

## Review article

# Association of sedentary behavior with the risk of breast cancer in women: update meta-analysis of observational studies



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## ABSTRACT

**Purpose:** Increasing studies focus on the health consequences of sedentary behavior, and whether sedentary behavior is associated with the risk of breast cancer remains uncertain. We applied quantitative techniques to synthesize relevant original observational studies to investigate this issue.

**Methods:** PubMed and Embase were searched through September 2014 to identify cohort and case-control studies that evaluated the association between sedentary behavior and breast cancer risk in women. Information on the characteristics of the included studies, risk estimates, and control for possible confounding factors, was extracted independently by two authors. A random effects model of meta-analysis was used to calculate the pooled risk estimate.

**Results:** Twenty one studies with 34 reports were included in our quantitative analysis. Sedentary behavior was found to slightly increase the risk of breast cancer in women and the pooled odds ratio (OR) and its 95% confidence interval (CI) were 1.08 and 1.04 to 1.13, without substantial heterogeneity ( $P = .579$ ,  $I^2 = 0.0\%$ ). Subgroup analysis showed that the risks of breast cancer for different domains of sedentary behavior were similar, although only occupational behavior showed statistical significance (OR, 1.10; 95% CI, 1.02–1.18) and the combined ORs of breast cancer are of borderline significance for sedentary behavior of daily life (OR, 1.10; 95% CI, 1.00–1.20) and sedentary behavior of leisure time (OR, 1.08; 95% CI, 0.98–1.19). Exclusion of any single study did not materially alter the combined risk estimate. Visual inspection of funnel plot, Begg's and Egger's tests did not indicate evidence of publication bias.

**Conclusions:** Integrated evidence from observational studies suggests a statistically significant slightly positive association of sedentary behavior with breast cancer risk.

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## Introduction

Breast cancer remains the most common malignancy in women worldwide. In 2013, it is estimated that there are 232,340 new cases of invasive breast cancer and 64,640 additional cases of breast cancer in situ among women in the United States [1]. Previous epidemiologic studies have showed that the development of breast cancer is associated with various risk factors, such as diet, obesity and weight gain, long-term postmenopausal hormone use, oral contraceptive use, alcohol or tobacco consumption, physical inactivity, and sedentary lifestyle [1].

Sedentary behavior, which is not a synonym for lack of exercise, is defined as activities done in sitting or reclining posture with an energy expenditure typically in the range of 1.0 to 1.5 multiples of the basal metabolic rate [2]. It is characterized by prolonged sitting or lying down and absence of whole body movement, such as watching television (TV) or other forms of screen-based entertainment (using computer or game consoles), desk-bound work, and car driving [3,4]. Sedentary behavior becomes more and more ubiquitous in modern life with the development of technology and industry. Studies have shown that individuals spent more than half of their waking time ( $\approx 7.7$  h/d) in sedentary activities in the United States in 2003 to 2004 [5]. Emerging studies have demonstrated that sedentary behavior is an independent risk factor for health problems and is distinct from the beneficial effects of moderate- to vigorous-intensity physical activity [6]. Sedentary behavior has been reported to be positively associated with obesity, weight gain [7], metabolic syndrome [8], and cardiovascular disease [9]. The relationship between sedentary behavior and cancers is a new field of epidemiologic study. A review

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published in 2010 summarized the original studies between sedentary behaviors and colorectal, breast, endometrial, ovarian, and prostate cancer risk, but quantitative techniques were not used [10]. From the findings of National Health and Nutrition Examination Survey (NHANES) (2003–2006), sedentary time was associated with biomarkers of breast cancer risk in postmenopausal women, indicating that sedentary time may independently contribute to breast cancer risk [11]. However, the results of several observational studies on this issue are inconsistent. Recently, a meta-analysis [12] analyzing relationship of TV viewing and other sedentary behaviors to cancer risk concluded that sedentary behavior was unrelated to breast cancer. However, this meta-analysis only identified 13 studies on sedentary behavior (mainly TV viewing) and breast cancer risk, and six other studies investigating association between job-titled sedentary behavior and the risk of breast cancer were missing. Given six missing studies in the previous meta-analysis and two additional recent literatures, an improved understanding of the effect of sedentary lifestyle on breast cancer risk should be necessary. Therefore, we conducted an updated meta-analysis of 21 observational studies to evaluate the association between sedentary behaviors and the risk of breast cancer.

## Methods

Ethical approval is not required for this meta-analysis.

This systematic review was performed in accordance with the meta-analysis of observational studies in epidemiology criteria [13]. Two authors (Y.Z. and C.P.) participated in the literature search, study selection, and data extraction independently. Discrepancy between researchers was resolved by discussion.

### Search strategy

PubMed and Embase databases were searched to identify relevant articles published until September 2014. The following search terms were used to form the search strategy for identifying articles specifically pertaining to sedentary behavior and breast cancer: “sedentary,” “sitting,” “television,” “TV,” “screen time,” “computer use,” “game-console use,” and “car driving” in combination with “breast cancer,” “breast carcinoma,” or “breast neoplasm.” We also conducted manual searches of the reference lists of the retrieved articles and review articles to identify additional eligible studies.

### Inclusion criteria and exclusion criteria

Studies were considered eligible if they met the following criteria: (1) It had a case-control or cohort study design, (2) Sedentary behavior was clearly defined or the time spent in sedentary behavior every day or week was reported (Specifically, sedentary behavior was defined by calculating time spent in “sitting” or “TV,” describing a job as “mostly sitting,” evaluating the job title based on specific criterion), (iii) Relative risk (RR) or odds ratio (OR) with 95% confidence intervals (CIs) on the association between sedentary behavior and breast cancer was reported or could be calculated from the data provided. Studies were excluded if “sedentary” was not particularly defined or only as a term used to denote no participation in moderate- to vigorous-intensity physical activity. For example, a study in which sedentary was classified as “low or very low physical activity, i.e. less than 10 min/day or less than 150 min/wk of moderate physical activity” was excluded in this analysis [14].

