Device-assessed total and prolonged sitting time: associations with anxiety, depression, and health-related quality of life in adults

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Published as: Biddle, S. J. H., Henson, J., Davies, M. J., Khunti, K., Sutton, S., Yates, T., & Edwardson, C. L. (2021). Device-assessed total and prolonged sitting time: associations with anxiety, depression, and health-related quality of life in adults. *Journal of Affective Disorders, 287*, 107–114. doi:10.1016/j.jad.2021.03.037

Abstract

Objective: Assessment of sitting has been challenging and nuances in the length of sitting are often missed.

Methods: The present study assessed total, short and prolonged sitting time, and number of breaks from sitting, and their association with anxiety, depression, and health-related quality of life (HRQoL). Adults (M=59.1 years) in three studies (n=1,574) wore the activPAL accelerometer (thigh) to obtain a measure of sitting, and the Actigraph accelerometer (hip) for estimating moderate-to-vigorous physical activity (MVPA). Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale, and HRQoL using the EQ-5D-5L (for health state and utility scores). Generalised linear modelling tested associations.

Results: Total and prolonged sitting were associated with higher depression [total: β = 0.132 (0.010, 0.254); prolonged: β = 0.178 (0.053, 0.304)] and worse HRQoL health state scores [(total: β = -0.985 (-1.471, -0.499); prolonged: β = -0.834 (-1.301, -0.367)] and utility scores [(total: β = -0.008 (-0.012, -0.003); prolonged: β = -0.008 (-0.012, -0.004], after controlling for covariates. MVPA was associated with better HRQoL health state and utility scores [health state: β =0.554 (0.187, 0.922); utility: β = 0.001 (0.001, 0.002)]. Total and prolonged sitting were associated with a 14% increased odds of being in the borderline/abnormal category for depression. No interactions were observed between MVPA status (active vs. inactive) and total or prolonged sitting. Anxiety was unrelated to any sitting variable.

Conclusion: Device-based measures of both total and prolonged sitting time were associated with depression and health-related quality of life, but not anxiety.

Key words: accelerometer, activPAL, Actigraph, sedentary, physical activity.

Introduction

Sedentary behaviour has been defined as sitting, lying, or reclining with low energy expenditure during waking hours [1], and has been the subject of growing interest and research over the past decade or so [2]. This interest has developed as a result of growing awareness of 'sedentary lifestyles' in contemporary society, reflected in trends such as the ubiquitous use of home-based entertainment, new technology, increasing car use, and the growth of seated occupations and computers in the workplace. Prevalence from studies using accelerometers to estimate sedentary time show that middle-to-older adults are sedentary for about 9-11 hours each day, reflecting 58-82% of device wear time [3]. Economic costs of physical inactivity (low levels of physical activity and not just sedentary time) are considerable, as demonstrated by Ding et al. [4] in their analysis of 142 countries.

Initial epidemiological data showed associations between self-reported sedentary behaviour and various health outcomes, such as greater risk for all-cause mortality [5-7]. Moreover, evidence has shown that reducing or breaking up prolonged sitting time can be beneficial for cardiometabolic health [8-10].

Sedentary behaviour research has focused mainly on physical health outcomes, although an increasing interest has been shown in mental health. For example, two meta-analyses have been published on sedentary behaviour and depression [11 12]. Both analyses report higher levels of sedentary behaviour being significantly associated with higher depression. However, only two studies (<10%) in Zhai et al's meta-analysis and none in Huang et al. included studies using wearable devices for the assessment of sedentary time. A meta-analysis concerning sedentary behaviour and risk of anxiety also synthesised primarily self-reported sedentary behaviour [13]. Only one study used accelerometers. The overall association between

93 sedentary behaviour and risk of anxiety was positive, significant, but small. These
94 systematic reviews show that further work is needed to test such associations using
95 device-based assessment rather than reported behaviours, with the latter having
96 significant issues concerning recall bias and validity.

97 The evidence linking sedentary behaviour with health-related quality of life
98 (HRQoL) has also relied on reported measures of sedentary behaviour or sitting
99 time. HRQoL measures will include assessments of mental health, such as anxiety
100 and depression. However, generic perceptions of life quality, including functional
101 status, are also assessed. This might be important in the context of sedentary
102 behaviour. For example, intervention studies that have reduced sitting in the
103 workplace have reported improvements in some domains of musculo-skeletal health
104 and quality of life [14 15]. Similarly, a prospective cohort study from Spain has shown
105 higher scores on health-related quality of life for older adults with lower levels of self-
106 reported leisure-time sitting [16]. It is important, therefore, to assess both psychological
107 and broader quality of life constructs in research on sedentary behaviour.

108 In addition to possible links between health and the amount of sedentary time,
109 researchers have also suggested that breaking up sedentary time might be
110 important. This can be assessed using device-based measures of sedentary breaks
111 or interruptions, and the number of 'sit-to-stand transitions'. Okely et al. [17], for
112 example, found in one of three cohorts studied that more sit-to-stand transitions were
113 associated with lower depression symptoms. Hallgren et al. [18], using self-reported
114 data from a large sample of Swedish adults, found that more frequent interruptions to
115 sedentary time were associated with lower odds of symptoms of depression and
116 anxiety.

There has been some debate concerning the distinction between sedentary behaviour and physical activity, and how best to account for both behaviours in analyses [19]. While it has been agreed that not meeting physical activity guidelines (low physical activity or 'inactivity') is not the same as time spent in low energy sitting ('sedentary behaviour'), the two behaviours may interact in respect of health outcomes. For example, in an analysis of harmonised data, premature mortality risk was greater for those with higher levels of sitting. But this was much less evident for those with very high levels of MVPA [20]. Although many studies statistically control for MVPA in their analyses of physical and mental health effects of sedentary behaviour, it is important to also test whether MVPA is an effect modifier. That is, do the associations between sedentary time and outcome measures, such as depression, differ by different levels of MVPA? In an analysis of nearly 9,000 women who reported sitting time and physical activity from the Australian Longitudinal Study on Women's Health, it was found that physical activity clearly attenuated the risk of depression that was associated with sitting [21]. The likelihood of depressive symptoms in women who sat more than 7 hours/day and did no physical activity was triple that of women who sat 4 or more hours/day and met physical activity guidelines. It is important, therefore, to assess both sedentary behaviour and physical activity, and to test for effect modification.

The main purpose of the present study, therefore, is to assess the association between sitting time, assessed by the activPAL accelerometer, and indices of mental health and HRQoL in adults, and whether associations are modified by levels of MVPA. We tested four aspects of sitting: total sitting time, prolonged sitting time, short sitting time, and number of breaks in sitting as well as MVPA time, and three measures of mental health and perceptions of well-being: anxiety, depression, and

health-related quality of life. Findings may help guide preventive intervention work and personalised treatments.

