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TITLE: Sitting behaviour and incident diabetes over 13 years: the Whitehall II cohort study

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WHAT ARE THE NEW FINDINGS

- The epidemiological literature on sitting and incident diabetes is very scant and rarely acknowledges the confounding role of adiposity
- Occupational, non-TV leisure time at home, and total non-TV sitting were not associated with incident diabetes risk over 13 years of follow-up
- TV time and total sitting were associated with diabetes but once baseline body mass index was taken into account these associations were attenuated

HOW MIGHT IT IMPACT ON CLINICAL PRACTICE IN THE NEAR FUTURE

- Our findings provide little support for developing interventions that specifically target sitting to reduce diabetes risk.
- The weak evidence for associations we found may be partly due to the protective effect of relatively high amounts of daily walking and other moderate to vigorous physical activity in this cohort.
- Strategies to increase walking and other physical activity and reduce BMI remain the cornerstone of diabetes prevention

ABSTRACT

Background/Aim: Although certain types of sedentary behaviour have been linked to metabolic risk, prospective studies describing the links between sitting with incident diabetes are scarce and often do not account for baseline adiposity. We investigate the associations between context-specific sitting and incident diabetes in a cohort of mid-aged to older British civil servants. **Methods:** Using data from the Whitehall II Study (n=4811), Cox proportional hazards models (adjusted for age, sex, ethnicity, employment grade, smoking, alcohol intake, fruit and vegetable consumption, self-rated health, physical functioning, walking and moderate-to-vigorous physical activity, and BMI) were fitted to examine associations between total sitting and context-specific sitting time (work, television (TV), non-TV leisure time sitting at home) at Phase 5 (1997-99) and fasting glucose-defined incident diabetes up to 2011. **Results:** Total sitting (HR of top compared to the bottom group: 1.26; 95%CI: 1.00 to 1.62; p=0.01) and TV sitting (1.33; 1.03 to 1.88; p=0.05) showed associations with incident diabetes; once BMI was included in the model these associations were attenuated for both total sitting (1.19; 0.92 to 1.55; p=0.22) and TV sitting (1.31; 0.96 to 1.76; p=0.14). **Conclusions:** We found limited evidence linking sitting and incident diabetes over 13 years in this cohort of civil servants.

Keywords: diabetes, cardiometabolic, sedentary behaviour, sitting, physical activity, epidemiology, public health, prevention

INTRODUCTION

Sedentary behaviour (SB) comprises a set of waking time activities that are characterised by an energy expenditure of ≤ 1.5 MET in a sitting or reclining posture.¹ Sitting is a ubiquitous behaviour in today's world and has been linked to broad outcomes such as all-cause mortality^{2 3 4}. A growing body of research has examined the cardiometabolic consequences of sitting in both population^{3 4} and laboratory⁵ settings. Data on sitting and risk for incident diabetes are scarce. A meta-analysis of 10 cross-sectional and prospective epidemiological studies concluded that the population groups with the greatest levels of SB time had 112% higher risk for type 2 diabetes compared with the lowest SB time groups.⁶ All included studies used television viewing (TV) as a proxy of total SB⁷⁻¹⁰ and only one⁷ adjusted for baseline adiposity. Adiposity is associated with both type 2 diabetes and SB time¹¹⁻¹³ and as such it may be a confounder that needs to be accounted for. A more recent meta-analysis on SB and cardiometabolic disease events and mortality³ also showed that across all outcomes the most consistent associations were seen for risk for type 2 diabetes (>90% increase in risk). All five included studies also had TV viewing as the exposure³. But it is unclear whether these findings are driven by the sitting that TV viewing involves *per se*. TV time is a poor indicator of total SB^{14 15} and sitting time¹⁶ that is confounded by multiple aspects of socioeconomic circumstances,¹⁷ dietary factors,^{6 3} and mental health¹⁸. Such a breadth of confounding has not been fully accounted for by studies in the field. Beyond TV time, a recent study of total sitting and incident diabetes in a sample of adults from Denmark found associations only among the physically inactive and the obese groups.¹⁹ Sitting can occur in many different contexts (e.g. work, leisure time, transportation) and there is a limited number of cohort studies^{9 20 21} that examined context-specific associations with diabetes risk (all US-based). TV time only,^{9 9 20} TV and total leisure-time sitting,²¹ but not work related sitting⁹

²⁰, were associated with diabetes; on one occasion these associations were eliminated once baseline BMI was taken into account²⁰.

The aim of this study was to examine the associations between context-specific sitting with incident diabetes among mid-aged and older British civil servants over a 13-years period.

We sought to highlight the role of adiposity by presenting these associations with and without adjustment for baseline BMI.

