Should leisure-time sedentary behavior be replaced with sleep or physical activity for prevention of diabetes?

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Working title:

Should leisure time sedentary behaviour be replaced with sleep or physical activity for prevention of diabetes? - prospective isotemporal substitution analyses in 87,339 Danish adults
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ABSTRACT (247 WORDS)
The aim was to examine the effects of replacing self-reported leisure time sedentary behaviour with sleep, light-to-moderate, or vigorous physical activity on incident diabetes among Danish adults using isotemporal substitution modeling.
Participants ≥ 25 years from the Danish Capital Region Health Survey 2007 (N=69,800, response rate 52.3%), 2010 (N=95,150, response rate 52.3%) and 2013 (N=95,150, response rate 43.5%) were included. Information on daily sleep duration, leisure time sedentary behaviour and movement behaviours was...
collected by questionnaire. Information on incident diabetes was obtained from National registers. Analyses included Cox proportional hazards regression models and isotemporal substitution analyses, with time (in years) from baseline to incident diabetes or censoring 31 December 2017. Potential confounders, sex, age, BMI, ethnicity, education, smoking, inflammatory joint disease, perceived stress, physical and mental component scale and work status, — were included.

Out of N=87,339 in the final study sample, n=3,007 had incident diabetes during a mean follow-up time of 7.4 years. Adults with incident diabetes included more men, higher mean age, and higher BMI, compared to respondents without incident diabetes. Theoretically substituting 30 minutes of leisure time sedentary behaviour with light-to-moderate PA (HR 0.96, 95%CI 0.94; 0.98) or with vigorous PA (HR 0.82, 95%CI 0.72; 0.94) decreased the risk of incident diabetes. We found no change in incident diabetes risk of substituting sedentary time with sleep (HR 1.00 95%CI 0.97;1.02).

Substituting 30 min per day of leisure time sedentary behaviour with light-to-moderate or vigorous PA, may significantly reduce the risk of incident diabetes among adults.

**Keywords:** Sedentary behaviour, Sitting time, Physical Behaviour, Incident diabetes, Isotemporal substitution, Longitudinal study, Public Health.

**INTRODUCTION**

Sedentary behaviour has been detrimentally associated with markers of cardiometabolic risk in observational studies, but it remains controversial to what extent sedentary behavior is linked to incident diabetes. In cross-sectional studies using self-reported (1) or accelerometer-assessed (2, 3) measurement of sitting time, leisure time sitting time has been associated with poor metabolic health, especially if sitting time was accumulated in uninterrupted bouts (4). Meta-analyses of cross-sectional and prospective epidemiological studies using self-reported TV-viewing as a proxy measure of sedentary behavior (5-7) have shown modest, but statistically significant positive associations with risk of type 2 diabetes (5-7). Likewise, recent cohort studies found a detrimental effect of self-reported total sitting time on incident
Previous studies have typically included a measure of moderate-to-vigorous physical activity (MVPA) as a co-variate, in order to adjust for the potential confounding effect of MVPA in the association between sedentary behavior and diabetes (1-4, 8, 9). Adjusting for MVPA when exploring the effect of sitting time on health outcomes, implies that potential health effects of sitting time and MVPA are regarded as independent factors. While in fact, sedentary behavior, physical activity and sleep should be examined from an integrated perspective, as these behaviors are by default interdependent within a confined time frame (10). From a public health perspective this approach makes good sense, as reduction of one type of behavior must necessarily be followed by an increase in some other type of behavior. Therefore, when public health guidelines recommend people to “sit less” for health benefits, information on which specific behavior sitting should be substituted with should also be included, e.g. “move more” (11). Isotemporal substitution modeling (ISM), estimates the health effects of theoretical time substitution, taking this interdependency of behaviours into account (12). However, as pointed out in a recent scoping review (13), no studies have examined the prospective relationship between sedentary behavior and incident diabetes using ISM. A few cross-sectional studies have found beneficial ISM substitution effects on prevalence of type 2 diabetes and cardio metabolic risk markers of replacing sedentary behavior with moderate-to-vigorous physical activity (14-17) and sleep (14), but where some have found beneficial health effects of substituting SB with light activity (15), others have not (16, 17).