Method

Participants and recruitment

Data from three studies were combined for the present analyses. This included baseline data from *Project STAND*, collected in 2010 [22 23], 36 month follow up data from *Walking Away from Diabetes*, collected in 2013-14 [24 25], and baseline data from *PROPELS* [26], collected in 2013-14. All have been described in detail elsewhere, as cited. Participants deemed to be at a high risk of developing type 2 diabetes (T2DM) were the target group for all three projects, although the inclusion criteria varied slightly between studies. All were ambulatory adults.

Project STAND. General Practice (GP) databases in the counties of Leicestershire and Northamptonshire, UK, were searched for adults aged 18-40 years with baseline BMI in the obese range (≥30kg/m^2;≥27.5kg/m^2 for South Asians) or, if they were in the overweight range (≥25kg/m^2; ≥23kg/m^2 for South Asians), they were required to have one or more additional risk factors for diabetes. These included i) family history of diabetes or cardiovascular disease in a first degree relative, ii) previous gestational diabetes, iii) polycystic ovarian syndrome, iv) HbA1c ≥5.8%, and v). impaired glucose tolerance and/or impaired fasting glucose. The study was approved by the Nottingham National Health Service (NHS) Research Ethics Committee.

Walking Away from Diabetes. Ten GP databases within Leicestershire, UK, were searched using a modified version of the automated Leicester Risk Score [27] and ranked individuals for diabetes risk using predefined weighted variables. Adults

aged 30-75 years scoring in the 90th percentile within each GP database were invited. The study was approved by the Nottingham NHS Research Ethics Committee.

PROPELS: GP databases within Leicestershire and Cambridge, UK, were searched for adults aged 40–74 years for white European, or aged 25–74 years for South Asian, who had a previous blood glucose or HbA1c result recorded in the prediabetes range [28] within the last 5 years. In Cambridge, existing research databases were also used to identify eligible individuals. The study was approved by the NHS East Midlands Research Ethics Committee.

All interested participants across studies were invited to a measurement session where the study was explained and informed consent was taken.

Demographics and anthropometric measures

Age, sex, ethnicity, smoking status, medical history and medication were assessed by a healthcare professional via a short interview. Height (Leicester Height Measure), body weight and body fat (both Tanita, West Drayton, UK), and waist circumference (midpoint between the lower costal margin and iliac crest) were measured to the nearest 0.5cm, 0.1 kg, 0.1%, and 0.5 cm, respectively. Body mass index (BMI) was calculated by the Tanita scales as kg/m^2. Three measurements of arterial blood pressure were taken in the sitting position (Omron Healthcare, Henfield, UK); the average of the last two measurements was used.

Device-measured sedentary behaviour and physical activity

The activPAL accelerometer (PAL Technologies, Glasgow, UK) was used to assess sitting (total sitting time, short sitting time of accumulated bouts lasting <30 minutes, and prolonged accumulated time in bouts lasting ≥30 minutes), standing,

and stepping time. The activPAL has been shown to be highly accurate in measuring these behaviours [29-31]. The device was worn on the thigh, using a 24hr wear protocol, for 10 days in Project STAND and 7 days in Walking Away from Diabetes and PROPELS. Default settings were used for initialisation of devices. To separate valid waking hours data from everything else, a validated algorithm was applied to the data [32]. Heat maps of processed data were created [33] to visually check the processed valid and invalid data. Any occasions where the algorithm appeared to incorrectly code data as valid/invalid, sleep/wear diaries were checked against the heat maps and data were corrected if necessary. Data were considered valid if a day consisted of ≥10 hours of waking wear data, ≥500 step events (i.e., 1000 steps) and <95% spent in any one behaviour (e.g., sitting, standing, or stepping) [32]. Participants were required to have at least one valid day to be included in the present study.

To assess moderate-to-vigorous physical activity (MVPA), participants wore the Actigraph accelerometer (ActiGraph LLC, Pensacola, FL, USA) on their waist during waking hours on the same days as the activPAL device was worn. All data were reintegrated into 60 second epochs for processing. Non-wear was defined as ≥60 minutes of consecutive zero counts with no allowance for counts greater than zero, and data were considered valid if a day consisted of ≥10 hours of waking wear data. MVPA was derived using a threshold of ≥1952 counts/min [34]. Data were processed using a commercially available package (KineSoft version 3.3.76, Loughborough, UK).

Anxiety and depression

Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) [35]. This includes 14 domains: seven for anxiety (e.g., “I feel tense or wound up”) and seven for depression (e.g., “I feel cheerful”), with each

item scored on a 4-point scale from 0-3 (e.g., 0='not at all'; 3='definitely'; some items were reverse-scored), thus allowing a score of 0-21 for both outcome measures. Higher numbers are indicative of an increase in the number and severity of symptoms, and a score of ≥8 on either variable can be used to identify at least 'borderline' levels of anxiety and depression. When using a threshold score of 8 to identify individuals with anxiety or depression disorders, sensitivity and specificity values between 0.7 and 0.9 have been reported [36]. HADS is widely used within primary care, community, and research settings, and it has been shown to be a valid measure for detecting clinical anxiety and depression [37].

Health-related quality of life

Health-related quality of life (HRQoL) was assessed using the European Quality of Life-5 dimensions scale (version EQ-5D-5L) [38]; it is used widely in health economic evaluations. It assesses perceptions of both mental and physical health, with five dimensions of mobility (e.g., "I have no problems in walking about"), self-care ("I am unable to wash or dress myself"), usual activities ("I have slight problems doing my usual activities"), pain/discomfort ("I have moderate pain or discomfort"), and anxiety/depression ("I am slightly anxious or depressed"). Each dimension has five levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. These can be presented as a health profile and converted to a single summary index score ('health utility score') with ranges from 'states worse than dead' (0 or below) to 1 (full health), anchoring dead at 0 [39]. The EQ-5D-5L also includes the EQ Visual Analogue Scale (EQ VAS; 'health state score'). Participants self-reported perceptions of today's health by placing a cross mark on a scale ranging from 0 ('worst health you can imagine') to 100 ('best health you can imagine') [40].

