneity among studies. RESULTS: We identified 32 observational studies, including 17 cross-sectional studies, 10 case-control studies and five longitudinal studies. PA (highest vs lowest) was inversely associated with risk for any-type CN (n=23 studies) and advanced CN (n=15 studies), with a RR of 0.77 (95% CI=0.71 to 0.83, I(2)=57.5%) and 0.73 (95% CI=0.63 to 0.82, I(2)=45.5%), respectively. There was no association between PA and non-advanced CN (n=5 studies). There was an association between PA and any-type CN in both sexes, and also for the distal colon. We found no dose-response relationship between PA and any-type or advanced CN. Based on three studies identified, SB time (longest vs shortest) was associated with an increased risk of advanced CN (RR=1.24, 95% CI 1.04 to 1.49, I(2)=14.4%). No publication bias was detected by Begg's test. CONCLUSION: We report a 23% lower relative risk of any type of CN and a 27% lower risk of advanced CN in people with the highest level of PA compared with those in the lowest. |
| <b>Timeframe:</b> Inception to 30 September 2018                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>Total # studies included:</b> 32 including 17 cross-sectional studies, 10 case-control studies and five longitudinal studies (3 studies on sedentary)                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>Other details (e.g. definitions used, exclusions etc)</b> Three studies reported data on sedentary behaviours and colorectal neoplasia (potential for overlap between two of these studies derived from the same cohort). meta-analysis of three studies. Comparator unclear and no dose-response reported                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>Outcomes addressed:</b> colorectal neoplasia                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |

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| <b>Harmonized MA</b><br><b>Citation:</b> Xu C, Furuya-Kanamori L, Liu Y, Færch K, Aadahl M, A Seguin R, LaCroix A, Basterra-Gortari FJ, Dunstan DW, Owen N, Doi SAR. Sedentary Behavior, Physical Activity, and All-Cause Mortality: Dose-Response and Intensity Weighted Time-Use Meta-analysis. J Am Med Dir Assoc. 2019 Oct;20(10):1206-1212.e3. doi: 10.1016/j.jamda.2019.05.001. Epub 2019 Jul 2. PMID: 31272857. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>Purpose:</b> To examine whether sedentary behaviour-related mortality risk can be offset by MVPA considered in a time-use fashion.                                                                                                                                                                                                                                                                                  | <b>Abstract:</b> Objectives: Previous studies have placed those with excessive sedentary behavior at increased risk of all-cause mortality. There is evidence of interdependency of sedentary behaviour with physical activity, and its elucidation will have implications for guidelines and practice. This study investigated if sedentary behaviour-related mortality risk can be offset by moderate-to vigorous-intensity physical activity (MVPA) considered in a time-use fashion. Design: PubMed was searched (from its inception till May 2018) for studies or meta-analyses that used data harmonized for MVPA. Of the 17 data-custodians located, 7 provided data on sitting time or TV viewing time, or both. A dose-response meta-analysis modelling log relative risks of all-cause mortality against uncompensated sedentary behaviour metabolic equivalent hours (USMh) was run using the robust error meta-regression method. (Registration: CRD42017062439) Setting: Individual subject data held by data custodians on this topic. Participants: General adults. Measurements: Sedentary time, MVPA. Results: Five harmonized cohorts of sitting time (258,688 participants) and 4 of TV viewing time (156,593 participants) demonstrated that sedentary behaviour was significantly associated with mortality, but this risk was attenuated with increasing energy expenditure through MVPA modelled in a time-use fashion. The average increment in mortality per USMh spent on sitting was 1% [relative risk (RR) 1.01, 95% confidence interval (CI) 1.00, 1.02; P=.01] and that per USMh spent on TV viewing was 7% (RR 1.07, 95% CI 1.04, 1.10; P < .001). The thresholds for risk started at 7 USMh for sitting and 3 USMh for TV viewing. Conclusions/Implications: Our findings suggest that overall daily sitting time energy expenditure of 7 MET-hours (or TV viewing of 3 MET-hours) in excess of that expended on MVPA is independently related to all-cause mortality. These findings support the view that sitting is strongly influenced by consideration of concurrent MVPA in its impact on adverse health consequences and that the USMh is a more practical metric of sedentary behaviour. |
| <b>Timeframe:</b> Inception to May 2018                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>Total # studies included:</b> 9                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>Other details (e.g. definitions used, exclusions etc)</b> Use of harmonized data from the authors of the cohort studies included in the 2016 Lancet meta-analysis by Ekelund et al.                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>Outcomes addressed:</b> Total mortality                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

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