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Physical activity and sedentary levels among people living with epilepsy: a systematic review and meta-analysis

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Running Head: Physical activity and sedentary behavior in epilepsy

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Abstract

How physically active and sedentary people with epilepsy are, is unclear. We conducted a meta-analysis to investigate physical activity and sedentary behavior levels compared with the general population in people with epilepsy across the lifespan. Embase, PubMed, PsycARTICLES and CINAHL Plus were searched from inception till 1/3/2019. A random effects meta-analysis was conducted. Adults with epilepsy (mean age range=30-47 years) were significantly less likely to comply with physical activity recommendations [odds ratio (OR)=0.68; 95%CI=0.53–0.87; P<0.001; N analyses=10; n epilepsy=1,599; n controls=137,80] and more likely to be inactive (as defined by individual study criteria) (OR=1.57; 95%CI=1.34-1.84; P < 0.001; N analyses=6; n epilepsy=6,032; n controls=928,184). Data in children (mean age range=10-12 years) were limited (N=4; n=170) and inconsistent, while there were no data available for middle-aged and old age (>65 years) people with epilepsy. Our data demonstrate that adults with epilepsy are less physically active than the general population. Public health campaigns specifically targeting the prevention of physical inactivity in adults with epilepsy are warranted. More research on physical activity and sedentary levels in children, adolescents, middle-aged and old age but also adult people with epilepsy is needed before specific recommendations can be formulated.

Keywords: Exercise; Physical Activity; Sedentary; Epilepsy

1. Introduction

People living with epilepsy have a high risk for co-morbid anxiety and depression [1, 2], which is also one of the most important factors contributing to a higher risk for physical co-morbidities and premature mortality in this population [3, 4]. In the general population, robust evidence demonstrates that higher levels of physical activity and lower levels of sedentary behavior reduce levels of depression and anxiety [5-11]. In the last decade, several reviews have considered physical activity as a therapeutic intervention in people with epilepsy, concluding that epileptic discharges can decrease or disappear during exercise, which may translate into reduced seizure recurrence [12-14]. The available evidence also suggests that physical activity should be encouraged in people with epilepsy in order to promote wellbeing and quality of life [12]. In light of the plethora of physical, mental and cognitive health benefits of physical activity across the lifespan [15-18], it is recommended that people achieve 150 or 75 minutes of moderate or vigorous PA per week.

Despite the benefits of an active lifestyle, people with epilepsy experience a range of barriers to engaging in more physical activity and becoming less sedentary, such as the presence of co-morbid anxiety and depression [19-21], fear of exercise-induced seizures [22], side-effects of antiepileptic drugs such as drowsiness, fatigue, headache or migraine, gastrointestinal disturbances, dizziness and faintness, rash or skin disorders [19] and perceived stigma [23, 24]. Given that an active lifestyle is related to a better seizure control and quality of life in people with epilepsy, understanding physical activity and sedentary levels among people with epilepsy is critical to improving long-term health outcomes.

Several important questions regarding the relationship between physical activity, sedentary behavior and epilepsy remain unanswered. For instance, mean levels of physical activity and sedentary behavior have yet to be established in this population. Along with obtaining an accurate estimate of the levels of physical activity and sedentary behavior among people with epilepsy, understanding predictors of physical activity and sedentary behavior in this population is also of relevance for improving daily clinical practice, while providing a basis for future research endeavors. In addition, it is of interest to explore demographic (e.g., age, gender) and clinical (e.g., illness duration, subtypes of epilepsy, active versus inactive epilepsy presence of co-morbidity, etc.) predictors as such information may assist in identifying those at a higher risk for lower physical activity participation and sedentary behavior. In

addition, it remains unclear if people with epilepsy engage in more or less physical activity and sedentary behavior compared to the general population.

In order to address the current gaps in the literature, the primary aims of this systematic review and meta-analysis were to establish: (a) the pooled mean time spent physically active (light, moderate and vigorous and total physical activity, and number of steps per day) and sedentary per day, and (b) the pooled percentage of people complying with the general population health recommendation of at least 150min of moderate intensity physical activity per week or being insufficiently active according to other (inter)national criteria. The secondary aims were to investigate predictors of physical activity and sedentary behavior using meta-regression analyses, and to explore differences in people with epilepsy versus the healthy population. As there are age-dependent variations in types of seizures [25] and in physical activity and sedentary levels, we evaluated physical activity and sedentary levels in children and adolescents (<18 years), adults (18 < 65years) and middle-age and old age people (65≤ years) with epilepsy versus the general population separately.

2. Material and methods

This systematic review adhered to the MOOSE guidelines [26] and PRISMA statement [27].