Therefore, the aim of the present study was to estimate the effects of substituting 30 minutes of self-reported leisure time sitting with 30 minutes of sleep, light-to-moderate and vigorous physical activity on incident diabetes in Danish adults using isotemporal substitution modeling.

METHODS

Study population

The present study includes data from the Danish Capital Region Health Survey, a cross-sectional survey conducted in the Capital Region of Denmark in 2007 (N=69,800, response rate 52.3%), 2010 (N=95,150, response rate 52.3%) and 2013 (N=95.150, response rate 43.5%). Individuals were randomly selected through the Danish Civil Registration system as a representative sample of the population stratified on the 29 municipalities that constitute the Capital Region of Denmark. In 2007, 1800 questionnaires were sent to the representative sample of 25-79-year-old inhabitants in each municipality, followed by one reminder. In 2010 and 2013, a total of 2450 questionnaires were sent to inhabitants aged 16 years and above in each
municipality. The sample size was increased in Frederiksberg Municipality (3000 in 2007, 4,500 in 2010 and 2013) The present study focusses on respondents aged 25 or above. In 2010 and 2013, two reminders were sent out: a postcard and a second letter with the questionnaire, and it was also possible to answer the survey on the internet (18).

The studies were approved by the Danish Data Protection agency according to the Danish Act on Processing of Personal Data. Approval from the Danish Health Research Ethics Committee system was not required according to Danish law, as the research project is solely based on data from questionnaires and from national registers. Written informed consent for publication of this paper and any accompanying images was given by the participants when returning the questionnaire (19).

**Exposure variables: Sedentary behavior, sleep and physical activity**

Information on leisure time sedentary behavior (sitting time), sleep duration and leisure time physical activity was collected by a self-report questionnaire, the Physical Activity Scale (PAS) version 2.1 (20). When comparing the PAS scale with combined accelerometer and heart-rate measurement, validation studies have found good face and construct validity despite some overestimation of physical activity and underestimation of sedentary behavior (20, 21). In the questionnaire, respondents were asked to report hours and minutes on an average weekday of sleep and leisure time sitting (e.g. watching TV, relaxing, reading or listening to music during). Likewise, participants reported hours and minutes per day of active commuting (walking or bicycling to and from work or studies), occupational sitting, standing or walking, and strenuous physical activity at work (including e.g. heavy lifting or walking stairs). Finally, hours and minutes per week engaging in leisure time physical activity of: 1. Light-to-moderate intensity (e.g. walking, light cleaning/sweeping, yoga, bowling), 2. moderate intensity (e.g. gardening, carrying loads upstairs, gymnastics, swimming, cycling (for leisure, not commuting) or strength training) and 3. vigorous intensity (e.g. jogging, running, football, tennis, aerobics) was reported by responders in the questionnaire. Self-reported daily leisure time sitting time and daily sleep duration were included in the analyses as continuous variables.

Likewise, for the analyses, time engaging in “Daily leisure time light-to-moderate intensity physical activity” was determined by merging the responses from the three questions on a. hours and minutes per day of active commuting, b. hours and minutes per week engaging in leisure time light-to-moderate intensity physical activity divided by seven, and c. hours and minutes per week engaging in leisure time moderate intensity physical activity divided by seven. Combining light-to-moderate intensity with moderate intensity leisure time physical activity was chosen, as the questions did not clearly distinguish between the two. This has also been reported by others when using self-report measures to assess light or moderate intensity
physical activity (22, 23). Finally, “Daily leisure time vigorous physical activity” was calculated from responses to the question on weekly hours and minutes engaging in leisure time vigorous physical activity by dividing the reported minutes and hours by seven.

For the analyses, respondents’ answers to questions on daily time spent a. sitting at work, b. standing or walking at work and c. engaging in strenuous physical activity at work were included as co-variates in the analyses. If the total number of reported hours per day/week exceeded 24 hours per day, the excess time was subtracted from each level of activity according to the relative distribution of time responses.

