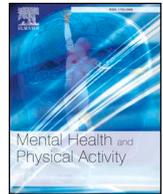




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## Objectively measured sedentary time and mental and cognitive health: Cross-sectional and longitudinal associations in The Rotterdam Study

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## A B S T R A C T

**Introduction:** Based on studies using self-reported sitting time, sedentary behavior has been suggested as a risk factor for poor mental health and cognition. However, it remains unclear whether objectively measured sedentary behavior is longitudinally associated with depression, anxiety disorders or cognition.

**Methods:** In the population-based Rotterdam Study, cross-sectional and longitudinal associations of objectively assessed sedentary time with depressive symptoms, anxiety disorders and cognition were assessed among 1841 participants (mean follow-up: 5.7 years). Participants wore a wrist actigraph for seven days between 2004 and 2007 to assess sedentary time (hours/day). Depression, anxiety disorders and cognition were assessed twice between 2004 and 2014. Depressive symptoms were continuously measured with the Centre for Epidemiologic Studies-Depression scale (CES-D) and a diagnoses of anxiety disorder (n = 147) was obtained by interview, using an adapted version of the Munich Composite International Diagnostic Interview (M-CIDI). Cognition was assessed using a test-battery. Linear regression was performed for all continuous outcomes, and logistic regression for all binary outcomes.

**Results:** In analyses adjusted for age, sex, cohort and time awake only, 1 h/day more sedentary time was cross-sectionally associated with a 0.25 point (95% confidence interval (95%CI): 0.08, 0.41) higher CES-D score, 1.11 (95%CI: 1.01, 1.21) higher odds of anxiety disorder, and 0.03 (95%CI: 0.05, -0.01) lower global cognition score. After adjustment for confounders, these associations no longer remained. Sedentary time at baseline was not associated longitudinally with changes in depressive symptoms, anxiety disorders and cognition.

**Conclusions:** No support was found for an association between actigraphically measured sedentary time and mental health or cognition. All observed associations were explained by confounders, in particular, disability, occupational status and smoking. The previously reported association between sitting time and mental health might reflect residual confounding, bias of subjective measures, or the social context of sedentary behavior.

## 1. Introduction

Sedentary behavior has been suggested as a risk factor cardiovascular disease, diabetes, poor mental health and low cognitive performance (de Rezende, Rodrigues Lopes, Rey-Lopez, Matsudo, & Luiz Odo, 2014). However, reviews of the association of sedentary behavior with mental health and cognitive performance concluded that results are inconsistent, even though several studies have related higher levels of sedentary behavior to an increased likelihood of depression (Sanchez et al., 2008; Yancey et al., 2004; Zhai, Zhang, & Zhang, 2015), anxiety disorders (Allen, Walter, & Swann, 2019; Cao et al., 2011; Stanczykiewicz et al., 2019; Teychenne, Costigan, & Parker, 2015), and impaired cognition (Falck, Davis, & Liu-Ambrose, 2017; Steinberg et al., 2015). For example, in middle-aged men and women, watching

television for 6 or more hours a day was associated with higher depressive symptoms and poorer cognitive function, compared to watching television for less than 2 h per day (Hamer & Stamatakis, 2014). It is important to understand the association between sedentary behavior and mental health and cognition in older adults, as these adults are at higher risk of engaging in sedentary behavior compared to younger adults (Koolhaas et al., 2017a), and problems with cognition are more prevalent (Rait et al., 2005). Moreover, a higher prevalence does not only make this a relevant public health problem but increases the power of a given sample size to study these associations.

There are important limitations to the studies included in the above mentioned reviews and meta-analyses. First, most studies were cross-sectional (Breland, Fox, & Horowitz, 2013; Cao et al., 2011; Sanchez et al., 2008; Santos, Virtuoso, Meneguci, Sasaki, & Tribess, 2017;

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Steinberg et al., 2015; Yancey et al., 2004), making it impossible to determine whether high sedentary time leads to impaired mental health and cognition or the converse. Second, only a few studies adjusted for disability (Hamer & Stamatakis, 2014; van Gool et al., 2003), which must be considered an important confounder of the association between sedentary behavior and mental health or cognition. Third, the majority of the studies included self-reported sedentary time, which might be subject to the influence of perception (Matthews, Moore, George, Sampson, & Bowles, 2012). The few studies that measured sedentary time objectively, had either no follow-up (Rosenberg et al., 2015; Vallance et al., 2011) or only examined the direction from anxiety to sedentary behavior (Uijtendewilligen et al., 2011). Subjective measures of sedentary behavior typically address television viewing, computer use or occupational sitting as proxies of sedentary behavior. This practice can influence the results (Hamer & Stamatakis, 2014; Hoang et al., 2016; Picavet et al., 2016; Sui et al., 2015), as associations might be driven more by the social context than the sedentary behavior itself (Teychenne, Ball, & Salmon, 2010). For example, it has been suggested that occupational sitting is not associated with mental health, because of the social context in which most jobs take place (Picavet et al., 2016). Furthermore, the purpose of the activity might be of importance for the association with mental health. Watching television for relaxation could be differently associated with mental health than occupational computer work in a demanding position. In summary, it remains unclear whether objectively measured sedentary time is longitudinally associated with depression, anxiety, and cognition.