METHODS

Participants and study background

The Whitehall II study was established in 1985 to examine the biological mechanisms that account for observed social inequalities in cardiovascular disease and diabetes. ²² The sample included in this study comprised 4811 individuals (3501 men and 1310 women) from clerical and office support grades, middle ranking executive grades and senior administrative grades. Baseline examination (Phase 1: 1985-88) involved a questionnaire and a clinical examination and subsequent measurement, phases have alternated between postal questionnaire alone and postal questionnaire accompanied by a clinical examination. Ethical approval was granted by the University College London Medical School Committee. Informed consent was obtained at baseline and renewed at each contact. The detailed measures of sitting and PA included in this report were undertaken during the 5th phase of data collection between 1997 and 1999 with follow-up for incident diabetes until December 2011.

Measurement of sitting behaviours

The questionnaire included items related to both occupational and leisure time sitting behaviours.²² Participants were asked ‘On average how many hours per week do you spend: sitting at work, driving or commuting?’ and ‘sitting at home e.g. watching TV, sewing, at a desk’, and responded by selecting one of eight time categories (none, 1 hour, 2-5, 6-10, 11-20, 21-30, 31-40, >40 hours). For sitting at home participants were given an open text response option to specify two types of sitting and then selected a time category for each. Using the midpoint of each time category (exactly 40hrs was used to represent the >40hrs category), 6 indicators of sitting expressed as hours per week were computed: 1) work related sitting time, 2) TV time, 3) Non-TV leisure sitting time at home, 4) Total leisure time sitting at home (sum of 2 and 3 above), 5) Total sitting time (sum of 1-3 above), and 6) non-TV total sitting time (the sum of 1 and 3 above). Five of these items (1-5) have been used previously^{9 11, 22} and although there is currently no objective criterion measure of context specific sitting, these questionnaire items have demonstrated concurrent validity with past weeks recall questionnaires (Pearsons $r=0.44$) and activity diaries ($r=0.41$).²³

Outcome measure

Outcomes included incident diabetes up to December 2011. As previously described²⁴, blood glucose was measured using the glucose oxidase method. Incident cases of diabetes were identified by fasting blood glucose concentration ($\geq 7.0\text{mmol/L}$), according to the 2006 World Health Organization (WHO) classification²⁵.

Covariates

Height (metres) and weight (kg) were measured at the clinical examinations. Body Mass Index (BMI) was computed by dividing squared height by bodyweight. Sociodemographic covariates included age, gender, ethnicity (white vs. non-white), employment grade (a comprehensive marker of socioeconomic circumstance related to salary, level of responsibility and social status), smoking status (current, previous, or never a smoker), alcohol consumption (units per week), frequency of fruit and vegetable consumption, self-rated health (excellent, very good, good, fair, or poor), and physical functioning score (continuous) using the SF-36 scale²⁶. PA was measured using a 20-items modified version of the previously validated Minnesota Leisure-Time Physical Activity Questionnaire that enquired about occupational, domestic and leisure time physical activities. These questions have been shown to have acceptable criterion validity against accelerometry²⁷ and have demonstrated excellent predictive validity for mortality²⁸ in the Whitehall II study. Physical activities were classified by metabolic equivalents (MET)²⁹ with moderate intensity activities ranging from 3-5.9 MET and vigorous intensity activities 6 MET or greater. As the energy cost of walking is dependent on walking pace and could not be determined from the Phase 5 questionnaire, walking time did not contribute to the MVPA and was entered as a separate covariate.

Statistical analyses

Participants with prevalent diabetes at baseline (based on the 2006 WHO fasting glucose definition²⁵) were excluded from analyses. Due to low numbers in some of the eight original time categories for each sitting exposure, each sitting time variable was regrouped into three categories of near equal numbers as the data permitted (exact tertiles were not possible due to abnormal distribution): work sitting was grouped as 0 to <15, ≥ 15 to <35, and ≥ 35

hours/week; TV sitting as 0 to <11, ≥ 11 to <16, and ≥ 16 hours/week; non-TV Leisure Time Sitting at home as 0 to <8, ≥ 8 to <16, and ≥ 16 hours/week; leisure time sitting as 0 to <15, ≥ 15 to <25, and ≥ 25 hours/week; total sitting as 0 to <33, ≥ 33 to <50, and ≥ 50 hours/week; and total sitting excluding TV as 0 to <33, ≥ 33 to <50, and ≥ 50 hours/week. Participants with missing data in any variables required for this analyses were excluded from analyses.