Outcome ascertainment: Incident diabetes

The Danish Civil Registration System identifies all inhabitants in Denmark by a unique 10-digit personal identification number (CPR) that allows data record linkage to national registers at individual level. Information on diabetes was obtained by linkage to the Danish National Patient Register (DNPR) (24), and the Danish Prescription Registry (DPR) (25). Information from these registers are available from 2002 to 2017, hence follow-up was limited to 31 December 2017. For this study, a person was defined as prevalent with diabetes if 1.) he or she had at least one DNPR entry (hospital or outpatient clinic) with the diagnose code E10-E14, H28.0 and H36.0 within the last five years, and/or 2.) Had at least one visit to a GP for “foot-therapy for diabetes” within the last five years, and/or 3.) had redeemed at least two prescriptions with ATC-code A10 within a time span of 12 months within the last five years according to the DPR registry. Prescriptions for Metformin® (ATC-code A10BA02) in women between 20 and 40 on the prescription date were ignored, since Metformin® is also used for treatment of polycystic ovary syndrome. Date of incident diabetes was defined among persons, who did not have prevalent diabetes at the time of questionnaire survey response, as whichever came first of the following three: 1. date of first DNPR contact with one of the above diagnoses. 2. Date for first contact with GP with the above reason and 3. date for the second redemption of a prescription with the above-mentioned ATC-codes within a time span of 12 months. To avoid including persons with prevalent diabetes, we decided that both prescriptions had to be redeemed after the start of follow-up time, for a person to be classified with incident diabetes by prescription medicine.

Time to diabetes

We followed all individuals from their baseline date to 31 December 2017, or to the date at which the individual emigrated, died or developed diabetes, whichever date came first. Information on death and emigration was obtained from the Cause of Death Register and the CPR. For the Danish Capital Region Health Survey 2007, questionnaires were sent out during 2006 to citizens from 5 municipalities, and baseline for these individuals was set as 1 January 2007. For citizens from the remaining municipalities in
the Health Survey 2007, questionnaires were sent out in September and returned no later than December 2007, and baseline was set as 1 January 2008. For the 2010 and 2013 surveys, baseline was defined as the date of response to the electronic survey questionnaire, or the day the paper version of the completed questionnaire was received.

**Co-variates**
Potential confounders were selected a priori based on theoretical considerations and previous findings in the literature on associations between sedentary behavior and incident diabetes. From central registers sociodemographic information on sex, age, ethnicity (Danish, Western, other) and education (basic, short, intermediate, high) was obtained, as was information on inflammatory joint disease, e.g. rheumatoid arthritis (yes/no). From the self-report questionnaire information on smoking (daily smokers/non-smokers/ex-smoker/never smoker), body mass index (continuous variable, calculated as kg/m^2 from self-reported weight and height), perceived stress (Cohens Perceived Stress Scale) (26), SF12 mental component score (dichotomized as high/low), SF12 physical component score (dichotomized as high/low) were selected (27).

**Statistical analyses**
The association between each exposure behavior (sleep, sitting, different intensities of physical activity) and risk of incident diabetes was analyzed using Cox proportional hazards regression models. Time (in years) was measured as the time from baseline to incident diabetes or censoring. Each exposure behavior was modelled in 30-minute intervals. While even short bouts of physical activity are known to be beneficial to health, only prolonged periods of leisure time sedentary behavior, i.e. for at least 30 minutes at a time, appear to be detrimental to metabolic health (28). Also, the Danish public health guidelines on physical activity recommend that all adults should engage in a minimum of 30 minutes of moderate-to-vigorous physical activity per day, which makes the 30-minute intervals relevant from the perspective of adoption of public health recommendations (29). Some previous studies have similarly used 30-minute intervals for isotemporal substitution analyses, which make comparisons across studies possible (14, 28, 30).”

Necessary assumptions on linearity and proportional hazards were tested. The covariates age and BMI were non-linear and were therefore included as linear spline variables, each with two knots.
First, associations between each of the exposure behaviors sleep, leisure time sitting, light-to-moderate intensity physical activity and vigorous intensity physical activity, were explored in relation to the outcome, incident diabetes, in single activity models, adjusted for all confounders (12, 30). Second, partition models
were built, including all exposure behavior variables, in order to estimate the effect of each exposure behavior on incident diabetes while keeping the others constant (12, 30). Finally, isotemporal substitution models (ISM) were built including all exposure physical behavior variables during leisure time and at work, except the one exposure behavior of interest, as well as a covariate for total time accounted for. The ISM assumes that time spent in one behavior will lead to an isotemporal displacement of another behavior while total time is kept constant. For example, to estimate the effect of substituting 30 minutes of leisure time sitting with 30 minutes of vigorous physical activity, leisure time sitting is left out of the model while including the total measured time (12, 30).