In this population-based study, the cross-sectional and longitudinal association of objectively measured sedentary time with mental and cognitive health were examined in older persons. Depressive symptoms, anxiety disorders, and cognition were assessed twice over an average follow-up period of 5.7 years.

## 2. Methods

### 2.1. Study population

This study was embedded in the Rotterdam Study (RS), a prospective population-based cohort among adults aged 50 years or older living in the Ommoord district in the municipality of Rotterdam, the Netherlands. The RS started in 1990 with a first cohort (RS-I) and was extended in 2000–2001 (RS-II) and in 2006–2008 (RS-III). Baseline invitations were sent to all the home addresses within Ommoord. The aim of the study was to examine the incidence of psychiatric, neurological, cardiovascular, and other chronic diseases. Details of the study have been published elsewhere (Ikram et al., 2017). Trained research assistants interviewed the participants at home to collect the baseline information and participants visited the research center twice, where clinical measurements were obtained.

From December 2004 to April 2007, 2632 successive participants of the Rotterdam Study, embedded in RS-I, RS-II or RS-III, were invited to participate in the actigraphy study. The current study was conducted in 2063 participants who agreed to participate (78%). The only requirement for participation was being able to understand the instructions for this study. To prevent missing data diluting the estimated hours of sedentary behavior per day, days with more than 3 h of continuous missing data (133 days) were excluded (Koolhaas et al., 2017b; Luik, Zuurbier, Hofman, Van Someren, & Tiemeier, 2013). Next, 168 recordings with technical problems or that contained fewer than 4 days were excluded (Berkemeyer et al., 2016) (see Supplementary Fig. 1). Additionally, sedentary data of 54 participants (2.8%) with unusually low (< 20% per day) or high (> 90% per day) sedentary time was considered unreliable after visual inspection and therefore excluded. The 1841 participants (87 from RS-I, 884 from RS-II and 870 from RS-III) with data on sedentary time all had information on at least one of the 5 outcomes relating to mental health or cognition (Supplementary Fig. 1). The number (%) of individuals with an anxiety disorder at

baseline was 147 (8.0%) and 22 (1.2%) were diagnosed with prevalent major depressive disorder (MDD).

All subjects provided written informed consent, and the study protocol was approved by the institutional review board (Medical Ethics Committee) of the Erasmus Medical Center and by the review board of The Netherlands Ministry of Health, Welfare and Sports. Information on the measurement of covariates is provided in the [supplement](#).

### 2.2. Measurement of sedentary time

Participants were asked to wear an actigraph around the non-dominant wrist (Actiwatch model AW4; Cambridge Technology, Cambridge, UK) for seven consecutive days and nights and to complete a 7-day sleep diary to report overnight sleep periods. The actigraph had to be removed from the wrist for water-based activities. Recordings were collected in 30-s intervals, during 24-h periods (Van Den Berg et al., 2008). The actigraph devices were introduced to the Rotterdam study to measure sleep in everyday life and were not calibrated to measure the level of physical activity. However, the actigraph device can validly measure active versus non-active intervals within a person. These data can be used as a proxy of sedentary behavior and test between-person differences (Routen, Upton, Edwards, & Peters, 2012).

To quantify sedentary time, only the waking hours were used. Waking hours were defined as all hours between the epochs classified as sleep end and sleep onset, as described previously (Van Den Berg et al., 2008). The time (hours/day) spent in sedentary behavior was determined using the standard count-based intensity threshold value of < 199 counts per minute (cpm) (Davis & Fox, 2007).

### 2.3. Measurement of clinical outcomes

#### 2.3.1. Depressive symptoms

At baseline (2004–2007) and the next follow-up measurement (2009–2014) depressive symptoms were assessed with the Dutch version of the Centre for Epidemiologic Studies Depression scale (CES-D) (Breslau, 1985), a scale designed to assess presence and severity of self-reported depressive symptoms (Hales et al., 2006). The CES-D has a high internal consistency (Cronbach's alpha ranging from 0.85 to 0.90 across studies (Radloff, 1977)). During the home interview, participants were asked 20 questions that correspond with criterion-based symptoms associated with depression and the summative scale ranges from score 0 to 60. A score of 16 or greater is traditionally accepted as cut-off to define clinically relevant depressive symptoms (McDowell, 2006).