Cox proportional hazards models for each exposure were fitted to examine the associations between each of the six sitting exposures and incident diabetes up to 2011. Hazard ratios and 95% confidence intervals (CI) were estimated for each category of sitting time, by type, with the lowest group as the reference category. Examination of Schoenfeld residuals and Nelson-Aalen cumulative hazards plots provided no evidence for deviations from proportionality in any of the Cox models. Analyses were limited to those who had completed both the survey and clinical examination, who were still working in the civil service or elsewhere, and who had no prevalent diabetes (590 cases excluded) or heart diseases (1145 cases excluded) at baseline. Models were first adjusted for age, gender, ethnicity, and employment grade (Model 1) and then further adjusted for smoking status, weekly alcohol intake, fruit and vegetable consumption, self-rated health, and physical functioning (Model 2). The final model was also adjusted for PA (Model 3). To test for linear trends in individual parameters the Wald chi-squared test was used and the Likelihood-ratio chi-squared test was used for non-linear relationships. As previously,³⁰ we examined the independence of the observed associations (only for the sitting exposures that were associated with incident diabetes in any of the three models) from adiposity in a separate analysis where in addition to all covariates specified in Model 3 we also adjusted for baseline BMI.

In a sensitivity analyses we repeated the above Cox analyses examining the associations between sitting behaviours in Phase 5 and incident diabetes using a 75 g oral glucose tolerance test (OGTT) at Phase 9 (which was the last Phase such a test was included).

OGTT involved determination of 2-hour postload glucose according to the WHO standards²⁵ (2-hour post-load glucose \geq 11.1 mmol/L). Analyses were conducted in 2016 using STATA version 13.2 (StataCorp, College Station, TX).

RESULTS

Sample characteristics

Out of the 10,308 participants at Whitehall II onset, 7870 took part in Phase 5. Among them, 517, 1145, and 1397 were excluded due to existing diabetes, existing CVD, and missing data in at least one of the variables needed for the multivariate analyses (Supplemental Table 1), respectively. The characteristics of the Phase 5 participants that were included in this analysis are shown in Table 1. As previously reported,²² compared with those in the sample of the present study, those lost to follow-up between the study's inception in 1985 and Phase 5 were slightly older at date of screening, consumed slightly less alcohol, and were more likely to be male, obese and in a higher employment grade in 1985. The mean follow up was 13.0 years corresponding to 62,463 person-years.

Incident diabetes

In total, 402 cases of fasting glucose defined incident diabetes occurred during the follow-up period. As Table 2 shows, leisure time sitting, total sitting, and TV time showed associations with incident diabetes in the models with minimal adjustment (Model 1) and these associations persisted for TV time and total sitting once the remaining potential confounders were taken into account. Work-time sitting, non-TV leisure time sitting, and total sitting excluding TV time were not associated with the outcome in any of the three models (Table 2). Baseline BMI was associated with incident diabetes (per unit HR: 1.15; 95%CI: 1.12 to

1.18, $p < 0.001$) after adjusting for total sitting time, age, sex, employment grade, ethnicity, smoking status, alcohol consumption, PA, general health, physical functioning and frequency of fruit & vegetable consumption.

Independence of the observed associations from baseline BMI

Table 3 presents the results additionally adjusted for BMI for those exposures that showed associations with incident diabetes in any of the three models. Once BMI was included in the model (Model 4), all associations were attenuated. For example, for TV time the HR of the top compared to the lowest group was attenuated to 1.31 (95% CI: 0.96 to 1.76).

Supplemental Table 2 presents the characteristics of the sample included in the sensitivity analysis with OGTT-defined incident diabetes between Phase 5 (1996-8) and Phase 9 (2006-08) ($n=4735$, 9.7 average years of follow up, 439 events, 45,864 person-years). Sensitivity analyses results were consistent with the main analyses described above and only TV sitting time and total sitting were associated with OGTT-defined incident diabetes (Supplemental Table 3). Once baseline BMI was taken into account these associations were also attenuated, although TV time maintained a borderline association (Supplemental Table 4).

DISCUSSION

Main findings and comparison with previous literature

Our study addresses several gaps in the SB literature by considering type-specific sitting in relation to incident diabetes over a long follow up. We found that total sitting and TV time were both associated with incident diabetes independently of PA and these associations were

attenuated once baseline BMI was taken into account. Our findings are a novel contribution, with previous prospective research being reliant on TV time as the sole marker of sitting and in most cases lacking adjustment for baseline adiposity.^{8 9 10}

A long-term prospective study, broadly comparable to ours, featured a sample of 4554 American women with gestational diabetes and examined the association between different types of sitting (TV, other domestic, non-domestic/work, car driving) and risk of type 2 diabetes over 16 years²⁰. The results of this study were concordant with ours as the TV time relative risk prior to adjustment for BMI was 1.41 (1.11-1.79) for the 11-20 hours/week of TV time group²⁰ (vs. 1.39, 1.03-1.88 for ≥ 16 hours/week in our study) and adjustments for baseline BMI attenuated substantially these associations.²⁰ In a multi-ethnic US cohort total leisure time sitting (62% of which was TV time) was associated with incident diabetes over 11 years of follow up²¹ in overweight and obese participants but not in participants with a BMI<25. A large Danish study of 72,608 adults with a relatively short follow up (<5 years) found that once BMI and physical activity were taken into account total sitting time was associated with HbA1c –defined incident diabetes only among the physically inactive and the obese groups¹⁹. Adjustment for baseline BMI attenuated the associations between weekly TV viewing frequency and clustered cardiometabolic risk in another prospective British study over a 21 year follow up.³⁰