### Quality assessment

The quality of studies was assessed according to the Newcastle-Ottawa quality assessment scale [15], which is a validated scale for

nonrandomized studies in meta-analyses. This scale awards a maximum of nine points to each study: (1) four for selection of participants and measurement of exposure, (2) two for comparability of cohorts on the basis of the design or analysis, and (3) three for assessment of outcomes and adequacy of follow-up. A high score ( $\geq 6$ ) out of a total of nine points indicated high methodological quality.

### Data extraction

Two investigators (Y.Z. and C.P.) independently extracted the data using a predesigned data extraction form. The following data were extracted from identified studies: first author’s name, publication year, study design, location or country where the study was performed, the number of patients and participants, definition and measurement of sedentary behavior, RR and/or OR with 95% CI, and confounding factors adjusted in the analysis. Discrepancies were resolved by discussion.

### Statistical analyses

RR and/or ORs reported separately by different subgroups of sedentary behavior in any single article were treated as separate reports. The pooled measure was calculated by the inverse variance weighted mean of the logarithm of ORs and RRs with 95% CI to assess the association of interest with random effects model. Statistical heterogeneity among reports was evaluated using  $I^2$  of Higgins and Thompson ( $I^2$  values of 0, 25, 50, and 75% represent no, low, moderate, and high heterogeneity, respectively).

To identify the stability of the primary results and to examine the resource of potential heterogeneity, we performed subgroup analyses by publication year, region where the study was conducted, study design, menopausal status, type of sedentary behavior, domain of sedentary behavior measurement, breast cancer type (invasive or in situ breast cancer), whether body mass index (BMI) or physical activity was adjusted, study quality, and referenced category. For sensitivity analyses, leave-one-out analyses [16] were used to investigate the magnitude of influence of each study on pooled risk estimates. We evaluated the publication bias by the Egger’s regression asymmetry test [17], Begg’s rank correlation test [18], and visual inspection of a funnel plot. All statistical analyses were conducted using Stata, version 11.0 (Stata-Corp, College Station, TX). Statistical tests were two sided and  $P$  less than 0.05 was considered statistically significant.

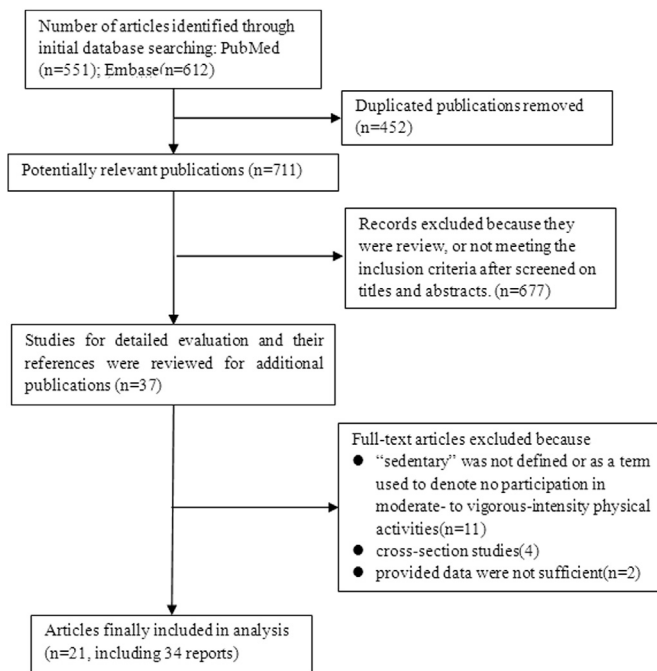
## Result

### Literature search results

The results of literature search process at each stage were shown in Figure 1. We retrieved 551 citations from the PubMed database and 612 citations from Embase. After 452 duplicate citations were excluded, we screened 711 citations through titles and abstracts, of which 677 were excluded because they were reviews, cross-sectional studies, or irrelevant studies. After reviewing the full text of the remaining 37 potentially eligible studies carefully, 16 of them were excluded because “sedentary” was not defined clearly and only as a term used to denote no participation in physical activity. Twenty one studies with 34 reports were identified for the final analysis. A manual search of the reference lists of these studies did not yield any new eligible studies.

### Study characteristics

Our search strategy identified 14 case-control studies and seven cohort studies, including 2,625,772 participants and 82,630 breast



**Fig. 1.** Flow chart of identification of relevant observational studies of sedentary behavior in relation to breast cancer.

cancer patients. Table 1 summarizes the general characteristics of the included studies that were published between 1993 and 2014. Of them, nine studies were conducted in Europe [23,26–28,31,32,34–36], two in China [33,38], one in India [30], seven in the United States of America [21,22,24,25,37,39], and two in Canada [19,29]. All the included studies used self-report measures such as questionnaires or interviews to assess the sitting time, TV time, job-related or other sedentary behavior in the domain of daily life, occupational, or leisure time. Of note, eight studies are included in this analysis with their sedentary behavior accessed by job titles based on predetermined occupational activity categories or in which “mostly sitting,” “mainly sitting,” and “job lasting for long sitting time” were an option for participants to select. The other 13 studies provided the specific time range spent in sitting, TV viewing each day or week. The risk estimates reported by the studies were adjusted for a comprehensive range of potentially confounding variables, including age, education, age at menarche and first birth, number of births, menopausal status, age at menopause, previous benign breast disease, history of breast cancer in first-degree relatives, and so on. Seven of the studies were adjusted with physical activity and 17 studies with the adjustment BMI. The study quality score ranged from 4 to 9 assessed by the modified Newcastle–Ottawa quality assessment scale, and 14 studies had 6 or more scores (indicating high quality).