#### 2.3.2. Depression diagnosis

Participants with a CES-D score of 16 or higher were invited for a semi-structured clinical interview with the Schedules for Clinical Assessment of Neuropsychiatry (SCAN) (Wing et al., 1990), an instrument commonly used to diagnose depression in older adults of the Dutch population (Van den Berg, Oldehinkel, Brilman, Bouhuys, & Ormel, 2000). The SCAN interview was conducted by a trained clinician at the participant's home. Using a digitalized algorithm of the DSM-IV, participants were considered having an MDD when they met the condition for MDD according to the DSM-IV.

#### 2.3.3. Anxiety disorders

The 12-month prevalence of 5 different anxiety disorders according to the DSM-IV-TR (Text Revision) Criteria (American Psychiatric Association, 1994) was assessed during the home interview, using an adapted version of the Munich version of the Composite International Diagnostic Interview (M-CIDI). The anxiety disorders under consideration were generalized anxiety disorder, panic disorder, agoraphobia, social phobia, and specific phobia as described previously (Hek et al., 2013). Participants were classified as having an anxiety disorder if they had at least one of these anxiety disorders. The M-CIDI was designed specifically to obtain DSM-IV diagnoses of mental disorders, and has a

satisfactory test-retest reliability (kappa value ranging from 0.45 to 0.72) (Wittchen, Lachner, Wunderlich, & Pfister, 1998).

### 2.3.4. Cognitive function

A detailed assessment of cognitive function was obtained using a test battery during the research center visit. The tests included the Mini-Mental State Examination (MMSE (Folstein, Folstein, & McHugh, 1975); Cronbach's alpha ranging 0.54–0.96 across studies (Tombaugh & McIntyre, 1992)), Stroop test (Houx, Jolles, & Vreeling, 1993) (time in seconds taken for completing each of the following 3 tasks: word reading, color naming, and a reading/color naming interference task), the letter-digit substitution task (Lezak, Howieson, Loring, & Fischer, 2004) (scored as the number of correct digits in 1 min), the verbal fluency test (Welsh et al., 1994) (scored as the number of mentioned animal species within 1 min), the 15-word learning test (Bleeker, Bolla-Wilson, Agnew, & Meyers, 1988) (recall and recognition of visually presented words), and the Purdue pegboard test for fine motor skills (Tiffin & Asher, 1948). For the Purdue pegboard test, the scores from the right hand, left hand, and both hands were summed.

A general cognitive factor (g-factor) was computed by performing principal component analyses incorporating the letter-digit substitution task, the verbal fluency test, 15-word learning delayed recall subtask, the inverse value of the Stroop color–word interference subtask and the sum of the Purdue pegboard scores. A higher g-factor indicates better performance. The g-factor explained 52.3% of all variance in cognitive tests at baseline and 51.6% at the follow-up measurement, which is in accordance with literature (Hoogendam, Hofman, van der Geest, van der Lugt, & Ikram, 2014).

### 2.3.5. Statistical analysis

Sedentary time was normally distributed (see Supplementary Fig. 2), and analyzed continuously (per 1 h/day). Baseline characteristics were compared across three categories of sedentary time: 1) < 8 h/day; 2) 8–11 h/day; 3) ≥ 11 h/day (Koolhaas et al., 2017b). All analyses were conducted in 2017.

To examine the cross-sectional and longitudinal associations of sedentary time with depressive symptoms, the g-factor and MMSE score, linear regression models were used. To examine the association of sedentary time with anxiety disorders and MDD, logistic regression models were used. Covariates measured at baseline were included in the models based on previous research (Falck et al., 2017; Teychenne et al., 2015; Zhai et al., 2015) or a 10% change in the effect estimate (Greenland & Mickey, 1989). Natural cubic splines were applied to test for non-linearity of each of the models (Hastie et al., 1991), but no evidence for a non-linear association of sedentary time was found with any outcome in any model.

For cross-sectional analyses, a basic model for all the outcomes was run, adjusting for age, sex, cohort indicator (RS-I, RS-II or RS-III) and time awake. In model 2, education, occupational status, marital status, smoking and BMI were added. In model 3, we added physical activity and the disability score, to examine the association between sedentary time and the separate outcomes, independent of physical activity and disability measures. The effect of adding each of these factors in the models was examined by computing the percentage change in the effect estimate for sedentary behavior after including the specific factor.