To explore the potential attenuating effect of the included confounders, Cox regression analyses substitution models were conducted in three steps; 1. as crude unadjusted models, 2. as adjusted models with inclusion of all potential confounders except body mass index, and 3. in fully adjusted models including body mass index. Finally, potential interactions with sex and age were tested in fully adjusted substitution models.

As data in the present study are population-representative survey data, all analyses were weighted for survey design and non-response, by using calibrated weights computed by Statistics Denmark, and based on information from central registers on sex, age, municipality of residence, highest completed education level, income, civil status and hospitalization in all individuals who were invited to the survey (18). Analyses were performed via Statistics Denmark using SAS version 9.4 (TS1M3) with STAT 14.1.

RESULTS
After exclusion of survey participants with prevalent or suspected diabetes (n=5,580 and n=54), missing information in register follow-up (n=35) or incomplete or missing information on self-reported behaviors (n=17,361), the final study sample included N=87,339 men and women 25 years of age or older (fig 1). Hereof, n=3,007 had incident diabetes during a mean follow-up time of 7.35 years (range 1 day – 11.0 yrs). The total number of reported hours per day spent on sedentary behavior, physical activity and sleep exceeded 24 hours per day in 4.178 (4.8 %) of the included sample. Among those reporting more than 24 hours per day, the mean hours reported per day was 26.2 hours and the highest mean adjustment for reporting of excess time, was made for the behaviour “sleep” (0.6 hours per day)”. Sensitivity analyses performed with and without the 4.8% of the study sample with corrections for excess time gave similar estimates.

Participants with incident diabetes were more likely to be men, smokers, not working, and had lower perceived stress than those without incident diabetes (Table 1). Furthermore, participants with incident
diabetes were ten years older on average (57.6 yrs vs. 47.8 yrs), had markedly higher BMI (29.3 kg/m² vs. 24.9 kg/m²), reported slightly longer daily sleep duration (7.6 h vs. 7.5 h), longer daily leisure sitting time (4.6 h vs. 3.6 h), and slightly less light-to-moderate (1.6 h vs. 1.7 h) and vigorous (0.1 h vs 0.2 h) physical activity per day compared to participants without incident diabetes (table 2).

Hazard Ratio estimates from confounder-adjusted single activity, partition and substitution models are presented in table 3. In single activity models, leisure time sitting, light-to-moderate and vigorous intensity physical activity, but not sleep, were significantly associated with incident diabetes. In the partition model only light-to-moderate (HR 0.97, 95% CI 0.95-0.99) and vigorous physical activity (HR 0.83, 95% CI 0.74-0.94) were significantly associated with incident diabetes (Table 3). In the fully adjusted substitution models the effect of theoretically displacing 30 minutes of sitting was statistically significant when substituted with light-to-moderate physical activity (HR 0.96, 95% CI 0.94-0.98) or vigorous physical activity (HR 0.82, 95% CI 0.72-0.94), but not when substituted with sleep. It is worth noting that there was also a statistically significant beneficial effect of substituting light-to-moderate physical activity with vigorous physical activity (HR 0.86, 95% CI 0.75-0.98) (Table 3).

Similarly, estimates were slightly attenuated by stepwise inclusion of confounders, but they remained statistically significant in the fully adjusted ISM models (figure 2).

Finally, we found no indication of interaction with age, but a statistically significant interaction with sex. In men, hazard ratio estimates for substitution of 30 minutes of leisure time sitting with light-to-moderate physical activity (HR 0.95; 95% CI 0.92-0.97) and vigorous physical activity (HR 0.78; 95% CI 0.67-0.89) were very similar to the estimates found in the full study population, whereas the estimates for women were smaller and only just statistically significant with respect to light-to-moderate physical activity (HR 0.97, CI 0.94-1.0), but not for vigorous physical activity (HR 0.97, 95% CI 0.78-1.21) (figure 3).