The role of BMI

Conceptually, adiposity and sitting may be associated in a bi-directional manner but not both directions of the association are empirically supported. Albeit limited in volume, existing literature^{12 13} (including a Whitehall II cohort study¹³) suggests that previous adiposity determines future SB and no prospective study, to our knowledge, has indicated that sitting

predicts markers of adiposity or obesity. Although some shared variance is likely to exist, it is more likely that BMI is a confounder rather than a mediator of the association between sitting and diabetes, an assertion that is indirectly supported by a recent laboratory study showing that the energy expenditure benefits of simply reducing sitting are negligible.³¹ While more work is needed in this area, our results and the above literature suggest that studies that examine the links between SB and diabetes without adjusting for adiposity may be compromised. Additional pathways linking SB, adiposity, and diabetes include the established relationships between TV viewing and obesogenic diets.³² SB may displace PA time leading to an decrease in energy expenditure and unfavourable weight changes.³³ It is worth noting that the top TV tertile in Whitehall II corresponded to >2.3 hours/day, which is well below the general population in England aged >55 where mean values are 3-4 hours/day³⁴). Despite this relatively low bound of the high TV group, only 0.007% (7/937) of its members reported less than 3.6 hour of TV per day and as such it is unlikely that our analyses under-estimated the associations due to a likely threshold effect.

Interpretation of main findings

During prolonged sitting, differences in energy balance have been proposed as a major determinant of the metabolic dysfunction (as indexed by compromised insulin action) observed among non-obese young and fit men and women.³⁵ Acknowledging the generally accepted theorem that increased adiposity (which BMI is thought to reflect reasonably at the population level) is the result of chronic energy imbalance, these findings suggest that future studies examining the links between SB and diabetes will benefit from incorporating more robust assessments of energy intake and expenditure.

One possible explanation for the limited evidence linking sitting and diabetes risk in the current study is the protective effect of the high volumes of total reported MVPA and in particular daily walking that is reported in the Whitehall cohort. For example, the mean reported daily walking time (42.73 ± 22.70 minutes/day) is over double the reported UK national average.³⁶ Several recent large prospective studies have showed that the associations between sitting time and incident diabetes¹⁹ or cardiovascular disease^{37 38} are only observed in the least active participants.

In general, previous literature is consistent in that TV time is prospectively associated with diabetes and other cardio metabolic outcomes^{3 39} but occupational sitting is not.⁴⁰ This contradiction suggests that examining total sitting volumes alone may not be sufficiently informative due to the existence of context-specific unmeasured confounding (e.g. dietary or socioeconomic). Another important consideration is the pattern of sitting (e.g. length of bouts and frequency of interruptions from sitting) that may be relevant to health outcomes but cannot be captured by self-report measures, including the questionnaires used in our study. A study of 164 London office workers⁴¹ who wore inclinometers for 7 days found that 69% of sitting bouts are <10 minutes with only <10% of all bouts lasting >60 minutes in duration. Both during work and in the evenings participants registered approximately two sit-to stand transitions per hour, a pattern that has been linked to measurable improvements in acute glycemic responses in laboratory studies testing interruptions of sitting with walking^{5 42}. Assuming the sitting patterns of the Whitehall II cohort are similar, the absence of notable effects may be partly attributed to the relatively frequent short physical activity bouts that confer glycemic protection in this occupational cohort.

Strengths and limitations

Strengths of our study include the prospective design, the long follow up, and the six sitting exposures (covering work, recreation, and commuting) that allowed us to take into account the sitting context. We were also able to take account of a broad range of important confounding factors, including physical functioning that is linked to acute injury and long-standing illness and may be a contributor to increased sitting. Our study also has limitations. Sitting was measured using self-report that may be subject to recall and social desirability biases. Leisure-time questions only captured sitting at home. Occupational cohorts are by definition sufficiently healthy at baseline to be in active employment which may reduce the extent to which our conclusions are generalizable. However, aetiological findings from Whitehall II are broadly consistent with those obtained from representative cohorts.⁴³ Despite threats to the ecological validity of our study, it is reassuring that our results are in agreement with a clinical US cohort.²⁰ We were able to take into account fruit and vegetable consumption that is an important for diabetes risk⁴⁴ aspect of diet.

Conclusions

In conclusion, our study makes a unique contribution in the literature by examining prospectively a broad range of type-specific sedentary behaviours in relation to incident diabetes over a long follow up period of 13 years in a physically active cohort of British civil servants. We found moderate evidence linking TV time and limited evidence linking total sitting with diabetes but these links were dependent on baseline BMI. It is important that prospective general population studies using objective measures of sitting patterns (in addition to sitting context-specific measures) and controlled trials replicate our findings.