For the longitudinal analyses 3 models were created, similar to the cross-sectional analyses. To account for the longitudinal design, model 1 was additionally adjusted for the time between the baseline and the follow-up measurement, and the baseline value of the outcome. For longitudinal analyses of anxiety disorders, participants with an anxiety disorder at baseline – according to the M-CIDI – were excluded. Because incidence of MDD in participants without MDD at baseline was limited (n = 7), longitudinal analyses of MDD were not conducted.

In sensitivity analyses, the associations stratified by age (younger or older than 65 years) and sex were examined. Additionally, cross-sectional analyses of the cognitive tests included in the g-factor were

**Table 1**  
Baseline participant characteristics by categories of sedentary time, the rotterdam study.

| Characteristics                   | Total population | Per category of sedentary behavior |             |             |
|-----------------------------------|------------------|------------------------------------|-------------|-------------|
|                                   |                  | < 8 h/d                            | 8–11 h/d    | ≥ 11 h/d    |
| <b>Demographics</b>               |                  |                                    |             |             |
| Participants, n (%)               | 1841             | 637 (34.6)                         | 958 (52)    | 246 (13.4)  |
| Age (years)                       | 62.6 (9.3)       | 60.1 (8.0)                         | 63.7 (9.5)  | 65.2 (10.6) |
| Female, n (%)                     | 1001 (54.4)      | 419 (65.8)                         | 478 (49.9)  | 104 (42.3)  |
| Educational level, n (%)          |                  |                                    |             |             |
| Primary education                 | 154 (8.4)        | 56 (8.7)                           | 71 (7.4)    | 27 (11)     |
| Lower education                   | 752 (40.8)       | 282 (44.3)                         | 386 (40.3)  | 84 (34.1)   |
| Intermediate education            | 555 (30.1)       | 182 (28.6)                         | 291 (30.3)  | 82 (33.3)   |
| Higher education                  | 378 (20.6)       | 117 (18.4)                         | 210 (21.9)  | 53 (21.5)   |
| Employed, n (%)                   | 623 (33.8)       | 262 (41.1)                         | 293 (30.6)  | 68 (27.7)   |
| Living with partner, n (%)        | 1436 (78.0)      | 513 (80.5)                         | 753 (78.6)  | 170 (69.1)  |
| <b>Lifestyle factors</b>          |                  |                                    |             |             |
| Smoking, n (%)                    |                  |                                    |             |             |
| Never                             | 579 (31.5)       | 224 (35.2)                         | 294 (30.7)  | 61 (24.8)   |
| Former                            | 942 (51.2)       | 327 (51.3)                         | 489 (51.0)  | 127 (51.5)  |
| Current                           | 320 (17.4)       | 86 (13.5)                          | 176 (18.3)  | 58 (23.7)   |
| BMI (kg/m <sup>2</sup> )          | 27.9 (4.2)       | 27.3 (4)                           | 27.9 (4.1)  | 29 (4.8)    |
| Disability score                  | 0.3 (0.4)        | 0.3 (0.3)                          | 0.3 (0.4)   | 0.4 (0.4)   |
| Alcohol (glasses/day)             | 1.1 (1.3)        | 0.9 (1.1)                          | 1.1 (1.3)   | 1.1 (1.4)   |
| Physical activity (METhours/week) | 60.6 (61.4)      | 68.8 (66.5)                        | 57.3 (64.7) | 50.2 (52.4) |
| <b>Mental Health</b>              |                  |                                    |             |             |
| Baseline CES-D score              | 5.4 (6.9)        | 5.2 (6.8)                          | 5.5 (6.9)   | 5.7 (7.2)   |
| Prevalent MDD, n (%)              | 22 (1.2)         | 6 (1.0)                            | 13 (1.4)    | 3 (1.3)     |
| Prevalent anxiety disorder, n (%) | 147 (8.0)        | 50 (8.1)                           | 77 (8.2)    | 20 (8.5)    |
| Baseline g-factor (Z-score)       | 0.0 (1.0)        | 0.2 (0.9)                          | −0.1 (1.0)  | −0.4 (1.1)  |
| MMSE score                        | 27.9 (1.9)       | 28 (1.8)                           | 27.9 (2.0)  | 27.9 (1.8)  |
| <b>Prevalent diseases</b>         |                  |                                    |             |             |
| Prevalent diabetes, n (%)         | 259 (14.1)       | 65 (10.2)                          | 142 (14.8)  | 52 (21.1)   |
| Prevalent CHD, n (%)              | 104 (5.6)        | 25 (3.9)                           | 52 (5.4)    | 27 (11)     |
| Prevalent stroke, n (%)           | 47 (2.6)         | 10 (1.6)                           | 31 (3.2)    | 6 (2.4)     |
| Prevalent cancer, n (%)           | 214 (11.6)       | 74 (11.6)                          | 105 (11.0)  | 35 (14.2)   |

Data are presented as mean (SD), unless otherwise stated.