#### Overall association between sedentary behavior and breast cancer risk

Of the included 34 reports, four reports showed a significantly positive relationship between sedentary behavior and breast cancer risk, and one study showed an inverse relationship. The other 29 suggested no statistically significant association of interest. Combining these estimates of association by a random effects meta-analysis, the pooled OR and 95% CI of breast cancer associated with sedentary behavior was 1.08 (1.04–1.13) and no significant heterogeneity among studies was observed ( $P = .579$ ,  $I^2 = 0.0\%$ ; Fig. 2).

#### Subgroup analysis and sensitivity analysis

According to different criteria of classification, we conducted 11 types of subgroup analyses involving 27 subgroups. The association between sedentary behavior and breast cancer risk did not vary obviously across different subgroups by published time (before 2010 or after 2010), menopausal status (premenopausal or postmenopausal), BMI adjustment (yes or no), physical activity adjustment, study quality, and so on (Table 2). Subgroup analyses by study design showed that pooled risk estimate from cohort studies (OR, 1.09; 95% CI, 1.04–1.15) was similar with that from case-control studies (OR, 1.09; 95% CI, 1.00–1.18), although pooled risk estimate from case-control studies was of borderline significance and had a more substantial heterogeneity (Fig. 3). Subgroup analysis by sedentary behavior domain showed that although sedentary behaviors of daily life and leisure time were both not significantly associated with breast cancer risk (daily life: OR, 1.10; 95% CI, 1.00–1.20 and leisure time: OR, 1.08; 95% CI, 0.98–1.19) and there was a statistically significant positive association between occupational sedentary behavior (OR, 1.10; 95% CI, 1.02–1.18; Fig. 4), the combined ORs were similar for these three domains of sedentary behavior. Subgroup analysis by breast cancer type indicated that sedentary behavior was associated with both invasive (OR, 1.11; 95% CI, 1.03–1.19) and in situ breast cancer (OR, 1.09; 95% CI, 0.80–1.48), with statistically significant results only for invasive cancer. Subgroup analysis by referenced category indicated that the pooled OR of studies that compared high levels of sedentary behavior with the most physically active group as the referent category (OR, 1.20; 95% CI, 1.08–1.34) was bigger than that of the other studies (OR, 1.05; 95% CI, 1.00–1.11; Table 2).

We excluded any single study in turn and pooled the results of remaining included reports with a range from 1.07 (95% CI: 1.02–1.14;  $I^2 = 9.60\%$ ;  $P = .309$ ) to 1.10 (95% CI: 1.04–1.15;  $I^2 = 0\%$ ;  $P = .721$ ). No single study had excessive influence on the pooled effect between risk of breast cancer and sedentary behavior. We included multiple effect estimates of different sedentary behavior domains from the same study which may give a different weight to the study in the meta-analysis. Therefore, we conducted sensitivity analysis by including only one risk estimate per domain from a given study and found that the pooled results did not changed substantially.

#### Publication bias

Visual inspection of a funnel plot did not identify substantial asymmetry (Fig. 5). The Begg’s rank correlation test and Egger’s linear regression test also indicated no evidence of obvious publication bias among the studies (Begg’s test:  $Z = 1.32$ ,  $P = .188$ ; Egger’s test:  $t = 1.35$ ,  $P = .181$ ).

#### Discussion

Sedentary behavior is more and more widespread in modern life, and the health consequences of it have been of increasing interest to the general public recently. We quantitatively reviewed the existing observational epidemiologic evidence and suggested a positive association between sedentary behavior and the risk of breast cancer. Compared with individuals in control groups, people who often experienced sedentary behavior had a slightly increased risk of 8% for breast cancer. There was no evidence of substantial heterogeneity among studies on the association between sedentary behavior and the risk of breast cancer, and no evidence of obvious publication bias among the studies was found.