In the analyses data were weighted for survey design and non-response of the full survey sample and were not re-calculated after the exclusions of those with missing values. However, there were only small differences in the distribution of the population characteristics among the intended sample of 110,535 persons and the final sample used in the analyses with 87,339 observations. The largest difference was found for age (weighted mean 49.8 years in intended sample vs. 47.7 years in the final sample). For all other variables there was less than 1%-point difference (data not shown).

**DISCUSSION**

In this prospective cohort study in a large population-based sample of Danish adults, theoretical substitution of 30 minutes of leisure time sitting per day with light-to-moderate or vigorous physical activity was associated with approximately 4% or 18% reduction in risk of incident diabetes, respectively, after
adjustment for BMI and other known confounders. No change in risk of incident diabetes was found when substituting sitting time with sleep.

Overall, these findings suggest that replacement of 30 minutes of leisure time sitting time per day may significantly reduce the risk of incident diabetes at population level. In everyday life this would correspond to replacing sitting during a single 30-minute “sitcom” TV episode with e.g. a brisk 30-minute walk, or - for even greater risk reduction – with vigorous physical activity, such as running or other high intensity physical activity. Although direct comparisons are difficult since previous studies have not used isotemporal substitution methods, our findings are in line with previous work suggesting that prolonged sitting time is linked to an increased risk of type 2 diabetes (5-7, 31). However, some prospective studies did not find an association between sedentary behaviour and incident diabetes (8, 9). In a large prospective cohort study in 72, 608 adults, Petersen et al examined the effect of total number of hours sitting per day on incident diabetes over 5 years (8). The crude association was substantially moderated by physical activity and BMI, and high amount of total sitting remained a risk factor in obese and inactive individuals only (8). Likewise, a study by Stamatakis et al from 2017 including 4811 Whitehall II civil servants found an initial association between both TV-viewing and total sitting time, and incident diabetes over 13 years of follow-up, but the associations were attenuated in fully adjusted analyses (9). In our study, adjusting for BMI and other confounders also attenuated the substitution effects on risk of incident diabetes, but replacing 30 minutes of sedentary behavior with light-to-moderate physical activity and especially with vigorous physical activity remained statistically significant.

In the present study, we found no significant decrease in risk of incident diabetes of substituting 30 minutes of sedentary behavior with 30 minutes of sleep. Short sleep duration, i.e. less than 6 hours per day, has previously been associated with risk of incident diabetes in observational studies (32-34). However, replacing leisure time sedentary behavior with sleep may only be beneficial if it leads to a more optimal sleep duration, as prolonged sleep duration may also increase the risk, as may poor sleep quality, shift work and specific sleep disturbances, such as abnormal sleep timing, sleep apnea or insomnia (32). This additional information on sleep characteristics was not available in the present study, but should be included in future ISM studies, as also pointed out by Rosique-Estaban et al (35), who found indications that sleep duration and sleep variability may act synergistically in relation to prevalence of type 2 diabetes (35).

We found no interaction with age, but a statistically significant interaction with sex and the effect of substituting 30 minutes of leisure time sitting per day was less pronounced in women compared to men. In stratified analyses, the effect of substituting sitting with vigorous physical activity in women was not
statistically significant, although the pattern was similar to what was seen in men. This finding may possibly reflect that markedly fewer women reported any vigorous physical activity, and that there were fewer incident diabetes cases among women. However, a potential gender difference should be further explored in future studies.