240 ***Statistical analysis***

241 Baseline characteristics were presented as mean (SD) or median
242 (interquartile range) for continuous variables and as number (%) for categorical
243 variables. There were four outcome variables - HADS anxiety score, HADS
244 depression score, EQ-5D health state score, and EQ-5D health utility score. These
245 were analysed at one time point using generalised linear models (GLM) and were
246 adjusted for socio-demographic and health data [age, sex, ethnicity (white and non-
247 white), smoking status (never and previous/current), heart disease, history of stroke,
248 taking blood pressure medication and lipid medication], and activPAL waking wear
249 time in Model 1. Further adjustments were made for MVPA and sitting time in Model
250 2, and for waist circumference in Model 3 (the most adjusted model). GLMs are
251 presented as beta coefficients (95% CI). As anxiety and depression scores were
252 positively skewed, the data were analysed using a gamma distribution with an
253 identity link. This also yielded the best model fit for the other outcomes of interest. A
254 small constant (10^{-3}) was added to any of the dependent variables recorded as zero.

255 Significant observations in Model 3 were followed up with interaction terms to
256 assess whether associations between the sitting variables and anxiety, depression,
257 EQ-5D health state or EQ-5D utility score were modified by levels of MVPA (active
258 vs. inactive). In order for individuals to be classed as active, they needed to have
259 undertaken at least 150 minutes of MVPA over 7 days [41]. Only those individuals with
260 ≥7 valid days were included in the interaction analyses. For those with >7 days, total
261 MVPA time was scaled backwards.

262 Categorical data were analysed using a binary response and reported as an
263 odds ratio (OR), representing the effects of sitting, prolonged sitting, and short sitting
264 on the odds of depression or anxiety. Anxiety and depression were categorised into

those without depression or anxiety (score of 0-7) and those with mild-severe depression or anxiety (a score of ≥8) [35].

Cases are included based on having at least one valid activPAL day data. Sensitivity analyses were carried out by including only those with at least four days of activPAL data. Results are presented per 60 minutes for sitting variables and per 10 minutes for MVPA. Two-tailed *p* values of 0.05 or less were considered statistically significant for main effects and $p<0.1$ for interactions. All analyses were performed using IBM SPSS Statistics v26.0 (Chicago, IL, USA).

Results

Descriptive statistics

As shown in Table 1, the sample comprised 1,574 adults with a mean age of 59 years. The sample was split reasonably equally by sex, with 76% being white European. From an average of 15.7 hours of valid waking wear time for the activPAL monitor, participants had a mean total sitting time of 9.2 hours/day, with 4.9 hours/day (53.3% of total sitting time) in prolonged sitting. The overall sample averaged just over 22 minutes/day of MVPA, but this value had a wide dispersion. In total, 53.3% of the individuals who had ≥7 valid days of accelerometer data achieved at least 150 minutes/week of MVPA. Anxiety and depression scores averaged in the 'normal' range, with 29.8% for anxiety and 15.2% for depression being at borderline-to-abnormal levels. EQ-5D utility score suggested that the sample reported quite positive HRQoL see [39], and the EQ-5D health state score was suggestive of reasonably positive perceptions of their overall health with a score of 80 from a possible 100.

289 Table 1 about here

290 Associations between sitting variables and MVPA and anxiety, depression,
291 and quality of life are shown in Table 2. Significant associations were evident for total
292 sitting time and prolonged sitting time with depression, health state and utility score
293 and for MVPA with health state and utility score. These remained significant at all
294 model levels of adjustment. Higher levels of total and prolonged sitting were
295 associated with higher scores for depression and lower scores for HRQoL and
296 higher levels of MVPA were associated with higher HRQoL scores. Supplementary
297 Table S1 shows the results of the sensitivity analyses for those with 4 or more days
298 of assessment with the activPAL. Results are largely unchanged from Table 2. There
299 were no significant associations for any of the sitting variables with anxiety or for
300 short sitting time and breaks from sitting with any outcome.

301 Table 2 about here

302 Results for anxiety and depression when dichotomised into normal vs.
303 borderline/abnormal scores are shown in Table 3. Total sitting time and prolonged
304 sitting were associated with greater odds of being in the borderline/abnormal
305 category for depression, after adjustments including MVPA [total: odds = 1.135
306 (1.040, 1.238); prolonged: odds = 1.141 (1.054, 1.236)]. No other associations were
307 observed.

308 Table 3 about here

309 No significant interactions were observed when examining associations between
310 those classed as physically inactive or active and total and prolonged sitting time (see
311 Supplementary Table S2).

312 **Discussion**

313 The main aim of this study was to assess cross-sectional associations
314 between device-measured sitting time and measures of mental health and health-
315 related quality of life while also accounting for levels of MVPA as a covariate and a
316 possible effect modifier. Higher levels of total and prolonged sitting time were
317 associated with less healthy scores for depression and quality of life, after adjusting
318 for key confounders including MVPA and waist circumference. When participants
319 were dichotomised into physically inactive or active, the interactions were non-
320 significant, suggesting that these associations were consistent across both activity
321 categories. Furthermore, MVPA was associated with better quality of life.

322 With strong evidence showing that MVPA can prevent and reduce depression
323 e.g., [42], it might be expected that those who are more physically active, but sit a lot,
324 would be protected from elevated levels of depression. More work is required on this.
325 Notwithstanding possible reverse causality, there are plausible mechanisms for
326 associations between sedentary behaviour and depression, such as through
327 underlying inflammatory pathways and neurotransmitter function [43]. Dempsey et al.
328 [44] hypothesise that sedentary behaviour may affect chronic disease risk factors
329 through mechanisms that include insulin resistance, hyperglycemia, obesity,
330 dyslipidemia, atherosclerosis, hypertension, and possibly cerebrovascular function.
331 However, Dempsey et al. also state that “current consensus of understanding on the
332 hypothesized mechanisms underlying sedentary behavior and chronic disease is
333 largely based on expert opinion or narrative reviews, both of which are prone to bias.
334 More targeted research is required to investigate the specific pathophysiological
335 pathways through which sedentary behavior may independently influence chronic
336 disease risk” (p. 53). This statement was made more in the context of
337 cardiometabolic and related chronic conditions rather than mental and cognitive

outcomes. Clearly more work is required bridging physical and psychological/cognitive processes in the context of sedentary behaviour.

Notwithstanding the reporting of significant associations in this study, it is also important to investigate effect sizes. An increase of one hour in total sitting is associated only with a 0.182 (least adjusted) and 0.132 (most adjusted) unit increase in HADS depression scores. This is not clinically meaningful (Lemay et al., 2019). Similar arguments could be made for HRQoL. However, both total and prolonged sitting were associated with greater odds of being in the borderline/abnormal category for depression. These data are suggestive of more meaningful effects, with a one hour increase in either total or prolonged sitting time being associated with a 14% increase in the odds of being in the higher depression category. As argued by Orben [45] in her analysis of the health effects of the growth in technology, it is important for stakeholders to see reports of the size of effects or associations and whether these are important. One additional argument regarding mental health is that if we are to better understand a wider range of effects of sedentary behaviour beyond typical cardiometabolic markers, measures of total or prolonged sitting will need to be contextualised alongside reported measures of different sedentary behaviours where social context and psychological engagement are assessed.