2.1. Inclusion criteria

We included studies that involved participants of any age with a diagnosis of epilepsy, irrespective of the diagnostic assessment method, and secondly measured physical activity or sedentary behavior using either a subjective questionnaire (e.g. International Physical Activity Questionnaire (IPAQ)[28]) or objective measure (e.g. accelerometer). Physical activity was defined as any bodily movement produced by skeletal muscles and which requires energy expenditure [29]. Sedentary behavior was defined as a behavior with an energy expenditure ≤1.5metabolic equivalents of task (METs), while in a sitting or reclining posture during waking hours and not simply the absence of physical activity [30] Third, studies could be observational (prospective or cross-sectional) or interventional (randomized controlled trial or clinical controlled trials) conducted in any setting. For prospective and interventional studies only the baseline data were included. Fourth, papers had to be published in an international peer-reviewed journal.

2.2. Exclusion criteria

Exclusion criteria were: (a) non-quantitative studies, (b) abstracts of conferences and review papers, (c) not including people with epilepsy, and (d) no adequate measure of physical activity or sedentary behavior (see outcomes).

2.3. Search strategy

Two independent authors (DV and BS) searched Embase, PubMed, PsycARTICLES and CINAHL Plus without language restrictions from inception till March 1st 2019, using the keywords: ‘epilepsy’ AND ‘physical activity’ OR ‘exercise’ OR ‘sports’ OR ‘sedentary’ OR ‘sitting’ OR ‘lying’ OR ‘screen time’. In addition, reference lists of all eligible articles and related systematic reviews were screened to identify potentially eligible articles.

2.4. Study selection

After removal of duplicates, two independent reviewers (DV and BS) screened titles and abstracts of all potentially eligible articles and a final list of included articles was reached through consensus. A third reviewer (PW) was available for mediation throughout this process.

2.5. Outcomes

The primary outcomes were the mean time (minutes) per day that people with epilepsy engaged in (1) physical activity, and (2) sedentary behavior. We collected separate data for light, moderate and vigorous intensity and total physical activity if these data were reported. We also extracted the percentage of people complying with the general health recommendation of at least 150 min of moderate intensity physical activity per week and the percentage of people with epilepsy being insufficiently active according to each individual study criteria. Finally, we also collected data on physical activity and sedentary behavior among matched controls from the general population (where reported).

2.6. Data extraction

One author (DV) extracted data using a predetermined data extraction form, which was subsequently validated by a second author (BS). The data extracted included first author, year of publication, participants included in the article (including mean age, % male, % inactive versus active epilepsy, subtypes of epilepsy, mean body mass index, mean oxygen uptake, % smoking, % of physical and mental co-morbidity), physical activity and sedentary behavior assessment method (objective or self-report), and the physical activity and sedentary behavior outcomes.

2.7. Meta-analysis

Due to the anticipated heterogeneity across studies, we conducted a random effects meta-analysis with Comprehensive Meta-Analysis software (CMA, Version 3). The meta-analysis was conducted in the following sequence. First, we calculated the mean amount of time (total and light, moderate and high intensity physical activity, and sedentary behavior) with the 95% confidence intervals (CIs). Second, we calculated pooled percentage of people complying with the general health recommendations and the percentage of people being insufficiently active according to individual study criteria and where possible, also according to the measurement (self-report versus objective measurement). Third, we investigated

potential moderators of physical activity and sedentary behavior in people with epilepsy with meta-regression analyses. The potential moderators of interest were mean age (years), % male, subtypes of epilepsy, % active and inactive epilepsy, mean body mass index (kg/m²), mean oxygen uptake (ml/min/kg), % smoking, % of physical and mental co-morbidity, and physical activity and sedentary behavior assessment method (objective vs self-report). Fourth, we conducted a comparative meta-analysis investigating differences in physical activity and sedentary behavior levels with matched controls from the general population calculating Hedges' g and the 95% CI as the effect size. In addition, we calculated the mean difference in minutes per day together with the 95% CI in levels of physical activity and sedentary behavior. Heterogeneity was assessed with the I^2 statistics for each analysis [31]. Publication bias was assessed with the Begg-Mazumdar Kendall's tau [32]. For all analyses we calculated the trim and fill adjusted analysis [33] to remove the most extreme small studies from the positive side of the funnel plot, and recalculated the effect size at each iteration, until the funnel plot was symmetric about the (new) effect size.

3. Results

3.1. Search results

The initial search yielded 6,953 results. After removal of duplicates and exclusion at the title and abstract level, 61 abstracts were retrieved in full. Following analyses of the abstracts, 16 papers were removed. At the full text review stage, 30 papers were subsequently excluded (see Figure 1 for reasons). Full details of the 15 included studies [21, 23, 34-46] including 22 physical activity and / or sedentary levels are summarized in Table 1.