Strengths of this study include the large population-based study sample, the longitudinal design with register-based information on incident diabetes and the availability and inclusion of multiple relevant confounders. Limitations include the inability to distinguish between type 2 and type 1 diabetes and the self-report nature of the exposures, sleep, sedentary behavior and physical activity. However, most incident diabetes cases are likely to be type 2 diabetes cases, as type 1 diabetes debuts relatively rarely among adults. While self-reported information on sleep and movement behaviours is not optimal, and prone to substantial social desirability bias, device-based measurement of movement behaviours was not a feasible option in these large population-based surveys at the time of data collection. Sitting time is likely to have been underestimated, and light, moderate and vigorous intensity physical activity overestimated (13, 21, 23). If so, the found estimates are most likely underestimated and the true benefits of substituting sitting with light-to-moderate or vigorous intensity physical activity may be somewhat greater. It should also be noted that we adjusted the reported time used on sedentary behaviour, physical activity and sleep if the total number of reported hours per day exceeded 24 hours. This occurred in 4.8% of participants, who reported a mean total time per day of 26.2 hours. The excess time was subtracted from each level of activity according to the relative distribution of time responses. However, activities of different intensities may have been overreported differentially, and subtracting any time reported over 24 hours equally across all activity categories may potentially have introduced information bias, most likely resulting in underrepresentation of moderate and vigorous intensity physical activity. But, as sensitivity analyses performed with and without the 4.8% of the study sample with corrections for excess time gave similar estimates, this is unlikely to have influenced the results (data not shown).

The lack of valid information on light physical activity, which takes up a substantial part of everyday life is considered a particular limitation in the present study. The questionnaire did not enable us to distinguish sufficiently between light and moderate intensity physical activity in the analyses, and the effect of substituting sitting with moderate PA may have been diluted, when collapsed into one category together with light PA. Finally, dietary energy intake should ideally have been adjusted for when examining the prospective association between movement behaviours and incident diabetes. Information on dietary intake was not available in the present study. We did, however, include BMI. Albeit based on self-report information of height and weight and as such prone to substantial social desirability bias (36), BMI is
relatively strongly correlated with energy intake and therefore to some extent reflects dietary energy intake (37).

While much media coverage has focused on the deleterious effects of sedentary behaviour \textit{per se} on chronic disease, and sedentary behavior has been inaccurately appointed “the new smoking” (38), our findings point to the importance of investigating the effect of reallocating time spent sedentary to time spent in physical behaviours (13). From a public health perspective this approach is particularly relevant, as results may be interpreted and easily communicated as health effects of substituting e.g. 30 minutes of sedentary behavior with 30 minutes of physical activity or sleep.

To the best of our knowledge, and as pointed out in a recent scoping review (13), no other studies have so far examined the prospective relationship between sedentary behavior and incident diabetes using ISM. While we used the method originally described by Mekary el al (12, 30, 39) and applied it in cox regression models, new methods for analyzing 24-hour time use data on physical activity, sedentary behavior and sleep are emerging (13). These methods all attempt to account for the fact that the duration of a day is fixed and finite, and a change in one movement-related behavior will result in an opposite change in other behaviours. Suggested methods include compositional data analyses (CoDA) (40) and multivariate pattern analyses (41). However, there is no definite consensus as to which method is superior to others, except that any form of isotemporal substitution is superior to standard regression methods for analyzing theoretical substitution of physical behaviours in relation to health outcomes using 24-hour time use data (13). As opposed to isotemporal substitution, standard regression methods do not take the inherent displacement of physical behaviours into account (13).

Findings from the present study are considered representative of the adult Danish population in the Capital Region of Denmark and are likely to be generalizable to adult populations in countries similar to Denmark, as we used population-representative survey data and all analyses were weighted for survey design and non-response.

**PERSPECTIVES**

In this large, prospective population-based study among Danish adults, theoretical substitution of 30 minutes of sitting time per day with light-to-moderate or vigorous physical activity was associated with a decreased risk of incident diabetes of approximately 4% and 18%, respectively. While this may not be a substantial risk reduction for the individual, it could potentially have a substantial impact at population level (42). Future population-based studies should consider using more accurate device-based
measurement methods, e.g. accelerometers, for measuring sedentary behavior, physical activity and sleep, in order to obtain more precise estimates of the potential effects of substituting sitting time with sleep or physical activity of light, moderate and vigorous intensity. This would contribute additional information to the knowledge base needed to inform future guidelines on physical activity, sedentary behavior and sleep for the prevention of diabetes and other chronic diseases.

ACKNOWLEDGEMENTS
The authors wish to acknowledge all the respondents who took the time to respond to the questionnaire in the Danish Capital Region Health Survey 2007, 2010 or 2013.