For the EQ-5D utility score, participants self-rated their mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The measure of HRQoL (health state) involved a rating on a visual analogue scale of current health perceptions for the day of assessment. All of these dimensions of quality of life might be expected to be associated with sedentary time, and especially prolonged sitting. Again, reverse causality is plausible, but higher and more prolonged periods of sitting may also create feelings of lethargy and inertia and thus contribute to poorer

363 physical function. Plausibly, higher levels of MVPA can be expected to have a strong
364 role to play.

365 If these findings are confirmed, interventions may need to be implemented
366 that target reductions in prolonged sitting [2 46], and this may include advice given
367 when managing patients with a variety of chronic conditions. The interventions will
368 need to involve displacing sedentary time with more light and moderate-intensity
369 movement, and these, in turn, may alleviate some of the negative symptoms of low
370 HRQoL. Experimental [47] and epidemiological [48] evidence supports such a proposal
371 for health biomarker outcomes.

372 Results suggested that neither total sitting time nor prolonged sitting are
373 associated with anxiety. This contrasts with the conclusion by Teychenne et al. [49]. In
374 their review of the early literature on this topic, they found nine studies (seven cross-
375 sectional), and concluded that small associations existed. However, nearly all papers
376 reviewed assessed screen time as a marker of sedentary behaviour, and no study
377 used an accelerometer to assess sedentary time. Similarly, the meta-analysis by
378 Allen et al. [13] showed that sedentary behaviour was associated with the risk of
379 anxiety in a small way, but included only one study assessing sedentary time with an
380 accelerometer.

381 Conceptually, it might be argued that high anxiety could be reflected in both
382 less and more active behaviours, and more sedentary time may occur through
383 screen time, such as passive TV viewing. However, the current study is unable to
384 shed light on this but more needs to be known about behaviours undertaken while
385 sitting, including the degree of passivity.

386 We found no evidence for associations between the outcome measures and
387 sedentary behaviour assessed as short sitting periods or breaking up sitting time.
388 There has been some debate about the importance of breaking up prolonged sitting
389 time since the publication of the seminal study by Healy and colleagues [50]. However,
390 that study investigated cardiometabolic outcomes and it remains to be seen if other
391 measures, including mental health, are associated with the patterning rather than
392 volume of sitting. Currently, messages recommending the breaking up of prolonged
393 sitting – common in national and international guidelines – is still contested [9 51].

394 Strengths of the present study include assessments of over 1,500 adults at
395 risk of diabetes and other health problems (e.g., BMI averaging 30, and 39% on
396 blood pressure medication). Moreover, device-based assessments of sitting and
397 MVPA were undertaken. Recognised measures of mental health and HRQoL were
398 used, and analyses included controlling for multiple confounders. Limitations of the
399 study include the cross-sectional design and the sampling of an at-risk group of
400 overweight or obese adults. Results may not apply to those with other health-risk
401 profiles. In addition, our measure of total sitting time may not reflect some of the
402 more unhealthy aspects of sitting, such as prolonged periods of passive behaviours
403 in front of the TV. It has been suggested that not all sedentary behaviours act on
404 health in the same way [52], probably due to co-existing behaviours, such as diet and
405 levels of passivity [53]. To assess sedentary behaviours in this way will require mixed
406 methods studies where device-based measures are combined with context-specific
407 self-reported behaviours.

408 The use of self-reported psychological instruments for the assessment of the
409 mental health outcomes of interest will be less valid than a structured clinical
410 interview. However, the instruments we chose were practical for the large samples

411 we were assessing, and the instruments have acceptable validity. Finally, the cross-
412 sectional design cannot rule out the possibility that those with poorer mental health
413 and HRQoL choose to sit more – the reverse causality argument.

414 In conclusion, in a sample of over 1,500 overweight and obese adults, device-
415 based measures of total sitting time and prolonged sitting time were detrimentally
416 associated with depression and health-related quality of life, but not anxiety. Total
417 and prolonged sitting time were associated with increased odds of being in the
418 borderline/abnormal category for depression. MVPA was beneficially associated with
419 health-related quality of life.

420

421

Author contributions

SJHB and CE conceived the idea for this manuscript and drafted the paper. JH performed the statistical analyses, which were informed by TY. CE processed the accelerometer data. All authors revised the manuscript and approved the final version.

Acknowledgements

We would like to acknowledge and thank the investigators of the STAND study (Trish Gorely, Myra Nimmo, Laura Gray) and PROPELS trial (Simon Griffin, Wendy Hardeman, Helen Eborall, Jacqui Troughton, Laura Gray). We would like to thank the individuals who participating in the studies as well as the clinical and administrative staff who contributed to the data collection.

Funding

The analysis was supported by the National Institute for Health Research (NIHR) Leicester Biomedical Research Centre which is a partnership between University Hospitals of Leicester NHS Trust, Loughborough University, and the University of Leicester, and the National Institute for Health Research Applied Health Research Collaboration–East Midlands (NIHR ARC–EM). The *STAND* study was funded by a grant from the Medical Research Council (UK) under the National Prevention Research Initiative (Project #91409). The *Walking Away from Diabetes* study was funded by the National Institute for Health Research (NIHR) Collaboration in Applied Health Research and Care for Leicestershire, Northamptonshire and Rutland (CLAHRC LNR) and the Collaboration for Leadership in Applied Health Research and Care – East Midlands (CLAHRC – EM). The *PROPELS* trial was funded by the Health Technology Assessment (HTA) Programme, National Institute for Health

446 Research. The views expressed are those of the authors and not necessarily those
447 of the NHS, NIHR, or Department of Health. There are no other conflicts of interest.