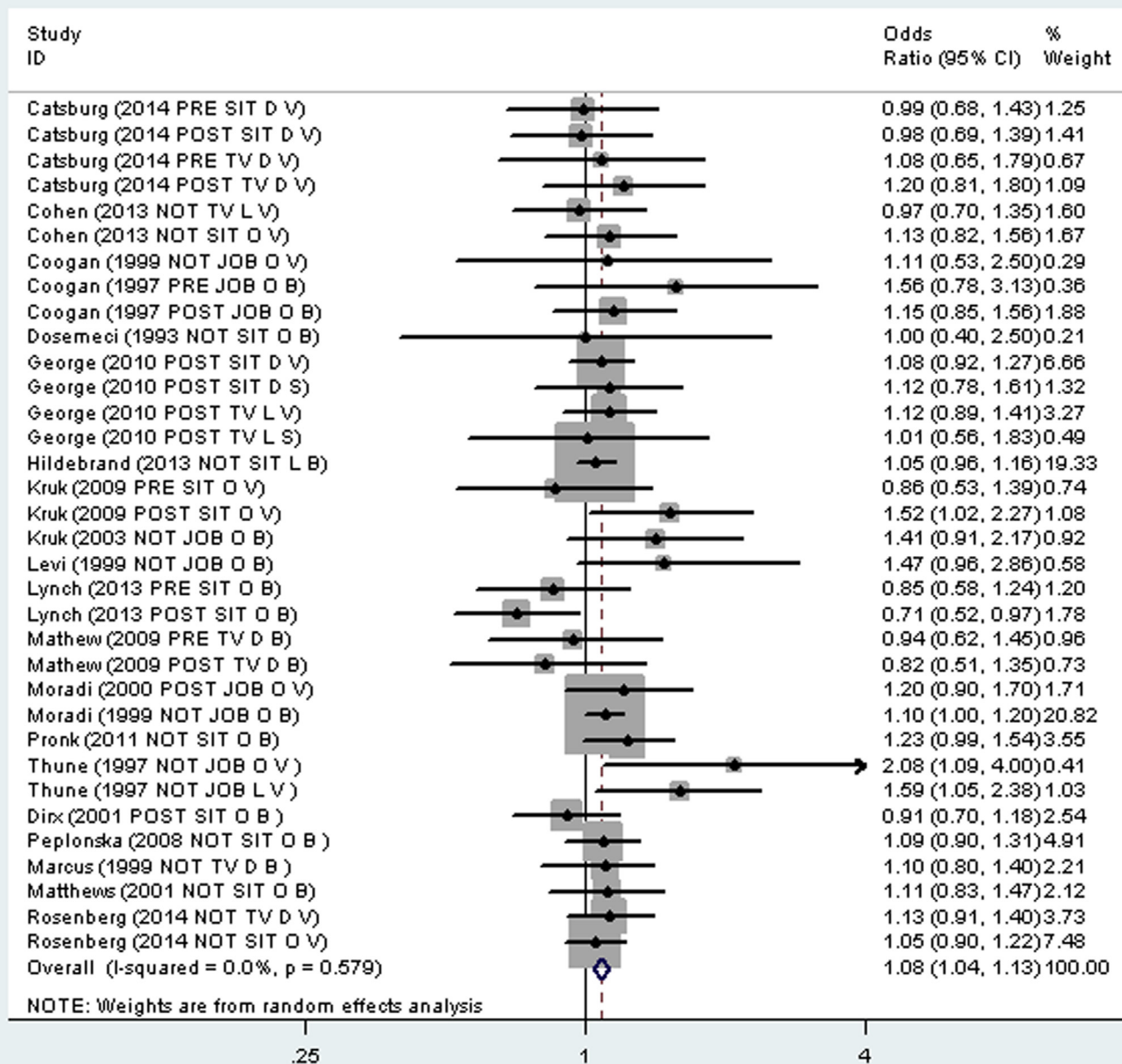
It has been reported in two previous articles that sedentary behavior occupied 70% of the prevalence of modifiable breast cancer risk factors [40] and the standardized incidence ratio of

**Table 1**  
Main characteristics of the included studies

First author and year	Design and region	Study participants	Number of cases	Outcome	Sedentary behavior measurement mode	Sedentary behavior domain	Measurement of sedentary behavior	Sedentary measure used in meta-analysis	Adjustment for confounders	NOS
Catsburg [19] 2014	Case control, Canada	4417	1097	Invasive breast cancer	Questionnaire	Daily life	Time spent in sitting and TV	Time spent in TV $\leq 1$ versus $\geq 21$ h/w and sitting $\leq 12.5$ h/w versus $\geq 54$ h/w	Age, menarche, use of oral contraceptives, use of hormone therapy, number of live births, age at first live birth, family history of breast cancer, alcohol intake	6
Cohen [20] 2013	Case control, USA	2730	546	Invasive breast cancer	Questionnaire	Daily life	Sitting time at work or watching TV and so on	Sitting at work none versus $\geq 3$ h/d, watching TV or movie $< 2$ versus $\geq 5$ h/d	Education, household income, cigarette smoking, ever use of hormone replacement therapy, parity, age at menarche, first-degree family history of breast cancer, having health insurance, and other sedentary behaviors as well as total activity	7
Coogan [21] 1997	Case control, USA	11646	4863	Breast cancer	Telephone interview	Occupational	Job titled	Sedentary versus heavy physical activity rating	Age, benign breast disease, family history of breast cancer, age at menarche, parity, age at first birth education, and alcohol consumption	5
Coogan [22] 1999	Case control, USA	903	233	Breast cancer	Telephone interview	Occupational	Job titled	Sedentary jobs versus medium or heavy jobs	Vital status, education, and total duration of work in years	5
Dosemeci [23] 1993	Case control, Turkey	485	241	Breast cancer	N/A	Occupational	Sitting $> 6$ h/d	Sedentary $> 6$ h/d versus $< 2$ h/d	Age, smoking, socioeconomic status	5
George [24] 2010	Cohort, USA	97,039	3436	Invasive breast cancer or breast cancer in situ	Questionnaire	Daily life	Hours spent sitting while watching TV or videos	TV or watching, $< 3$ versus $\geq 9$ h/d	Age, energy intake, parity or age at first live birth, menopausal hormone therapy use, number of breast biopsies, smoking, alcohol intake in grams per day, race education	6
Hildebrand [25] 2013	Cohort, USA	73,615	4760	Breast cancer	Questionnaire	Leisure time	Sitting time	Sitting time $\leq 3$ versus $\geq 6$ h/d	Age, race, education, BMI, weight change, alcohol use, smoking status, number of live births, age at first live birth, age at menopause, family history of breast cancer, breast cysts, hysterectomy, oophorectomy, and mammogram within last year.	9
Kruk [26] 2003	Case control, Poland	822	257	Breast cancer	Questionnaire	Occupational	Job titled (job remaining long sitting time)	Sedentary versus medium physical activity	BMI, age at menarche, sport and recreational activities, intake of vegetables and fruits, and experience of stress	5
Kruk [27] 2009	Case control, Poland	1943	858	Invasive breast cancer	Questionnaire	Occupational	Sitting time	Long versus short	Age, BMI, age at menarche, age at first full-term pregnancy, parity, months of breast-feeding, active and passive smoking	9
Levi [28] 1999	Case control, Sweden	620	246	Breast cancer	Interview with questionnaire	Occupational	Job titled (mainly sitting)	Mainly sitting versus stirring	Age, education, age at menarche, age at first birth, number of births, menopausal status, age at menopause, calorie intake, previous benign breast disease, and history of breast cancer in first-degree relatives.	5
Lynch [29] 2013	Case control, Canada	2452	1222	Breast cancer	In-person interviews	Occupational	Lifetime total occupational sitting time (h/w)	Lifetime total occupational sitting time 0 versus $> 7.3$ h/w	Current age, educational level, caloric intake, ever alcohol consumption, smoking status, waist-hip ratio, total number of mammograms, first-degree family history of breast cancer, ever use of hormone replacement therapy, number of children breast-fed	7