FUNDING
The data collection for the Danish Capital Region Health Survey 2007, 2010 and 2013 was funded by The Capital Region of Denmark, who provided the data for this study.

CONFLICT OF INTEREST
The authors have no conflicts of interest to declare.

CONTRIBUTION
MA and CJL were responsible for the conception and design of the study. AHA analyzed data and AH, NG, CBH, CJL and MA discussed data analyses and interpretation. MA wrote first draft of the manuscript and AH, NG, CBH, AHA and CJL contributed to subsequent versions of the manuscript. All authors critically revised the manuscript and approved the final version of the manuscript.

Table 1. Study population characteristics by incident diabetes status. Data presented as numbers and frequencies (%) (N=87,339).

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<th>Characteristics</th>
<th>Not incident diabetes</th>
<th>Incident diabetes</th>
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<td>N=3,007</td>
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<table>
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<td><strong>Sex</strong></td>
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<td>High level</td>
<td>13,012</td>
<td>17.8</td>
<td>622</td>
<td>24.3</td>
</tr>
<tr>
<td><strong>Mcs12</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=80,886)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>6,092</td>
<td>9.2</td>
<td>270</td>
<td>11.6</td>
</tr>
<tr>
<td>High</td>
<td>72,063</td>
<td>90.8</td>
<td>2,461</td>
<td>88.4</td>
</tr>
<tr>
<td><strong>Pcs12</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=80,886)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>5,394</td>
<td>6.9</td>
<td>487</td>
<td>19.1</td>
</tr>
<tr>
<td>High</td>
<td>72,761</td>
<td>93.1</td>
<td>2,244</td>
<td>80.9</td>
</tr>
<tr>
<td><strong>Arthritis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=87,339)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1,781</td>
<td>1.9</td>
<td>169</td>
<td>5.8</td>
</tr>
<tr>
<td>No</td>
<td>82,551</td>
<td>98.1</td>
<td>2,838</td>
<td>94.2</td>
</tr>
<tr>
<td><strong>Work status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(87,339)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Working</td>
<td>62,806</td>
<td>77.3</td>
<td>1,635</td>
<td>55.0</td>
</tr>
<tr>
<td>Not working</td>
<td>21,526</td>
<td>22.7</td>
<td>1,372</td>
<td>45.0</td>
</tr>
</tbody>
</table>
**Table 2.** Age, BMI and activity time-use by incident diabetes status. Data presented as means and Standard deviations (SD). (N=87,339).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Not incident diabetes</th>
<th>Incident diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=84,332</td>
<td>n=3,007</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Age years</td>
<td>47.8</td>
<td>15.1</td>
</tr>
<tr>
<td>BMI</td>
<td>24.9</td>
<td>4.1</td>
</tr>
<tr>
<td>Sleep h/day</td>
<td>7.4</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Leisure time</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sitting h/day</td>
<td>3.6</td>
<td>2.0</td>
</tr>
<tr>
<td>Moderate h/day</td>
<td>1.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Vigorous PA h/day</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Work</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sitting h/day</td>
<td>3.4</td>
<td>3.1</td>
</tr>
<tr>
<td>Standing/walking h/day</td>
<td>2.2</td>
<td>2.5</td>
</tr>
<tr>
<td>Strenuous h/day</td>
<td>0.5</td>
<td>1.21.1</td>
</tr>
<tr>
<td><strong>Total time accounted for h/day</strong></td>
<td>18.9</td>
<td>2.9</td>
</tr>
</tbody>
</table>

**Table 3.** Hazard Ratio estimates of associations between 30 min units of sleep, leisure time sitting, light-to-moderate and vigorous physical activity on incident diabetes (N= 87,332), from Single Activity, Partition and Substitution models. (PA=physical activity, LMPA=Light-to-moderate physical activity, VPA=Vigorous physical activity)