Abbreviations: BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression; CHD, coronary heart disease; d, day; h, hour; MET, metabolic equivalent of task; MDD, major depressive disorder; MMSE, mini mental state examination.

performed.

Substantial data was missing for physical activity (24.5%) and disability (25.5%), other covariates had < 2% missing data. Multiple imputations (n = 20 imputations) were performed using a Markov Monte Carlo imputation method. All analyses were conducted using SPSS software version 21 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp) and R (3.4.1).

### 2.3.6. Non-response analysis

When participants who agreed were compared to those who refused to wear an actigraph, it was visible that the former were slightly older, more often men, had better scores for the g-factor and MMSE and had a lower disability score (Supplementary Table 1).

## 3. Results

Table 1 shows the baseline characteristics of the 1841 participants included in the study according to categories of sedentary time. Mean age was 62.6 years (standard deviation (SD): 9.3), 54.4% of the sample was female, and the mean daily sedentary time was 8.8 h (SD: 2.0). Almost all participants (n = 1826; 99.2%) had at least one weekend day included in the sedentary time estimate. The mean (SD) follow-up

**Table 2**

Cross-sectional associations of objectively assessed sedentary time with depressive symptoms and anxiety disorders, analyzed per 1 h/day more sedentary time.

| Model   | Depressive symptoms score (n = 1826) |             |              | Major depressive disorder <sup>a</sup> (n = 1817) |            |      | Anxiety disorders <sup>a</sup> (n = 1788) |            |             |
|---|--------------------------------------|-------------|--------------|---|------------|------|---|------------|-------------|
|   | $\beta$                              | 95%CI       | p            | OR  | 95%CI      | p    | OR  | 95%CI      | p           |
| Model 1 <sup>b</sup> : basic model                              | 0.25                                 | 0.08, 0.41  | <b>0.004</b> | 1.17  | 0.96, 1.44 | 0.12 | 1.11                                      | 1.01, 1.21 | <b>0.03</b> |
| Model 2 <sup>c</sup> : + sociodemographic and lifestyle factors | 0.18                                 | 0.01, 0.34  | <b>0.04</b>  | 1.14  | 0.92, 1.41 | 0.23 | 1.07                                      | 0.98, 1.17 | 0.15        |
| Model 3 <sup>d</sup> : + activity and disability                | 0.08                                 | -0.09, 0.24 | 0.37         | 1.10  | 0.88, 1.38 | 0.41 | 1.04                                      | 0.95, 1.14 | 0.40        |

Abbreviations: CI, confidence interval; OR, odds ratio; ref, reference.

Note: Boldface indicates statistical significance ( $p < 0.05$ ).<sup>a</sup> There were 22 participants with a major depressive disorder and 147 participants with an anxiety disorder.<sup>b</sup> Model 1 is adjusted for age, sex, cohort and time awake.<sup>c</sup> Model 2 is model 1 additionally adjusted for education, occupational status, marital status, smoking and body mass index.<sup>d</sup> Model 3 is model 2 additionally adjusted for physical activity and the disability score.

time was 5.7 (0.6) years. Scores for the CES-D ranged between 0 and 44, MMSE-scores ranged between 7 and 30 and the g-factor ranged between -3.22 and 3.10. For the CES-D score, an average 0.41 point increase (SD: 7.51) was observed over time; for the MMSE score a 0.06 point decline (SD: 1.89) was found; and the g-factor showed an average 0.18 point (SD: 0.51) decline.

### 3.1. Sedentary time in association with depressive symptoms and MDD

In cross-sectional analyses adjusted for age, sex, cohort and time awake (model 1), 1 h/day more sedentary time was associated with 0.25 point higher CES-D score (95%CI: 0.08, 0.41) (Table 2). After additional adjustment for confounders in model 2, the effect estimate was slightly reduced ( $\beta$ : 0.18; 95%CI: 0.006, 0.34). The association was clearly attenuated after additional adjustment for activity variables in model 3 ( $\beta$ : 0.08; 95%CI: -0.09, 0.24). The change in the effect estimate was particularly large (54%) after adding the disability score to the model (Supplementary Table 2A). Additionally, occupational status, marital status, and smoking were associated with changes in the effect estimate of more than 10%. No cross-sectional association of sedentary time with MDD was found in any model (Table 2).