References

1. Tremblay MS, Aubert S, Barnes JD, et al. Sedentary Behavior Research Network (SBRN): terminology consensus project process and outcome. *International Journal of Behavioral Nutrition and Physical Activity* 2017;14 doi: 10.1186/s12966-017-0525-8
2. Owen N, Healy GN, Dempsey PC, et al. Sedentary behavior and public health: integrating the evidence and identifying potential solutions. *Annual Review of Public Health* 2020;41(1):265-87. doi: 10.1146/annurev-publhealth-040119-094201
3. Ekelund U, Tarp J, Fagerland MW, et al. Joint associations of accelerometer-measured physical activity and sedentary time with all-cause mortality: a harmonised meta-analysis in more than 44 000 middle-aged and older individuals. *British Journal of Sports Medicine* 2020;54(24):1499-506. doi: 10.1136/bjsports-2020-103270
4. Ding D, Lawson KD, Kolbe-Alexander TL, et al. The economic burden of physical inactivity: a global analysis of major non-communicable diseases. *The Lancet* 2016;388(10051):1311-24. doi: 10.1016/S0140-6736(16)30383-X
5. Katzmarzyk PT, Powell KE, Jakicic JM, et al. Sedentary behavior and health: update from the 2018 Physical Activity Guidelines Advisory Committee. *Medicine & Science in Sports & Exercise* 2019;51(6):1227-41. doi: 10.1249/mss.0000000000001935
6. Wilmot EG, Edwardson CL, Achana FA, 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. Biddle SJH, Bennie J, Bauman A, et al. Too much sitting and all-cause mortality: is there a causal link? *BMC Public Health* 2016;16(1):635. doi: 10.1186/s12889-016-3307-3
8. Dunstan DW, Kingwell BA, Larsen R, et al. Breaking up prolonged sitting reduces postprandial glucose and insulin responses. *Diabetes Care* 2012;35(5):976-83. doi: 10.2337/dc11-1931
9. Biddle SJH, Bennie JA, De Cocker K, et al. Controversies in the science of sedentary behaviour and health: Insights, perspectives and future directions from the 2018 Queensland Sedentary Behaviour Think Tank. *International Journal of Environmental Research and Public Health* 2019;16:4762. doi: 10.3390/ijerph16234762
10. Chastin SF, Egerton T, Leask C, et al. Meta-analysis of the relationship between breaks in sedentary behavior and cardiometabolic health. *Obesity* 2015;23(9):1800-10. doi: 10.1002/oby.21180
11. Zhai L, Zhang Y, Zhang D. Sedentary behaviour and the risk of depression: a meta-analysis. *British Journal of Sports Medicine* 2015;49:705-09. doi: 10.1136/bjsports-2014-093613
12. Huang Y, Li L, Gan Y, et al. Sedentary behaviors and risk of depression: a meta-analysis of prospective studies. *Translational Psychiatry* 2020;10(1):26. doi: 10.1038/s41398-020-0715-z
13. Allen MS, Walter EE, Swann C. Sedentary behaviour and risk of anxiety: a systematic review and meta-analysis. *Journal of Affective Disorders* 2019;242:5-13. doi: 10.1016/j.jad.2018.08.081

14. Pronk NP, Katz AS, Lowry M, et al. Reducing occupational sitting time and improving worker health: The Take-a-Stand Project, 2011. *Preventing Chronic Disease* 2012;9:110323. DOI: http://dx.doi.org/10.5888.pcd9.23.
15. Edwardson CL, Yates T, Biddle SJH, et al. Effectiveness of the Stand More AT (SMArT) Work intervention: cluster randomised controlled trial. *The BMJ* 2018;363:k3870. doi: 10.1136/bmj.k3870
16. Balboa-Castillo T, León-Muñoz LM, Graciani A, et al. Longitudinal association of physical activity and sedentary behavior during leisure time with health-related quality of life in community dwelling older adults. *Health and Quality of Life Outcomes* 2011;9:47. doi: 10.1186/1477-7525-9-47
17. Okely JA, Čukić I, Shaw RJ, et al. Positive and negative well-being and objectively measured sedentary behaviour in older adults: evidence from three cohorts. *BMC Geriatrics* 2019;19(1):28. doi: 10.1186/s12877-019-1026-1
18. Hallgren M, Nguyen T-T-D, Owen N, et al. Associations of interruptions to leisure-time sedentary behaviour with symptoms of depression and anxiety. *Translational Psychiatry* 2020;10(1):128. doi: 10.1038/s41398-020-0810-1
19. van der Ploeg HP, Hillsdon M. Is sedentary behaviour just physical inactivity by another name? *International Journal of Behavioral Nutrition and Physical Activity* 2017;14(1):142. doi: 10.1186/s12966-017-0601-0
20. 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
21. van Uffelen JGZ, Gellecum YRv, Burton NW, et al. Sitting-time, physical activity, and depressive symptoms in mid-aged women. *American Journal of Preventive Medicine* 2013;45(3):276-81. doi: 10.1016/j.amepre.2013.04.009
22. Wilmot EG, Davies M, Edwardson C, et al. Rationale and study design for a randomised controlled trial to reduce sedentary time in adults at risk of type 2 diabetes mellitus: project stand (Sedentary Time ANd diabetes). *BMC Public Health* 2011;11(1):908. doi: 10.1186/1471-2458-11-908
23. Biddle SJH, Edwardson CL, Wilmot EG, et al. A randomised controlled trial to reduce sedentary time in young adults at risk of type 2 diabetes mellitus: Project STAND (Sedentary Time ANd Diabetes). *PLoS ONE* 2015;10(12):e0143398. doi: 10.1371/journal.pone.0143398
24. Yates T, Davies MJ, Henson J, et al. Walking away from type 2 diabetes: trial protocol of a cluster randomised controlled trial evaluating a structured education programme in those at high risk of developing type 2 diabetes. *BMC Family Practice* 2012;13(1):46. doi: 10.1186/1471-2296-13-46
25. Yates T, Edwardson CL, Henson J, et al. Walking Away from Type 2 diabetes: a cluster randomized controlled trial. *Diabetic Medicine* 2017;34(5):698-707. doi: 10.1111/dme.13254
26. Yates T, Griffin S, Bodicoat DH, et al. PRomotion Of Physical activity through structured Education with differing Levels of ongoing Support for people at high risk of type 2 diabetes (PROPELS): study protocol for a randomized controlled trial. *Trials* 2015;16(1):289. doi: 10.1186/s13063-015-0813-z
27. Gray LJ, Taub NA, Khunti K, et al. The Leicester Risk Assessment score for detecting undiagnosed Type 2 diabetes and impaired glucose regulation for