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COMPETING INTERESTS

None of the authors has a conflict of interest to declare.

AUTHORS' CONTRIBUTIONS:

E. Stamatakis: conceived the idea, designed the study, drafted the manuscript, provided initial interpretation of the data, carried out multiple manuscript revisions

R Pulsford: assisted with data acquisition, contributed to study design, did and updated the statistical analysis several times, assisted with data acquisition, drafted parts of the manuscript

E. Brunner: assisted with data acquisition and study design, critical revision of the manuscript for important intellectual content; results interpretation

A. Britton: assisted with data acquisition, critical revision of the manuscript for important intellectual content; results interpretation

A. Bauman: critical revision of the manuscript for important intellectual content; results interpretation

S. Biddle: critical revision of the manuscript for important intellectual content; results interpretation

M. Hillsdon: assisted with data acquisition, contributed to study design, critical revision of the manuscript for important intellectual content; results interpretation

TRANSPARENCY DECLARATION

The first author (ES) and the second author (RP) affirm that the manuscript is an honest, accurate, and transparent account of the data being reported; that no important aspects of the study have been omitted; and that no discrepancies from the study as planned have occurred.

EXCLUSIVE LICENCE STATEMENT

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REFERENCES

1. Sedentary Behaviour Research Network. Standardized use of the terms “sedentary” and “sedentary behaviours”. *Appl Physiol Nutr Metab* 2012;37:540-42.
2. Chau JY, Grunseit AC, Chey T, et al. Daily Sitting Time and All-Cause Mortality: A Meta-Analysis. *PLoS ONE* 2013;8(11):e80000. doi: 10.1371/journal.pone.0080000
3. Biswas A, Oh PI, Faulkner GE, et al. Sedentary Time and Its Association With Risk for Disease Incidence, Mortality, and Hospitalization in Adults A Systematic Review and Meta-analysis Sedentary Time and Disease Incidence, Mortality, and Hospitalization. *Annals of Internal Medicine* 2015;162(2):123-32. doi: 10.7326/M14-1651
4. Ekelund U, Steene-Johannessen J, Brown WJ, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *Lancet* 2016;388(10051):1302-10. doi: 10.1016/s0140-6736(16)30370-1 [published Online First: 2016/08/01]
5. Chastin SF, Egerton T, Leask C, et al. Meta-analysis of the relationship between breaks in sedentary behavior and cardiometabolic health. *Obesity (Silver Spring)* 2015;23(9):1800-10. doi: 10.1002/oby.21180 [published Online First: 2015/08/27]
6. Wilmot E, Edwardson C, Achana F, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. *Diabetologia* 2012;55(11):2895-905. doi: 10.1007/s00125-012-2677-z
7. Krishnan S, Rosenberg L, Palmer JR. Physical activity and television watching in relation to risk of type 2 diabetes: the Black Women's Health Study. *American journal of epidemiology* 2009;169(4):428-34. doi: kwn344 [pii]
- 10.1093/aje/kwn344 [published Online First: 2008/12/06]
8. Hu FB, Leitzmann MF, Stampfer MJ, et al. Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men. *Arch Intern Med* 2001;161(12):1542-8. doi: ioi00636 [pii] [published Online First: 2001/06/28]
9. Hu FB, Li TY, Colditz GA, et al. Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA* 2003;289(14):1785 - 91.
10. Ford ES, Schulze MB, Kroger J, et al. Television watching and incident diabetes: Findings from the European Prospective Investigation into Cancer and Nutrition-Potsdam Study. *J Diabetes* 2010;2(1):23-7. doi: 10.1111/j.1753-0407.2009.00047.x [published Online First: 2010/10/07]
11. Pulsford RM, Stamatakis E, Britton AR, et al. Sitting behavior and obesity: Evidence from the Whitehall II study. *American Journal of Preventive Medicine* 2013;44(2):132-38.
12. Pedisic Z, Grunseit A, Ding D, et al. High sitting time or obesity: Which came first? Bidirectional association in a longitudinal study of 31,787 Australian adults. *Obesity* 2014;22(10):2126-30. doi: 10.1002/oby.20817
13. Ekelund U, Brage S, Besson H, et al. Time spent being sedentary and weight gain in healthy adults: reverse or bidirectional causality? *The American Journal of Clinical Nutrition* 2008;88(3):612-17.
14. Scholes S, Coombs N, Pedisic Z, et al. Age- and sex-specific criterion validity of the health survey for England physical activity and sedentary behavior assessment questionnaire as compared with accelerometry. *American journal of epidemiology* 2014;179(12):1493-502. doi: 10.1093/aje/kwu087 [published Online First: 2014/05/28]
15. Clark BK, Healy GN, Winkler EA, et al. Relationship of television time with accelerometer-derived sedentary time: NHANES. *Med Sci Sports Exerc* 2011;43(5):822-8. doi: 10.1249/MSS.0b013e3182019510 [published Online First: 2010/10/29]
16. Clark BK, Lynch BM, Winkler EA, et al. Validity of a multi-context sitting questionnaire across demographically diverse population groups: AusDiab3. *The international journal of*