In longitudinal analyses, no association between sedentary time was observed and the CES-D score in any model (Table 3).

**Table 3**

Longitudinal associations of objectively assessed sedentary time with depressive symptoms and anxiety disorders, analyzed per 1 h/day more sedentary time.

| Model   | Depressive symptoms score (n = 1530) |             |      | Anxiety disorders <sup>a</sup> (n = 1347) |            |      |
|---|--------------------------------------|-------------|------|---|------------|------|
|   | $\beta$                              | 95%CI       | p    | OR  | 95%CI      | p    |
| Model 1 <sup>b</sup> : basic model                              | 0.13                                 | -0.04, 0.31 | 0.13 | 1.13                                      | 0.99, 1.28 | 0.08 |
| Model 2 <sup>c</sup> : + sociodemographic and lifestyle factors | 0.08                                 | -0.09, 0.26 | 0.36 | 1.07                                      | 0.93, 1.23 | 0.33 |
| Model 3 <sup>d</sup> : + activity and disability                | 0.05                                 | -0.13, 0.23 | 0.57 | 1.06                                      | 0.92, 1.22 | 0.42 |

Abbreviations: CI, confidence interval; OR, odds ratio; ref, reference.

<sup>a</sup> There were 59 incident cases of anxiety disorders.<sup>b</sup> Model 1 is adjusted for age, sex, cohort and time awake, the time between the baseline and follow-up measurement and the baseline measurement of depression symptoms.<sup>c</sup> Model 2 is model 1 additionally adjusted for smoking, education, body mass index, occupational status and marital status.<sup>d</sup> Model 3 is model 2 additionally adjusted for physical activity and the disability score.

### 3.2. Sedentary time in association with anxiety disorders

Per 1 h/day more sedentary time, the odds of having an anxiety disorder were 1.11 times higher (95%CI: 1.01, 1.21) in cross-sectional analysis adjusted for age, sex, cohort and time awake. However, after additional adjustment for lifestyle factors, the association did not remain (Table 2). The effect estimate changed most (26.9%) when disability score was added to the model. Additionally, physical activity, smoking, and BMI were associated with changes in the effect estimate of more than 10% (Supplementary Table 2B).

There was no longitudinal association between sedentary time and anxiety disorders (Table 3).

### 3.3. Sedentary time in association with cognition: g-factor and MMSE score

In cross-sectional analyses adjusted for age, sex, cohort and time awake, 1h more sedentary time was associated with 0.03 lower score for the g-factor (95%CI: -0.05, -0.01). The association disappeared with additional adjustment for sociodemographic and lifestyle factors in model 2 and 3 (Table 4). Smoking, BMI and the disability score were all associated with large changes in the effect estimate (Supplementary Table 2C). There was no cross-sectional or longitudinal association between sedentary time and the MMSE-score (Table 4). The cross-sectional analyses with the separate components of the g-factor showed a similar trend as the overall g-factor (Supplementary Table 3).

In longitudinal analyses, no association was found between sedentary time and the g-factor in any model (Table 4).

### 3.4. Sensitivity analyses

In the sensitivity analyses stratified by age, most associations were non-significant in line with the main analyses. No major differences were observed between the age-groups.

(Supplementary Tables 4–7). Furthermore, in sex-stratified analyses similar associations for men and women were observed (Supplementary Tables 8–11).

## 4. Discussion

In this population-based cohort study, no evidence was found for a cross-sectional or longitudinal association of actigraphically assessed sedentary time with depressive symptoms, anxiety disorders or cognition. The observed cross-sectional associations between sedentary time and the mental health or cognitive outcome measures were explained by external factors, and were not observed longitudinally.

In several cross-sectional studies, associations of higher self-reported or objectively measured sedentary time with depression (Sanchez et al., 2008; Yancey et al., 2004) and anxiety (Cao et al., 2011), and with impaired cognitive function (Steinberg et al., 2015)

**Table 4**  
Cross-sectional and longitudinal associations of objectively assessed sedentary time with cognition, analyzed per 1 h/day more sedentary time.