use in a multiethnic UK setting. *Diabetic Medicine* 2010;27(8):887-95. doi: 10.1111/j.1464-5491.2010.03037.x
28. National Institute for Health & Care Excellence. Type 2 diabetes: prevention in people at high risk - Public health guideline. https://www.nice.org.uk/guidance/ph38/resources/type-2-diabetes-prevention-in-people-at-high-risk-pdf-19963041921972012.
29. Edwardson CL, Rowlands AV, Bunnewell S, et al. Accuracy of posture allocation algorithms for thigh- and waist-worn accelerometers. *Medicine & Science in Sports & Exercise* 2016;48(6):1085-90. doi: 10.1249/MSS0000000000000865
30. Sellers C, Dall P, Grant M, et al. Validity and reliability of the activPAL3 for measuring posture and stepping in adults and young people. *Gait & Posture* 2016;43:42-47. doi: 10.1016/j.gaitpost.2015.10.020
31. Kozey-Keadle S, Libertine A, Lyden K, et al. Validation of wearable monitors for assessing sedentary behavior. *Medicine and Science in Sports & Exercise* 2011;43(8):1561-67. doi: 10.1249/mss.0b013e31820ce174
32. Winkler EAH, Bodicoat DH, Healy GN, et al. Identifying adults' valid waking wear time by automated estimation in activPAL data collected with a 24 h wear protocol. *Physiological Measurement* 2016;37(10):1653. doi: 10.1088/0967-3334/37/10/1653
33. Edwardson CL, Winkler EAH, Bodicoat DH, et al. Considerations when using the activPAL monitor in field-based research with adult populations. *Journal of Sport and Health Science* 2017;6(2):162-78. doi: 10.1016/j.jshs.2016.02.002
34. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Medicine and Science in Sports & Exercise* 1998;30(5):777-81.
35. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavia* 1983;67:361-70. doi: 10.1111/j.1600-0447.1983.tb09716.x
36. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale: An updated literature review. *Journal of Psychosomatic Research* 2002;52(2):69-77. doi: 10.1016/S0022-3999(01)00296-3
37. Stern AF. The Hospital Anxiety and Depression Scale. *Occupational Medicine* 2014;64:393-94. doi: 10.1093/occmed/kqu024
38. Euroquol. Euroquol- a new facility for the measurement of health related quality of life. *Health policy* 1990;16:199-208. doi: 10.1016/0168-8510(90)90421-9
39. van Hout B, Janssen MF, Feng Y-S, et al. Interim scoring for the EQ-5D-5L: Mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value in Health* 2012;15(5):708-15. doi: 10.1016/j.jval.2012.02.008
40. Devlin NJ, Shah KK, Feng Y, et al. Valuing health-related quality of life: an EQ-5D-5L value set for England. *Health Economics* 2018;27(1):7-22. doi: 10.1002/hec.3564
41. Department of Health & Social Care. UK Chief Medical Officers' physical activity guidelines. https://www.gov.uk/government/publications/physical-activity-guidelines-uk-chief-medical-officers-report#history2019.
42. Schuch FB, Vancampfort D, Richards J, et al. Exercise as a treatment for depression: a meta-analysis adjusting for publication bias. *Journal of Psychiatric Research* 2016;77:42-51. doi: 10.1016/j.jpsychires.2016.02.023
43. Hamer M, Smith L. Sedentary behaviour and depression. In: Leitzmann MF, Jochem C, Schmid D, eds. Sedentary behaviour epidemiology. Cham, Switzerland: Springer 2018:299-310.

44. Dempsey PC, Matthews CE, Dashti SG, et al. Sedentary behavior and chronic disease: mechanisms and future directions. *Journal of Physical Activity and Health* 2020;17(1):52-61. doi: 10.1123/jpah.2019-0377
45. Orben A. The Sisyphean cycle of technology panics. *Perspectives on Psychological Science* 2020;15(5):1143-57. doi: 10.1177/1745691620919372
46. Dempsey PC, Larsen RN, Winkler EAH, et al. Prolonged uninterrupted sitting elevates postprandial hyperglycaemia proportional to degree of insulin resistance. *Diabetes, Obesity and Metabolism* 2019;20(6):1526-30. doi: 10.1111/dom.13254
47. Henson J, Davies MJ, Bodicoat DH, et al. Breaking up prolonged sitting with standing or walking attenuates the postprandial metabolic response in postmenopausal women: a randomized acute study. *Diabetes Care* 2016;39(1):130-38. doi: 10.2337/dc15-1240
48. Healy GN, Winkler EAH, Owen N, et al. Replacing sitting time, standing or stepping: associations with cardio-metabolic risk biomarkers. *European Heart Journal* 2015;36(39):2643-49. doi: 10.1093/eurheartj/ehv308
49. Teychenne M, Costigan SA, Parker K. The association between sedentary behaviour and risk of anxiety: a systematic review. *BMC Public Health* 2015;15:513. doi: 10.1186/s12889-015-1843-x
50. Healy GN, Dunstan DW, Salmon J, et al. Breaks in sedentary time: beneficial associations with metabolic risk. *Diabetes Care* 2008;31(4):661-66. doi: 10.2337/dc07-2046
51. Stamatakis E, Ekelund U, Ding D, et al. Is the time right for quantitative public health guidelines on sitting? A narrative review of sedentary behaviour research paradigms and findings. *British Journal of Sports Medicine* 2019;53(6):377-82. doi: 10.1136/bjsports-2018-099131
52. Dempsey PC, Hadgraft NT, Winkler EAH, et al. Associations of context-specific sitting time with markers of cardiometabolic risk in Australian adults. *International Journal of Behavioral Nutrition and Physical Activity* 2018;15(1):114. doi: 10.1186/s12966-018-0748-3
53. Hallgren M, Dunstan DW, Owen N. Passive versus mentally active sedentary behaviours and depression. *Exercise and Sport Sciences Reviews* 2020;48(1):20-27. doi: 10.1249/JES0000000000000211

Table 1: Participants characteristics and baseline descriptive data.

	STAND N=125	WALKING AWAY N=456	PROPELS N=993	All N=1574
Demographic, anthropometric, medical history and medication variables				
Age (years)	32.8 ± 5.6	66.4 ± 7.7	59.4 ± 9.1	59.1 ± 12.1
Male	38 (30.4)	277 (60.7)	494 (49.7)	809 (51.4)
Ethnicity White Non-white	 91 (72.8) 34 (27.2)	 403 (88.4) 53 (11.6)	 699 (70.4) 294 (29.6)	 1193 (75.8) 381 (24.2)
Current smokers	23 (18.4)	32 (7.0)	89 (9.0)	144 (9.1)
Heart Disease	1 (0.8)	79 (17.3)	115 (11.6)	195 (12.4)
Stroke	1 (0.8)	15 (3.3)	21 (2.1)	37 (2.4)
BP medication	6 (4.8)	216 (47.4)	381 (38.4)	603 (38.3)
Lipid medication	1 (0.8)	136 (29.8)	277 (27.9)	414 (26.3)
BMI (kg/m^2)	34.6 ± 4.9	31.6 ± 5.4	29.2 ± 5.6	30.3 ± 5.8
Waist circumference (cm)	103.3 ± 13.9	104.1 ± 12.2	98.8 ± 14.0	100.7 ± 13.7
Accelerometer variables				
activPAL waking wear time (hours/day)	15.2 ± 1.1	15.5 ± 1.2	15.8 ± 1.2	15.7 ± 1.2
(Total) Sitting time (hours/day)	8.8 ± 1.8	9.4 ± 1.9	9.1 ± 1.9	9.2 ± 1.9
Prolonged sitting time (hours/day)	4.6 ± 1.1	5.2 ± 1.9	4.8 ± 1.9	4.9 ± 1.9
Short sitting time (hours/day)	4.6 ± 1.1	4.2 ± 1.2	4.3 ± 1.2	4.3 ± 1.2
MVPA (minutes/day)	27.2 (13.4, 39.1)	16.1 (7.4, 33.0)	24.5 (12.3, 42.6)	22.3 (10.7, 39.0)
*Achieved 150 minutes of MVPA	173 (41.0)	81 (64.8)	483 (57.7)	737 (53.3)