- behavioral nutrition and physical activity* 2015;12:148. doi: 10.1186/s12966-015-0309-y [published Online First: 2015/12/08]
17. Stamatakis E, Coombs N, Rowlands A, et al. Objectively-assessed and self-reported sedentary time in relation to multiple socioeconomic status indicators among adults in England: a cross-sectional study. *BMJ Open* 2014;4(11) doi: 10.1136/bmjopen-2014-006034
 18. Hamer M, Stamatakis E, Mishra GD. Television- and Screen-Based Activity and Mental Well-Being in Adults. *American Journal of Preventive Medicine* 2010;38(4):375-80.
 19. Petersen CB, Bauman A, Tolstrup JS. Total sitting time and the risk of incident diabetes in Danish adults (the DANHES cohort) over 5 years: a prospective study. *British journal of sports medicine* 2016;epub ahead of print doi: 10.1136/bjsports-2015-095648
 20. Bao W, Tobias DK, Bowers K, et al. Physical activity and sedentary behaviors associated with risk of progression from gestational diabetes mellitus to type 2 diabetes mellitus: a prospective cohort study. *JAMA internal medicine* 2014;174(7):1047-55. doi: 10.1001/jamainternmed.2014.1795 [published Online First: 2014/05/21]
 21. Joseph JJ, Echouffo-Tcheugui JB, Golden SH, et al. Physical activity, sedentary behaviors and the incidence of type 2 diabetes mellitus: the Multi-Ethnic Study of Atherosclerosis (MESA). *BMJ open diabetes research & care* 2016;4(1):e000185. doi: 10.1136/bmjdr-2015-000185 [published Online First: 2016/07/13]
 22. Pulsford RM, Stamatakis E, Britton AR, et al. Associations of sitting behaviours with all-cause mortality over a 16-year follow-up: the Whitehall II study. *Int J Epidemiol* 2015;10.1093/ije/dyv191. doi: 10.1093/ije/dyv191
 23. Wolf AM, Hunter DJ, Colditz GA, et al. Reproducibility and validity of a self-administered physical activity questionnaire. *Int J Epidemiol* 1994;23(5):991-9. [published Online First: 1994/10/01]
 24. Tabak AG, Jokela M, Akbaraly TN, et al. Trajectories of glycaemia, insulin sensitivity, and insulin secretion before diagnosis of type 2 diabetes: an analysis from the Whitehall II study. *Lancet* 2009;373(9682):2215-21. doi: 10.1016/s0140-6736(09)60619-x [published Online First: 2009/06/12]
 25. World_Health_Organisation. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: Report of a WHO/IDF Consultation: World Health Organisation, 2006:1-3.
 26. Jenkinson C, Wright L, Coulter A. Criterion validity and reliability of the SF-36 in a population sample. *Qual Life Res* 1994;3(1):7-12. [published Online First: 1994/02/01]
 27. Sabia S, van Hees VT, Shipley MJ, et al. Association between questionnaire- and accelerometer-assessed physical activity: the role of sociodemographic factors. *American journal of epidemiology* 2014;179(6):781-90. doi: 10.1093/aje/kwt330 [published Online First: 2014/02/07]
 28. Sabia S, Dugravot A, Kivimaki M, et al. Effect of intensity and type of physical activity on mortality: results from the Whitehall II cohort study. *American journal of public health* 2012;102(4):698-704. doi: 10.2105/ajph.2011.300257 [published Online First: 2011/09/24]
 29. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* 2000;32(9 Suppl):S498-504. [published Online First: 2000/09/19]
 30. Stamatakis E, Hamer M, Mishra GD. Early adulthood television viewing and cardiometabolic risk profiles in early middle age: Results from a population, prospective cohort study. *Diabetologia* 2012;55(2):311-20.
 31. Júdeice P, Hamilton M, Sardinha L, et al. What is the metabolic and energy cost of sitting, standing and sit/stand transitions? *Eur J Appl Physiol* 2015;116(2):263-73. doi: 10.1007/s00421-015-3279-5
 32. Pearson N, Biddle SJ. Sedentary behavior and dietary intake in children, adolescents, and adults. A systematic review. *Am J Prev Med* 2011;41(2):178-88. doi: 10.1016/j.amepre.2011.05.002 [published Online First: 2011/07/20]