| Model   | Cross-sectional              |              |              |                       |             |      | Longitudinal                 |             |      |                       |             |      |
|---|------------------------------|--------------|--------------|-----------------------|-------------|------|------------------------------|-------------|------|-----------------------|-------------|------|
|   | g-factor, Z-score (n = 1539) |              |              | MMSE score (n = 1828) |             |      | g-factor, Z-score (n = 1012) |             |      | MMSE score (n = 1444) |             |      |
|   | $\beta$                      | 95%CI        | p            | $\beta$               | 95%CI       | p    | $\beta$                      | 95%CI       | p    | $\beta$               | 95%CI       | p    |
| Model 1 <sup>a</sup> : basic model <sup>b</sup>                 | -0.03                        | -0.05, -0.01 | <b>0.005</b> | -0.01                 | -0.06, 0.04 | 0.66 | -0.01                        | -0.02, 0.01 | 0.37 | 0.02                  | -0.03, 0.06 | 0.46 |
| Model 2 <sup>c</sup> : + sociodemographic and lifestyle factors | -0.02                        | -0.04, 0.004 | 0.12         | -0.002                | -0.05, 0.04 | 0.94 | -0.01                        | -0.02, 0.01 | 0.44 | 0.02                  | -0.03, 0.06 | 0.46 |
| Model 3 <sup>d</sup> : + activity and disability                | -0.01                        | -0.03, 0.01  | 0.23         | -0.0004               | -0.05, 0.05 | 0.98 | -0.004                       | -0.02, 0.01 | 0.61 | 0.02                  | -0.02, 0.07 | 0.31 |

Abbreviations: CI, confidence interval; MMSE, mini mental state examination; OR, odds ratio; ref, reference.

Note: Boldface indicates statistical significance ( $p < 0.05$ ).

<sup>a</sup> Model 1 is adjusted for age, sex, cohort and time awake.

<sup>b</sup> The longitudinal model 1 is additionally adjusted for the time between the baseline and follow-up measurement and the baseline measurement of the g-factor or MSSE score.

<sup>c</sup> Model 2 is model 1 additionally adjusted for education, occupational status, marital status, smoking and body mass index.

<sup>d</sup> Model 3 is model 2 additionally adjusted for physical activity and the disability score.

have been reported. In the current study, high levels of sedentary time were cross-sectionally associated with more depressive symptoms, higher odds for anxiety disorders, and worse cognitive performance. However, these associations were largely explained by disability, smoking and occupational status. In the associations between sedentary time and mental and cognitive health, the effect estimate for sedentary time changed notably after inclusion of the disability score. Having a disability increases the risk of worse mental and cognitive health (Krall, Carlson, Fried, & Xue, 2014; McKnight & Kashdan, 2009; Schieman & Plickert, 2007), and is associated with higher levels of sedentary time (Dunlop et al., 2015). Therefore, in this study, disability was considered a confounder; an antecedent of the exposure (sedentary time) and the outcome (mental and cognitive health), and not on the causal pathway (Rothman, Greenland, & Lash, 2008). However, it might be argued that prior sedentary behavior had led to disabilities, which in turn led to poor mental health and impaired cognition. Several scientists have warned for overadjustment bias when analyses are adjusted for an intermediate variable that is on a causal pathway from the exposure to the outcome (Schisterman, Cole, & Platt, 2009). In the elderly, it is more likely that having physical disabilities will lead to more sedentary time than the converse. It is certainly important to understand the association between sedentary time and mental health and cognition independent of the effect of disease, thus it is important to include a measure of disability or functional limitations. However, in the meta-analyses regarding the association of sedentary behavior with depression and cognition, only 4 out of 20 (Zhai et al., 2015) and 2 out of 8 (Falck et al., 2017) studies adjusted for a measure of disability, respectively. None of the studies in the meta-analyses of sedentary behavior and anxiety adjusted for disability (Teychenne et al., 2015). Previous studies might have been affected by (residual) confounding, but future studies examining the association between sedentary behavior and mental health should be aware of the possibility of residual confounding if not adjusting for by disability.

In longitudinal analyses in the current study, no association was found between objectively measured sedentary time and depressive symptoms, anxiety or cognitive performance after a follow-up period of 5.7 years, whether disability and other confounders were accounted for or not. In contrast, previous longitudinal studies using self-reports provided support for the notion that high sedentary time and poor mental health and cognitive performance co-occur (Falck et al., 2017; Teychenne et al., 2015; Zhai et al., 2015). The follow-up time in previous studies ranged from 1 to 10 years, with most studies including 6 years of follow-up, similar to the current study (Hamer & Stamatakis, 2014; Kesse-Guyot et al., 2012, 2014; Lampinen & Heikkinen, 2003; Lucas et al., 2011; Peeters, Burton, & Brown, 2013; Sanchez-Villegas et al., 2008; Thomée, Eklöf, Gustafsson, Nilsson, & Hagberg, 2007; Thomee, Harenstam, & Hagberg, 2012; van Gool et al., 2003).