No. of breaks in sitting/day	52.6 ± 14.8	44.2 ± 13.8	48.3 ± 15.1	47.6 ± 14.9
Anxiety, depression and QoL outcomes				
HADS anxiety	7 (4.5, 10.5)	4 (2, 7)	5 (3, 9)	5 (3, 8)
HADS depression	4 (2, 7)	2 (1, 5)	3 (1, 6)	3 (1, 6)
EQ-5D health state score	68 (50, 80)	80 (70, 90)	85 (75, 95)	80 (70, 90)
EQ-5D utility score	1.000 (0.909, 1.000)	0.937 (0.860, 1.000)	0.937 (0.860, 1.000)	0.922 (0.829, 1.000)

Continuous results presented as mean ± standard deviation (SD) or median (interquartile range). Categorical variables are presented as number (column percentage)
* Includes only individuals with ≥7 days of valid accelerometer data (STAND n=125; Walking Away n=422; PROPELS=837 ;Total n=1384)

MVPA= Moderate-to-vigorous physical activity

Table 2: GLM estimates (95% CI) of the effect of sitting, prolonged sitting, short sitting, MVPA time and breaks on anxiety, depression and quality of life

	n	Total sitting time[a] *β (95% CI)*	P value	Prolonged sitting time[a] *β (95% CI)*	P value	Short sitting time[a] *β (95% CI)*	P value	MVPA[b] *β (95% CI)*	P value	Breaks[a,b] *β (95% CI)*	P value
Model 1											
Anxiety	1542	0.078 (-0.086, 0.241)	0.354	0.100 (-0.062, 0.261)	0.226	-0.070 (-0.323, 0.183)	0.587	-0.050 (-0.170, 0.070)	0.392	-0.003 (-0.024, 0.017)	0.758
Depression	1574	0.182 (0.070, 0.294)	**0.001**	0.238 (0.116, 0.360)	**<0.001**	-0.145 (-0.334, 0.044)	0.133	-0.100 (-0.180, -0.020)	**0.020**	-0.012 (-0.026, 0.002)	0.097
EQ-5D health state	1548	-1.591 (-2.054, -1.128)	**<0.001**	-1.460 (-1.906, -1.014)	**<0.001**	-0.025 (-0.755, 0.704)	0.946	1.078 (0.720, 1.434)	**<0.001**	0.050 (-0.008, 0.109)	0.093
EQ-5D utility score	1567	-0.012 (-0.016, -0.009	**<0.001**	-0.013 (-0.017, -0.009)	**<0.001**	0.003 (-0.003, 0.009)	0.291	0.002 (0.001, 0.003)	**<0.001**	0.001 (-0.001, 0.001)	0.423
Model 2											
Anxiety	1542	0.050 (-0.129, 0.229)	0.584	0.074 (-0.096, 0.244)	0.395	-0.069 (-0.326, 0.187)	0.596	-0.037 (-0.165, 0.089)	0.561	-0.003 (-0.024, 0.018)	0.790
Depression	1544	0.160 (0.037, 0.283)	**0.011**	0.219 (0.091, 0.37)	**0.001**	-0.151 (-0.344, 0.041)	0.123	-0.052 (-0.147, 0.043)	0.286	-0.011 (-0.025, 0.002)	0.107
EQ-5D health state	1518	-1.349 (-1.834, -0.865)	**<0.001**	-1.228 (-1.689, -0.766)	**<0.001**	0.019 (-0.708, 0.746)	0.959	0.780 (0.413, 1.148)	**<0.001**	0.048 (-0.010, 0.106)	0.105
EQ-5D utility score	1537	-0.010	**<0.001**	-0.011	**<0.001**	0.004	0.231	0.001	**<0.001**	0.001	0.406

		(-0.015, -0.006)		(-0.015, -0.007)		(-0.002, 0.010)		(0.001, 0.002)		(-0.001, 0.001)	
Model 3											
Anxiety	1535	0.027 (-0.155, 0.210)	0.768	0.052 (-0.120, 0.225)	0.551	-0.066 (-0.325, 0.193)	0.619	-0.020 (-0.150, 0.110)	0.726	-0.001 (-0.022, 0.021)	0.943
Depression	1537	0.132 (0.010, 0.254)	**0.033**	0.178 (0.053, 0.304)	**0.005**	-0.131 (-0.319, 0.058)	0.174	-0.001 (-0.100, 0.099)	0.926	-0.007 (-0.021, 0.007)	0.329
EQ-5D health state	1511	-0.985 (-1.471, -0.499)	**<0.001**	-0.834 (-1.301, -0.367)	**<0.001**	-0.168 (-0.881, 0.545)	0.645	0.554 (0.187, 0.922)	**0.003**	0.011 (-0.047, 0.069)	0.706
EQ-5D utility score	1530	-0.008 (-0.012, -0.003)	**<0.001**	-0.008 (-0.012, -0.004)	**<0.001**	0.003 (-0.003, 0.009)	0.347	0.001 (0.001, 0.002)	**0.005**	0.001 (-0.001, 0.001)	0.961

Model 1: adjusted for age, sex, ethnicity (white/non-white), smoking status (never and previous/current), heart disease, history of stroke, taking blood pressure medication and lipid medication, and activPAL waking wear time
Model 2 was adjusted for the above covariates and [a]MVPA or [b]sitting time
Model 3 was adjusted for the same covariates as Model 2 and waist circumference

Table 3: Odds ratios for the effects of sitting, prolonged sitting, short sitting and MVPA on anxiety and depression (grouped into normal vs borderline/abnormal).