33. Mekary RA, Willett WC, Hu FB, et al. Isotemporal Substitution Paradigm for Physical Activity Epidemiology and Weight Change. *American journal of epidemiology* 2009;170(4):519-27. doi: 10.1093/aje/kwp163
34. Joint Health Surveys Unit. Self-reported physical activity in adults. In: Craig R, Mindell J, Hirani V, eds. Health Survey for England 2008. London: The Information Centre for Health and Social Care 2010:21-58.
35. Stephens BR, Granados K, Zderic TW, et al. Effects of 1 day of inactivity on insulin action in healthy men and women: interaction with energy intake. *Metabolism* 2011;60(7):941-9. doi: 10.1016/j.metabol.2010.08.014 [published Online First: 2010/11/12]
36. Statistics. OfN. The Time Use Survey, 2005 Office for National Statistics 2006.
37. Petersen C, Bauman A, Gronbaek M, et al. Total sitting time and risk of myocardial infarction, coronary heart disease and all-cause mortality in a prospective cohort of Danish adults. *International Journal of Behavioral Nutrition and Physical Activity* 2014;11(1):13.
38. Chomistek AK, Manson JE, Stefanick ML, et al. Relationship of Sedentary Behavior and Physical Activity to Incident Cardiovascular DiseaseResults From the Women's Health Initiative. *Journal of the American College of Cardiology* 2013;61(23):2346-54. doi: 10.1016/j.jacc.2013.03.031
39. Grøntved A, Hu FB. Television Viewing and Risk of Type 2 Diabetes, Cardiovascular Disease, and All-Cause Mortality. *JAMA: The Journal of the American Medical Association* 2011;305(23):2448-55. doi: 10.1001/jama.2011.812
40. van Uffelen JG, Wong J, Chau JY, et al. Occupational sitting and health risks: a systematic review. *Am J Prev Med* 2010;39(4):379-88. doi: 10.1016/j.amepre.2010.05.024 [published Online First: 2010/09/15]
41. Smith L, Hamer M, Ucci M, et al. Weekday and weekend patterns of objectively measured sitting, standing, and stepping in a sample of office-based workers: the active buildings study. *BMC Public Health* 2015;15(1):1-9. doi: 10.1186/s12889-014-1338-1
42. Pulsford RM, Blackwell J, Hillsdon M, et al. Intermittent walking, but not standing, improves postprandial insulin and glucose relative to sustained sitting: A randomised cross-over study in inactive middle-aged men. *Journal of science and medicine in sport* 2016 doi: 10.1016/j.jsams.2016.08.012 [published Online First: 2016/09/17]
43. Batty GD, Shipley M, Tabák A, et al. Generalizability of Occupational Cohort Study Findings. *Epidemiology* 2014;25(6):932-33. doi: 10.1097/ede.0000000000000184
44. Carter P, Gray LJ, Troughton J, et al. Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis. *British Medical Journal* 2010;341(c4229) doi: 10.1136/bmj.c4229

TABLES

Table 1. Subject characteristics at baseline (Phase 5, 1997-2011)^a

		Whole sample	Total reported sitting ^b (h/week)		
			≥0 & <33	≥33 & <50	≥50
n (cases)		4811 (402)	1671 (145)	1498 (103)	1642 (154)
Age (years)		43.83 (5.93)	46.43 (5.83)	43.50 (5.79)	41.49 (5.04)
Male (%)		72.77	31.88	32.16	35.96
Female (%)		27.23	42.37	28.40	29.24
BMI		25.68 (3.77)	25.61 (3.67)	25.61 (3.74)	25.80 (3.89)
Waist Circumference (cm)		89.03	88.00 (11.29)	89.14	89.88 (11.43)
Weight (kg)		77.40	75.64 (12.83)	77.53	78.95 (13.43)
Walking (min/day)		42.73	44.93 (24.33)	42.50	40.73 (21.26)
MVPA (h/week)		14.27	15.96 (13.10)	14.17	12.66 (10.44)
Employment	Administrative	47.04	28.68	33.63	37.69
Grade (%)	Prof/ Executive	43.17	37.17	29.90	32.93
	Clerical/Support	9.79	53.08	24.63	22.29
Alcohol consumption (units/week)		13.99	12.56 (14.23)	14.01	15.42 (15.66)
Smoking Status (%)	Never	52.09	33.64	30.77	35.59
	Ex	38.25	36.14	32.61	31.25
	Current	9.67	35.05	27.31	37.63
Self-rated health (%)	Very Good	53.69	36.82	30.82	32.37
	Good	37.00	32.19	31.01	36.80
	Fair or Poor	9.31	32.81	33.48	33.71

^a Data are mean (SD) unless otherwise stated; ^bWork-related sitting (includes sitting during commuting and driving) and leisure time sitting at home