Mathew [30] 2009	Case control, India	3739	1866	Breast cancer	In-person interviews	Daily life	The time of watching TV	Nil or <60 m per d versus ≥180 m/d	Age and center, religion, marital status, education, socioeconomic status, residence status, waist and hip sizes, parity, age at first child birth, and duration of breast-feeding	7
Moradi [31] 1999	Cohort, Sweden	1,940,510	51,520	Breast cancer	Questionnaire	Occupational	Job titled	Occupational sedentary versus high/very high occupational physical activity lever	Age by 5-y intervals, calendar year of follow-up by year, place of residence, socioeconomic status	7
Moradi [32] 2000	Case control, Sweden	6802	3347	Invasive breast cancer	Self-administered questionnaire and telephone interview	Occupational	Job titled	Occupational sedentary versus high/very high occupational physical activity lever	Age, age at menarche, parity and age at first birth, height, use of hormone replacement therapy, age at menopause, and use of oral contraceptives	6
Pronk [33] 2011	Prospective cohort, China	73,049	717	Breast cancer	Questionnaire	Occupational	Average sitting time	≥4 h/d versus ≤1.20 h/d	Age, education, family history of breast cancer, age at first birth, and number of pregnancies	5
Thune [34] 1997	Cohort, Norway	25,624	351	Invasive breast cancer	Questionnaire	Occupational and leisure time	Leisure time spent reading, watch TV, or engaging in other sedentary activities; work mostly sedentary	Sedentary at work versus heavy manual labor	Age at entry, height, county of residence, and number of children	7
Dirx [35] 2001	Cohort, Netherlands	62,537	1208	Breast cancer	Interview	Occupational	Sitting time per day (h)	6–8 h/d versus <2 h/d	Age, age at menarche, age at menopause, benign breast disease, parity, age at first birth, maternal breast carcinoma, breast carcinoma in sister(s), education, height, and baseline alcohol and energy intake	7
Peplonska [36] 2008	Case control, Poland	4502	2176	Breast cancer	Questionnaire	Occupational	Occupational sitting time	Occupational sitting <11.3 h/d versus >47.8 h/d	Age, study site, education, BMI, age at menarche, menopausal status, age at menopause, number of full-term births, age at first full-term birth, breast-feeding, family history of breast cancer, and previous screening mammography	6
Marcus [37] 1999	Case control, USA	1650	863	Breast cancer	Interview	Daily life	TV viewing time	Daily or almost daily versus never	Age at diagnosis/selection, sampling design, matching factors: age, race	4
Matthews [38] 2001	Case control, China	3015	1459	Breast cancer	Interview	Occupational	Job titled	Occupational sitting time: Q5 (long) versus Q1 (short)	Age, education, household income, first-degree family history of breast cancer, history of breast fibroadenoma, age at menarche, age at first live birth, and age at menopause; matching factor: age	6
Rosenberg [39] 2014	Cohort, USA	307,672	1364	Invasive breast cancer	Questionnaire	Daily life and Occupational	Time of sitting and watching TV or sitting at work	TV: <1 h/d versus ≥5 h/d; work: <1 h/d versus ≥5 h/d	Age (single year), years of education, BMI, parity, vegetable/fruit dietary pattern, and meat/fried foods dietary pattern, and vigorous activity; sitting and watching TV adjusted for sitting at work and vice versa	8

h/d = hours per day; h/w = hours per week; m/d = minutes per day; NOS = Newcastle-Ottawa quality assessment scale; USA = The United States.



**Fig. 2.** Forest plots of sedentary behavior and risk for breast cancer. B = breast cancer; D = daily life; JOB = job title–based classification or job relative definition of sedentary behavior; L = leisure time; NOT = not mention the menopausal status; O = occupational life; POST = postmenopausal women; PRE = premenopausal women; S = breast cancer in situ; SIT = sitting time; TV = TV viewing time; V = invasive breast cancer.

breast cancer in women with long sitting time was significantly higher than those with short sitting time [41]. However, these two articles were excluded in this meta-analysis because they are not case-control or cohort studies, or no OR or hazard ratio was presented in the results. Our result was similar with the two studies and provided more robust epidemiologic evidence. However, our result was different from the result of a previous meta-analysis [12], which included 13 studies and suggested there was no statistically significant association between sedentary behaviors and the risk of breast cancer (RR = 1.03; 95% CI: 0.95–1.12). The different results between our meta-analysis and the previous meta-analysis may be due to the different types and numbers of original studies included.

Compared with the foregoing meta-analysis, we included eight additional studies which were missing in the previous meta-analysis possibly because of incomprehensive literature searching or different understanding and measurement of sedentary behaviors, and two were reported after the preceding meta-analysis.