	n	Total sitting time[a] *Exp (B) (95% CI)*	P value	Prolonged sitting time[a] *Exp (B) (95% CI)*	P value	Short sitting time[a] *Exp (B) (95% CI)*	P value	MVPA[b] *Exp (B) (95% CI)*	P value	Breaks [a,b] *Exp (B) (95% CI)*	P value
Model 1											
Anxiety	1542	1.080 (1.013, 1.150)	**0.018**	1.054 (0.992, 1.120)	0.088	1.049 (0.951, 1.157)	0.341	0.997 (0.992, 1.002)	0.216	1.003 (0.995, 1.011)	0.431
Depression	1574	1.189 (1.096, 1.290)	**<0.001**	1.188 (1.102, 1.279)	**<0.001**	0.948 (0.838, 1.074)	0.402	0.992 (0.985, 0.999)	**0.018**	0.996 (0.986, 1.007)	0.480
Model 2											
Anxiety	1542	1.066 (0.997, 1.139)	0.512	1.037 (0.973, 1.104)	0.264	1.056 (0.957, 1.166)	0.280	0.998 (0.993, 1.004)	0.512	1.004 (0.995, 1.012)	0.391
Depression	1544	1.175 (1.078, 1.281)	**<0.001**	1.176 (1.088, 1.271)	**<0.001**	0.943 (0.832, 1.068)	0.354	0.996 (0.988, 1.003)	0.224	0.996 (0.986, 1.007)	0.491
Model 3											
Anxiety	1535	1.050 (0.981, 1.124)	0.157	1.021 (0.957, 1.090)	0.526	1.058 (0.958, 1.169)	0.263	0.999 (0.993, 1.004)	0.672	1.005 (0.997, 1.013)	0.260
Depression	1537	1.135 (1.040, 1.238)	**0.004**	1.141 (1.054, 1.236)	**0.001**	0.950 (0.838, 1.078)	0.425	0.998 (0.990, 1.005)	0.531	0.998 (0.988, 1.009)	0.499

Model 1: adjusted for age, sex, ethnicity (white/non-white), smoking status (never and previous/current), heart disease, history of stroke, taking blood pressure medication and lipid medication, and activPAL waking wear time
Model 2 was adjusted for the above covariates and [a]MVPA or [b]sitting time
Model 3 was adjusted for the same covariates as Model 2 and waist circumference

Supplementary Table S1: GLM estimates (95% CI) of the effect of sitting, prolonged sitting, short sitting and MVPA time and breaks on anxiety, depression and quality of life (>=4 days of activPAL assessment)

	n	Total sitting time[a] *β (95% CI)*	P value	Prolonged sitting time[a] *β (95% CI)*	P value	Short sitting time[a] *β (95% CI)*	P value	MVPA[b] *β (95% CI)*	P value	Breaks [a,b] *β (95% CI)*	P value
Model 1											
Anxiety	1504	0.037 (-0.135, 0.208)	0.675	0.056 (-0.112, 0.223)	0.513	-0.055 (-0.317, 0.208)	0.683	-0.040 (-0.161, 0.081)	0.392	-0.002 (-0.023, 0.019)	0.861
Depression	1507	0.150 (0.032, 0.267)	**0.013**	0.203 (0.077, 0.329)	**0.002**	-0.125 (-0.319, 0.068)	0.205	-0.090 (-0.173, 0.001)	0.051	-0.010 (-0.025, 0.005)	0.179
EQ-5D health state	1481	-1.613 (-2.092, -1.135)	**<0.001**	-1.481 (-1.945, -1.017)	**<0.001**	-0.074 (-0.820, 0.672)	0.846	1.119 (0.759, 1.479)	**<0.001**	0.051 (-0.008, 0.110)	0.093
EQ-5D utility score	1500	-0.012 (-0.016, -0.008	**<0.001**	-0.012 (-0.016, -0.009)	**<0.001**	0.003 (-0.003, 0.009)	0.411	0.002 (0.001, 0.003)	**<0.001**	0.001 (-0.001, 0.001)	0.512
Model 2											
Anxiety	1479	0.020 (-0.184, 0.189)	0.980	0.027 (-0.148, 0.202)	0.765	-0.058 (-0.324, 0.209)	0.672	-0.039 (-0.169, 0.090)	0.551	-0.001 (-0.023, 0.020)	0.912
Depression	1482	0.125 (-0.002, 0.253)	0.054	0.182 (0.051, 0.314)	**0.007**	-0.138 (-0.334, 0.058)	0.166	-0.054 (-0.149, 0.043)	0.274	-0.010 (-0.025, 0.004)	0.154
EQ-5D health state	1456	-1.298 (-1.801, -0.796)	**<0.001**	-1.210 (-1.691, -0.730)	**<0.001**	0.061 (-0.684, 0.806)	0.872	0.839 (0.466, 1.212)	**<0.001**	0.049 (-0.009, 0.108)	0.098
EQ-5D utility score	1475	-0.010	**<0.001**	-0.011	**<0.001**	0.004	0.287	0.001	**<0.001**	0.001	0.498

		(-0.014, -0.006)		(-0.015, -0.006)		(-0.003, 0.010)		(0.001, 0.002)		(-0.001, 0.001)	
Model 3											
Anxiety	1472	-0.019 (-0.209, 0.170)	0.840	0.006 (-0.172, 0.183)	0.950	-0.053 (-0.322, 0.216)	0.699	-0.025 (-0.159, 0.109)	0.715	0.001 (-0.021, 0.023)	0.944
Depression	1475	0.091 (-0.036, 0.219)	0.161	0.137 (0.007, 0.267)	**0.039**	-0.111 (-0.305, 0.083)	0.262	-0.001 (-0.100, 0.094)	0.921	-0.006 (-0.021, 0.009)	0.419
EQ-5D health state	1449	-0.929 (-1.436, -0.422)	**<0.001**	-0.820 (-1.309, -0.331)	**0.001**	-0.094 (-0.827, 0.638)	0.800	0.641 (0.268, 1.014)	**0.001**	0.016 (-0.043, 0.075)	0.597
EQ-5D utility score	1468	-0.007 (-0.011, -0.003)	**0.002**	-0.008 (-0.012, -0.003)	**<0.001**	0.003 (-0.004, 0.009)	0.391	0.001 (0.001, 0.002)	**0.005**	0.001 (-0.001, 0.001)	0.982

Model 1: adjusted for age, sex, ethnicity (white/non-white), smoking status (never and previous/current), heart disease, history of stroke, taking blood pressure medication and lipid medication, and activPAL waking wear time
Model 2 was adjusted for the above covariates and [a]MVPA or [b]sitting time
Model 3 was adjusted for the same covariates as Model 2 and waist circumference

Supplementary Table S2. Interaction terms across MVPA categories (active [>150min/wk of MVPA] vs. inactive [<150min/wk of MVPA])

	n	Total sitting time*MVPA	Prolonged sitting time*MVPA
Anxiety	1065	0.906	0.962
Depression	1064	0.684	0.944
EQ-5D health state	1043	0.393	0.859
EQ-5D utility score	1056	0.157	0.553
Adjusted for age, sex, ethnicity (white/non-white), smoking status (never and previous/current), heart disease, history of stroke, blood pressure and lipid medication, activPAL waking wear time and waist circumference.			