Table 2. 13-year risk of incident type II diabetes according to categories of sitting behaviours and total sitting

	n/ cases	Person years (x100)	Rate (per 1000)	Model 1 ^b HR (95% CI)	Model 2 ^c HR (95% CI)	Model 3 ^d HR (95% CI)
Work sitting^a (h/week)						
≥0 & <15	1794/152	22.73	6.69	1	1	1
≥15 & <35	1069/92	13.95	6.60	1.12 (0.85, 1.47)	1.15 (0.87, 1.51)	1.14(0.87, 1.51)
≥35	1772/142	23.62	6.01	1.14 (0.88, 1.49)	1.18 (0.90, 1.54)	1.17(0.89, 1.53)
<i>P</i> _{trend}				0.57	0.44	0.48
TV sitting (h/week)						
≥0 & <11	1235/87	16.27	5.35	1	1	1
≥11 & <16	1212/107	15.75	6.80	1.35 (1.02, 1.80)	1.31 (0.98, 1.74)	1.33 (1.00, 1.77)
≥16	937/90	11.87	7.58	1.49 (1.11, 2.01)	1.38 (1.02, 1.86)	1.39 (1.03, 1.88)
<i>P</i> _{trend}				0.02	0.07	0.05
Non-TV Leisure Time Sitting at Home (h/week)						
≥0 & <8	738/70	9.61	7.28	1	1	1
≥8 & <16	1650/119	21.57	5.51	0.79 (0.59, 1.07)	0.78 (0.58, 1.05)	0.78 (0.57, 1.05)
≥16	793/76	10.29	7.39	1.05 (0.76, 1.46)	0.99 (0.71, 1.37)	0.98 (0.70, 1.36)
<i>P</i> _{trend}				0.11	0.15	0.15
Leisure Time Sitting at Home (h/week)						
≥0 & <15	1311/96	17.10	5.61	1	1	1
≥15 & <25	1698/141	22.24	6.34	1.28 (0.98, 1.66)	1.25 (0.96, 1.63)	1.26 (0.97, 1.64)
≥25	1726/159	22.11	7.19	1.40 (1.07, 1.81)	1.27 (0.98, 1.65)	1.27 (0.98, 1.66)
<i>P</i> _{trend}				0.04	0.16	0.15
Total sitting (h/week)						
≥0 & <33	1671/145	21.11	6.87	1	1	1
≥33 & <50	1498/103	19.77	5.20	0.90 (0.70, 1.17)	0.87 (0.67, 1.14)	0.87 (0.67, 1.13)
≥50	1642/154	21.58	7.14	1.35 (1.05, 1.72)	1.28 (1.00, 1.65)	1.26 (1.00, 1.62)
<i>P</i> _{trend}				0.01	0.01	0.01
Total sitting excluding TV (h/week)						
≥0 & <33	1162/98	14.77	6.64	1	1	1
≥33 & <50	1040/76	13.66	5.67	0.96 (0.70, 1.31)	0.93 (0.68, 1.28)	0.93 (0.68, 1.27)
≥50	1181/109	15.47	7.05	1.28 (0.95, 1.73)	1.25 (0.92, 1.68)	1.23 (0.91, 1.66)
<i>P</i> _{trend}				0.12	0.14	0.15

^a includes sitting during commuting and driving; ^b adjusted for age, gender, ethnicity and last known employment grade (including Phase 5); ^c also adjusted smoking, alcohol consumption, frequency of fruit and vegetable consumption, physical functioning and self-rated health; ^d also adjusted for moderate to vigorous physical activity and walking time.

Table 3. 13-year risk of incident type II diabetes events according to categories of sitting behaviours and total sitting following adjustments for baseline BMI.

	n/ cases	Person- years (x1000)	Rate (per 1000 per year)	Model 3 ^a HR (95% CI)	Model 4 ^b HR 95% CI
TV sitting (h/week)					
≥0 & <11	1235/87	16.27	5.35	1	1
≥11 & <16	1212/107	15.75	6.80	1.33 (1.00, 1.77)	1.29 (0.96, 1.73)
≥16	937/90	11.87	7.58	1.39 (1.03, 1.88)	1.31 (0.96, 1.76)
<i>P_{trend}</i>				0.05	0.14
Leisure Time Sitting at Home (h/week)					
≥0 & <15	1311/96	17.10	5.61	1	1
≥15 & <25	1698/141	22.24	6.34	1.26 (0.97, 1.64)	1.24 (0.95, 1.61)
≥25	1726/159	22.11	7.19	1.27 (0.98, 1.66)	1.24 (0.95, 1.61)
<i>P_{trend}</i>				0.15	0.22
Total sitting (h/week)					
≥0 & <33	1671/145	21.11	6.87	1	1
≥33 & <50	1498/103	19.77	5.20	0.87 (0.67, 1.13)	0.86 (0.66, 1.12)
≥50	1642/154	21.58	7.14	1.26 (1.00, 1.62)	1.19 (0.92, 1.55)
<i>P_{trend}</i>				0.01	0.06

^aadjusted for age, gender, ethnicity and last known employment grade (including Phase 5), smoking, alcohol consumption, frequency of fruit and vegetable consumption, physical functioning, self-rated health, and moderate to vigorous physical activity and walking time; ^b also adjusted for baseline body mass index