Several hypothesized biological mechanisms exist to underpin how sedentary behavior increase breast cancer risk, including possible effects of sedentariness on weight gain, hyperinsulinism or insulin resistance, and breast density, which were supposed to be contributing to the development and progression of breast cancer [11,42,43]. For example, excess body weight, the most apparent consequence caused by sedentary behavior, was an

**Table 2**  
Results of subgroup analyses

Subgroup	Number of studies	Number of reports	OR	95% CI	<i>I</i> <sup>2</sup>	<i>P</i> for heterogeneity
Publication year						
Before 2010	14	18	1.12	1.05–1.20	4.3%	.403
After 2010	7	16	1.06	1.00–1.12	0.0%	.732
Region						
North America	9	19	1.05	1.00–1.11	0.0%	.892
Europe	9	11	1.17	1.04–1.31	31.5%	.147
Asia	3	4	1.11	0.95–1.29	0.00%	.407
Study design						
Case-control studies	14	22	1.09	1.00–1.18	10.70%	.312
Cohort studies	7	12	1.09	1.04–1.15	1.60%	.428
Menopause state						
Premenopausal	5	6	0.97	0.81–1.16	0.0%	.745
Postmenopausal	8	12	1.05	0.95–1.16	19.3%	.254
Not mentioned	8	16	1.10	1.05–1.16	0.00%	.670
Definition and measurement of sedentary behavior						
Sitting time	9	16	1.05	0.99–1.11	2.00%	.430
TV time	6	9	1.07	0.96–1.20	0.00%	.955
Job titled	6	9	1.20	1.06–1.34	10.50%	.348
Sedentary behavior domain						
Daily life	5	10	1.10	1.00–1.20	0.00%	.638
Leisure time	4	5	1.08	0.98–1.19	6.60%	.369
Occupational	12	19	1.10	1.02–1.18	23.80%	.168
Controlling for BMI						
Yes	13	26	1.07	1.02–1.13	4.8%	.394
No	8	8	1.10	1.03–1.19	0.00%	.764
Controlling for physical activity						
Yes	8	16	1.07	1.02–1.12	0.00%	.475
No	13	18	1.12	1.03–1.21	0.0%	.585
Type of breast cancer						
In situ	1	2	1.09	0.80–1.48	0.00%	.770
Invasive	8	15	1.11	1.03–1.19	0.00%	.562
Not mentioned type	12	17	1.07	1.00–1.13	8.3%	.358
NOS						
≥6	15	26	1.07	1.02–1.12	1.0%	.448
<6	6	8	1.21	1.06–1.38	0.00%	.944
Referenced category						
The most physically active group	7	9	1.20	1.08	1.34	.348
Group not experiencing defined sedentary behavior	14	25	1.05	1.00	1.11	.800

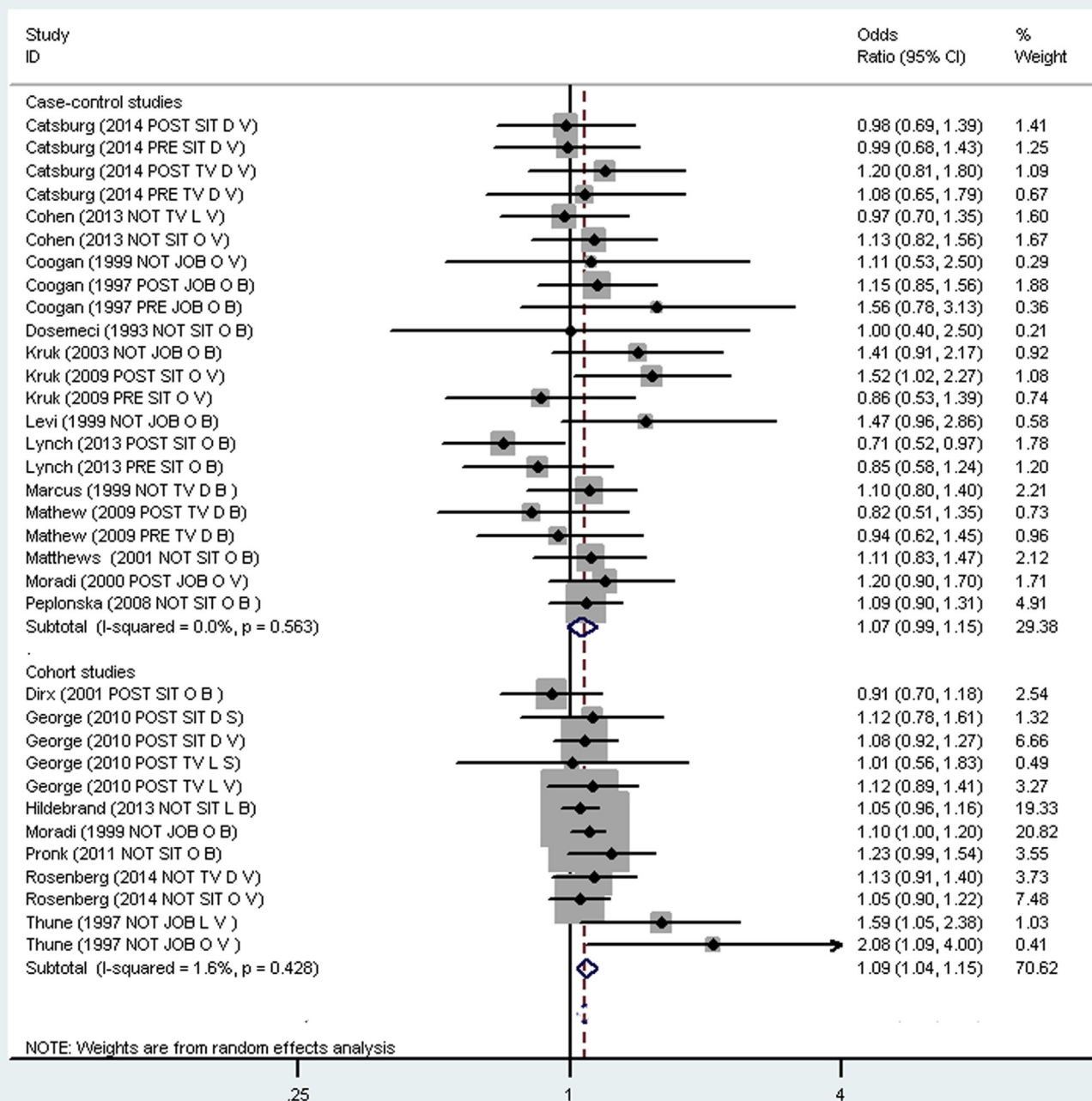
NOS = Newcastle-Ottawa quality assessment scale.