Furthermore, the age-range of participants in previous studies is similar to the population in the current study. Therefore, it seems unlikely that these factors contribute to the inconsistent findings between studies. Instead, the explanation for these inconsistencies might be related to the measure of sedentary behavior. For self-report, there is a possibility of shared method variance bias or reporter bias (Podsakoff, MacKenzie, Lee, & Podsakoff, 2003). In previous studies based on self-reported sedentary behavior, the information on the dependent and independent variable were both obtained from the same individual with subjective measures. Furthermore, with more objective methods, like actigraphy, all sedentary time during the day is captured, whereas questionnaires often do not specifically include information on sitting during breakfast, lunch, or dinner. Noteworthy, all of the studies observing a longitudinal association between sedentary behavior and mental health or cognition included watching television in their measure, whereas the studies using computer or internet use as a proxy for sitting time more often observed no association with mental health (de Wit, van Straten, Lamers, Cuijpers, & Penninx, 2011; Teychenne et al., 2015; Thomee et al., 2012; Zhai et al., 2015). This suggests that not all types of sedentary behaviors are related to poor mental health and cognition. The social context and the purpose of the sitting activity can be of importance. For example, in contrast to the (socially) interactive character of computer/internet use, television viewing is a passive form of sedentary behavior. On the one hand, viewing television is a possible risk factor for poor mental health over and above sitting. On the other hand, watching television for the purpose of relaxation might benefit mood (Nabi, Prestin, & So, 2016), whereas driving a car in busy traffic could result in stress.

Taken together, the results of the current study suggest that sedentary behavior itself might not be related to impaired mental health and cognition. The context of sitting may be more important than the posture. However, comparing objective and subjective sedentary measures was not possible in the current study. Future studies using comprehensive questionnaires to capture sedentary behavior in addition to objective measures are recommended to better understand the association with mental health and cognition. Factors such as the purpose and the social context of the behavior should be taken into account in analyses. Meanwhile, since there is evidence that high levels of sedentary time are associated with worse cardiometabolic health (de Rezende et al., 2014), public health efforts should continue encouraging adults to be active.

#### 4.1. Strengths and limitations

The strengths of this study are the objective measurement of sedentary behavior, the prospective population-based design and the relatively large sample size over a follow-up period of six years. However,

several potential limitations must be acknowledged. Participants that agreed to wear an Actiwatch were more often men, showed a lower disability score and better cognitive performance than individuals not participating in the current study. This might affect the generalizability towards the total population of older adults. Additionally, a limitation of the wrist-worn actigraph is that it cannot classify all (in)activity accurately (Rosenberger et al., 2013). Consequently, lower body activity might be classified as sedentary behavior. As a result, regression dilution bias might attenuate the association between sedentary behavior and mental and cognitive health (Hutcheon, Chioloro, & Hanley, 2010). However, an advantage of a wrist-worn device is that it can be worn 24-h per day, thereby leading to a comprehensive overview of sedentary behavior. Furthermore, in the longitudinal analyses in this study, there might be some survival effect, since only those alive at follow-up could complete the next measurements of the mental health factors. Moreover, other selection biases may have occurred, since participants with missing information on any of the outcome measures might be in worse health than those with complete information. For example, g-factor was only computed if all the cognitive tests were completed. Those with missing test scores for the cognitive test battery might be cognitively more compromised than those who completed all tests. However similar associations were seen when the respective cognitive tests were analyzed individually. Another limitation is that the follow-up measurements were not always collected in the same season as the baseline measurement. Seasonal variation of mood has been reported (Harmatz et al., 2000) and this could have influenced the results in the current study. Finally, levels of sedentary behavior were only measured at baseline. Since participants might have changed their level of sedentary behavior over time, this might have led to misclassification of the exposure. Additionally, only two measures of mental and cognitive health were obtained, and no additional information on these measures was collected between baseline and follow-up. Since especially mental health measures typically fluctuate over time (Stegenga, Kamphuis, King, Nazareth, & Geerlings, 2012; Sutin et al., 2013), this limitation reduces the power of the analyses.

## 5. Conclusions

In conclusion, in this population of middle-aged and elderly adults, high levels of sedentary time were not associated with depressive symptoms, anxiety or cognition. Previously observed longitudinal associations might be explained by specific types of sedentary behavior or the subjective assessment of sedentary behavior.

## Conflicts of interest statement

All authors declare that there are no competing interests.

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## Author contributions

CK, FJAvR, DK, AIL, MAI, OHF and HT participated actively in each of the following aspects for this article: conception and design or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content and final approval of the version to be published.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mhpa.2019.100296>.

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