<table>
<thead>
<tr>
<th>Activity type</th>
<th>Sleep</th>
<th>Sitting</th>
<th>Light-to-moderate</th>
<th>Vigorous</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td><strong>Model</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single Activity(^a)</td>
<td>1.01 (0.99;1.04)</td>
<td>1.02 (1.01;1.03)</td>
<td>0.96 (0.94;0.98)</td>
<td>0.81 (0.72;0.92)</td>
</tr>
<tr>
<td>Partition(^b)</td>
<td>1.01 (0.98;1.03)</td>
<td>1.01 (0.99;1.03)</td>
<td>0.97 (0.95;0.99)</td>
<td>0.83 (0.74;0.94)</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Substitution&lt;sup&gt;c&lt;/sup&gt;</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Replace sleep with</td>
<td>Dropped</td>
<td>1.00 (0.98;1.03)</td>
<td>0.96 (0.93;0.99)</td>
</tr>
<tr>
<td>Replace sitting with</td>
<td>1.00 (0.97;1.02)</td>
<td>Dropped</td>
<td>0.96 (0.94;0.98)</td>
</tr>
<tr>
<td>Replace LMPA with</td>
<td>1.04 (1.01;1.07)</td>
<td>1.04 (1.02;1.07)</td>
<td>Dropped</td>
</tr>
<tr>
<td>Replace VPA with</td>
<td>1.21 (1.07;1.38)</td>
<td>1.21 (1.07;1.38)</td>
<td>1.16 (1.02;1.33)</td>
</tr>
</tbody>
</table>

<sup>a</sup>All models adjusted for sex, ethnicity, education, smoking, inflammatory joint disease, perceived stress, mental component scale, physical component scale, work status and BMI.

<sup>b</sup>Partition model additionally includes all activity types as co-variates, but not time not accounted for.

<sup>c</sup>Substitution model additionally includes total time as co-variate, but not the replacement activity type (“dropped”).

References


FIGURE LEGENDS

Figure 1. Study population, the Danish Capital Region Health Survey from 2007, 2010 and 2013 (25-79-year-old men and women).

Figure 2. The Effects of substituting 30 minutes of leisure time sitting with sleep, light-to-moderate physical activity (LMPA) or vigorous physical activity (VPA) on incident diabetes. LIGHT GREY: Unadjusted estimates. GREY: Estimates adjusted for sex, age, ethnicity, education, smoking, inflammatory joint disease, perceived stress, mental component scale, physical component scale and work status. BLACK: Estimates additionally adjusted for BMI. (N= 87,339)
Figure 3. The effects of substituting 30 minutes of leisure time sitting with sleep, light-to-moderate physical activity (LMPA) or vigorous physical activity (VPA) on incident diabetes. Separate estimates for BLUE: Men (n=38,731) and RED: Women (n=48,608), from fully adjusted ISM models including sex, age, BMI, ethnicity, education, smoking, inflammatory joint disease, perceived stress, mental component scale, physical component scale and work status.
Figure 1.

Health Survey 2007  
N= 36,472

n=4 participated in two municipalities, first response only included

Health Survey 2007  
N= 36,468

Health Survey 2010  
N= 44,566

n=2,727 also participated in 2007, excluded from 2010 survey

Health Survey 2010  
N= 41,839

n=2,603 also participated in 2007, n=1993 also in 2010, n=273 also in 2007 & 2010, excluded from 2013 survey

Health Survey 2013  
N= 37,132

n=2,603 also participated in 2007, n=1993 also in 2010, n=273 also in 2007 & 2010, excluded from 2013 survey

Health Survey 2013  
N= 32,263

n=35 not identified because of missing date of birth

Health Survey 2007 + 2010 + 2013  
N= 110,535

n=5,580 prevalent diabetes  
n=54 suspected diabetes (prescription medicine)  
n=59 died before onset of follow-up  
n=142 missing information about diabetes prevalence

Health Survey 2007 + 2010 + 2013  
N= 104,700

n=17,361 incomplete or missing information on physical activity, sleep and/or sitting time

Health Survey 2007 + 2010 + 2013  
N= 87,339

Hereof n=3,007 with incident diabetes

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Figure 2.

Substitution of 30 min of leisure time sitting with sleep, LMPA or VPA and HR for incident diabetes
Figure 3.

Substitution of 30 min of leisure time sitting with sleep, LMPA or VPA and HR for incident diabetes in Men and Women.