independently associated breast cancer risk in postmenopausal women, suggesting adiposity accumulated through sedentary behavior is likely an independent contributor to breast cancer and a mediating variable on the other pathways [44]. Hyperinsulinemia, another independent risk factor of breast cancer, was proved to be associated with sedentary behavior in the bed rest studies, showing increased sedentary time could induce a range of deleterious metabolic effects such as significant decrease in whole-body insulin sensitivity [45]. Moreover, sedentary time was positively associated with high breast density [43], which has been shown to be a strong, independent risk factor for the development of breast cancer with a four- to six-fold risk increased compared with the least dense breasts [46,47]. Other proposed mechanisms by which sedentary behavior may increase the risk of breast cancer include decreasing level of vitamin D [48,49], imbalance of proinflammatory and anti-inflammatory factors [50–52] as well as sex hormones [46,53].

Taking into consideration the potential influence of physical activity and BMI on the association between sedentary behavior and breast cancer risk, we conducted subgroup analyses by adjusted variables of them. The finding showed that whether they were adjusted or not did not change the relationship of interest, suggesting that sedentary behavior could be an independent determinant of breast cancer distinct from that of physical inactivity. An interesting finding of subgroup analysis was that although the combined ORs were similar for different domains of sedentary

behavior, sedentary behaviors of daily life and leisure time were both not significantly associated with breast cancer risk and there was a statistically significant positive association between occupational sedentary behavior. This finding suggested that potential difference between occupational history and other domains of sedentary behavior should be further identified by more future studies with large samples. Generally, occupational sedentary behavior is easily measured and more difficult to be changed by health education. Therefore, to decrease the breast cancer risk, jobs involving sedentariness and women doing these types of jobs should be concerned and if necessary and possible, some measures should be taken. Subgroup analysis by referenced category indicated that studies which compared sedentary behavior with the most physically active behavior showed bigger breast cancer risk than studies which compared sedentary behavior with non-sedentary behavior. This finding suggested that it should be possible that physical activity could more decrease breast cancer risk than only reducing sedentary behavior.

Several strengths of the present systematic review should be highlighted. First, this meta-analysis systematically quantified the strength of association between sedentary behavior and breast cancer up to now. Second, it included a wide range of domain and measurement modes of sedentary behavior allowing for an accurate and comprehensive assessment of the association between sedentary behavior and the risk of breast cancer. Besides, consistent results from sensitivity analysis and the low



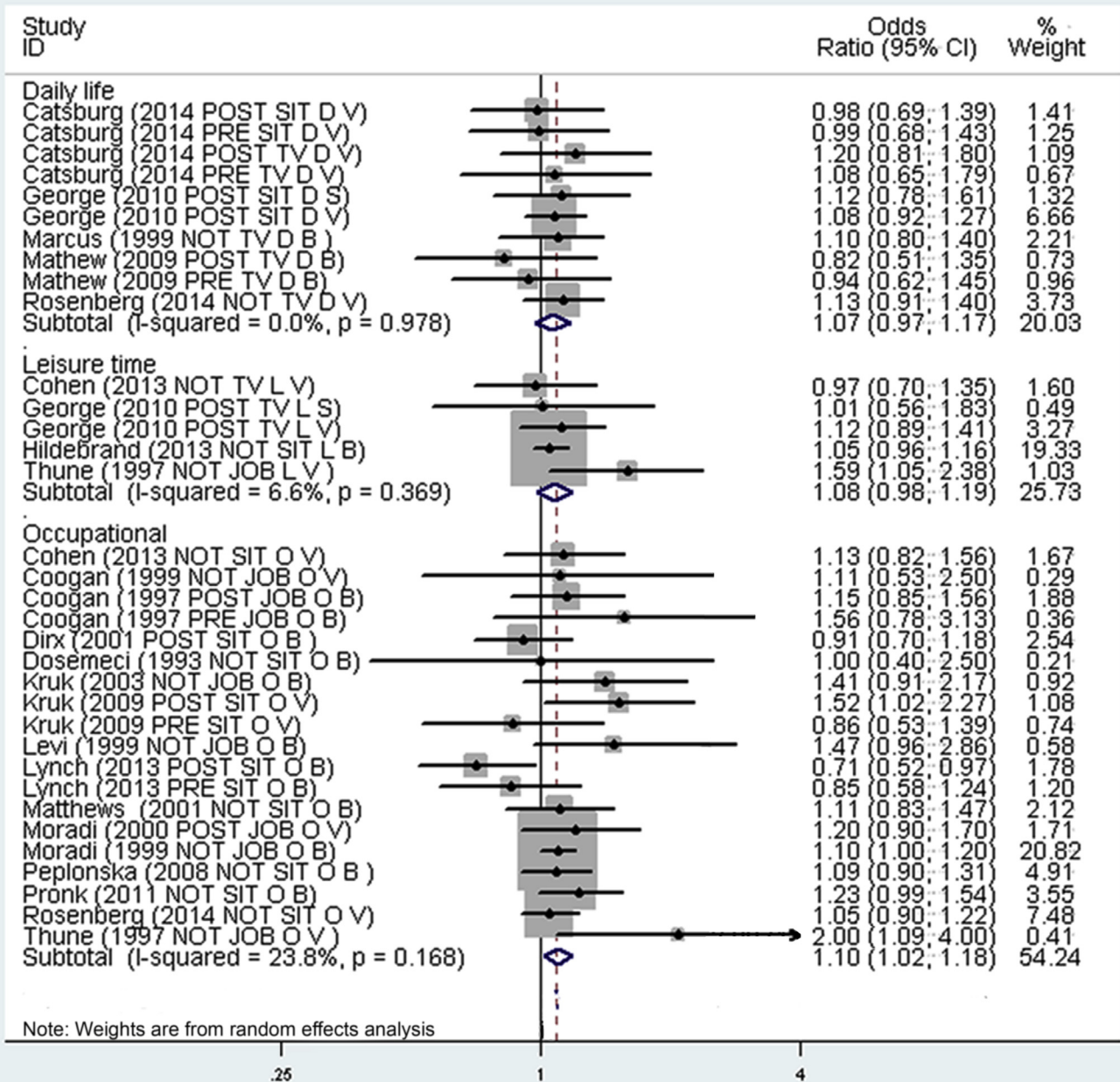
**Fig. 3.** Results of subgroup analysis by study design. B = breast cancer; D = daily life; JOB = job title–based classification or job relative definition of sedentary behavior; L = leisure time; NOT = not mention the menopausal status; O = occupational life; POST = postmenopausal women; PRE = premenopausal women; S = breast cancer in situ; SIT = sitting time; TV = TV viewing time; V = invasive breast cancer.

heterogeneity among included studies indicated that our findings were reliable and convincing. Finally, publication bias was unlikely responsible for our findings, as validated by visual inspection of a funnel plot, the Begg's rank correlation test, and the Egger's linear regression test.

With some limitations, the results of this meta-analysis should be interpreted cautiously in mind. First, although data analysis did not suggest substantial heterogeneity among the included studies, the nomenclature and measurement of sedentary behavior in these studies were highly heterogeneous and a wide range of

definitions of “sedentary” have been used (i.e., the use of time spent in sitting, TV viewing, or job described as “mostly sitting,” and so forth). Although the positive association with overall sedentary behaviors and the risk of breast cancer was found in this meta-analysis, the subgroup analysis of sitting time and TV time did not show significant association with the risk of cancer, which is consistent with the results of previous meta-analysis. Second, questionnaire is the only tool to assess the sedentary behavior in all included studies, which would suffer from recall and selection bias in the included case-control studies. Studies relied on job





**Fig. 4.** Results of subgroup analysis by domain of sedentary behavior. B = breast cancer; D = daily life; JOB = job title–based classification or job relative definition of sedentary behavior; L = leisure time; NOT = not mention the menopausal status; O = occupational life; POST = postmenopausal women; PRE = premenopausal women; S = breast cancer in situ; SIT = sitting time; TV = TV viewing time; V = invasive breast cancer.

title–based classification and self-reported engagement in sedentary behavior, which was likely to cause the misclassification of exposure, and may underestimate or exaggerate the reported associations. Finally, nine of the 34 reports used TV viewing as the surrogate marker of sitting time in this meta-analysis. Although TV viewing time through self-report measures has been regarded as reasonably reliable and valid as the commonly measured sedentary behavior particularly in leisure time [54], we cannot dismiss the potential measurement error associated because TV time cannot represent total sedentary behavior.

**Conclusions**

In summary, this meta-analysis of observational epidemiologic studies with the most up-to-date evidence indicated that sedentary behavior should be positively associated with an increased risk of breast cancer. Excessive sedentary behaviors may have potential detrimental effects on the development of breast cancer. It might be important to recommend the public to modify their lifestyle and reduce the time of sedentary behavior, such as watching TV and operating the computer.

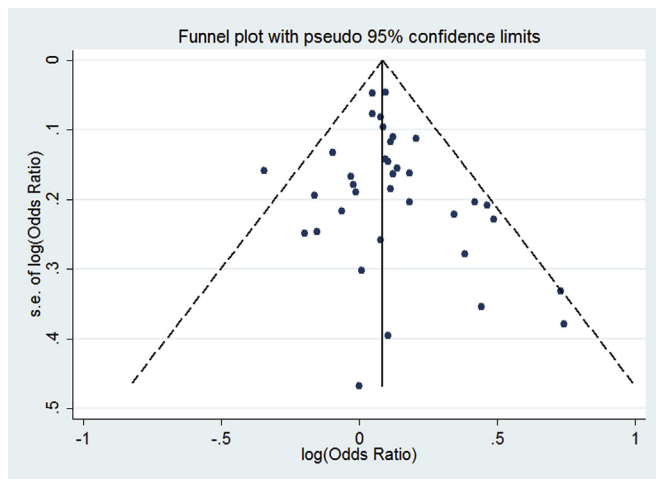


Fig. 5. Funnel plot with 95% CIs.

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