Insert Figure 1 about here

3.2. *Study and participants' characteristics*

Except for one single-group repeated-measures study [34], all studies were cross-sectional. Eleven studies focused on adults [14, 21, 23, 34, 37-39, 41-44] and four on children and adolescents [35, 36, 40, 45]. There were no studies in middle-aged and old age people with epilepsy (i.e. 65 years or older). Three studies used pedometers [34, 35, 40]. The other studies assessed physical activity and sedentary levels with questionnaires. Four studies reported physical activity levels for subgroups, e.g. for inactive epilepsy, active epilepsy and /or history of epilepsy [39, 41, 44] or different years of data collection [38] separately. Across the 15 unique studies, including 22 physical activity and/or sedentary levels, there were 8,074 people with epilepsy of which 170 were children and adolescents and 7,904 were adults. The mean age ranged from 10 [36] to 47 [34] years, the proportion of male participants from 35% [36] to 58% [46]. The sample size ranged from 8 [40] to 2,555 [42]. The number of matched general population controls was 1,066,124. The sample size ranged from 20 [37] to 400,055 [42]. All demographical and clinical data of the 15 studies including 22 physical activity and/or sedentary levels are summarized in Table 1, physical activity and sedentary outcomes (versus matched general population control data) in Table 2.

Insert Tables 1 and 2 about here

3.3. Narrative review and meta-analysis of the physical activity and sedentary levels in people with epilepsy

Results of the meta-analyses are summarized below. Full details are presented in Table 3. Three studies reported the total number of steps per day [34, 35, 40]. This number of steps per day was 7,268 [95%

confidence interval (CI) = 3,696 – 10,840]. Five adult studies including 9 analyses reported compliance with guidelines rates [23, 37, 39, 41, 44]. In total 44.4% (95% CI = 37.3 – 51.8) of the adults with epilepsy complied with the physical activity guidelines of 150 min of moderate to vigorous physical activity per week. One study in children and adolescents demonstrated that only 6% met the Canadian Assessment of Physical Literacy recommendations compared to 24% of their peers from the general population (Pohl et al., 2019). Five adult studies including 8 analyses reported on the percentage of people being inactive as defined by the authors of each study [21, 38, 42, 43, 46]. The pooled prevalence of adults with epilepsy being insufficiently active was 32.8% (95 CI = 15.6 - 56.4). Only one study assessed the daily time spend in screen time in children with idiopathic epilepsy (Rauchenzauner et al., 2017). This study found that children with epilepsy did not spend significantly more time in front of the TV or computer (11.6 ± 7.6 vs 10.2 ± 8.1 hours per week). Similarly, only one study explored the time spent sedentary per day in children with epilepsy compared with their siblings without epilepsy and found no significant difference (3.7 ± 1.6 vs 3.8 ± 1.7 hours per day) (Wong and Wirrell, 2006).

Insert table 3 about here

3.4. Subgroup analyses

There were insufficient data to perform any subgroup analyses.

3.5. Differences with matched general population controls

Data from 6 studies including 10 analyses showed that adults with epilepsy were significantly less likely to comply with physical activity recommendations [23, 35, 37, 39, 41, 44]. The odds ratio (OR) for complying with the guidelines in people with epilepsy (versus controls) is 0.68 (95% CI = 0.53 – 0.87) (P<0.001) (n with epilepsy = 1,599; n controls = 137,803). Three studies including 6 analyses demonstrated that adults with epilepsy have a higher odds for being inactive (OR= 1.57; 95 %CI = 1.34 - 1.84; P<0.001; n with epilepsy = 6,032; n controls = 928,184) [38, 42, 43].

4. Discussion

The current study is, to our knowledge, the first to systematically review and meta-analyze physical activity and sedentary behavior levels in people with epilepsy. Across 1,599 people with epilepsy, we found that adults with epilepsy were significantly less likely to meet international physical activity recommendations (OR=0.68; 95% CI = 0.53 – 0.87, P<0.001) compared to 137,803 controls. Similarly, data from 6,032 adults with epilepsy demonstrated that they were more likely to be physically inactive (OR= 1.57; 95 %CI = 1.34 - 1.84, P<0.001) than 928,184 controls. Studies in children and adolescents were limited (N=4) with low samples size (n total = 170) with inconsistent findings, and data in middle-aged and old age people with epilepsy were entirely absent. While in the past, patients were often advised against participating in physical activity and exercise, mostly because of fear, overprotection, and ignorance [47], our data clearly demonstrate that adults living with epilepsy should be advised to augment their physical activity levels

However, specific accurate information about the exact amount, frequency and intensity of physical activity and sedentary behavior levels was absent and minimal information was available which could be tested to explore factors that may influence these levels. Thus, formulating detailed physical activity recommendations for adults with epilepsy and strategies to address common barriers and facilitators is difficult due to the paucity of detailed information on the amount of time people with epilepsy spend in light, moderate and vigorous physical activity and sedentary behavior. Similarly, knowledge about predictors of physical activity and sedentary levels which could help to identify high-risk persons that may require more intense and targeted interventions is currently lacking. For example, it is unknown whether there are differences in physical activity and sedentary levels between different subtypes of epilepsy, between people with active and inactive epilepsy and between people with epilepsy with and without mental and/or physical co-morbidity. Previous individual studies have demonstrate that presence of co-morbid anxiety and depression [19-21], fear of exercise-induced seizures [22], side-effects of antiepileptic drugs [19], and perceived stigma [23, 24] contribute to lower physical activity levels in people with epilepsy.

Our current systematic review and meta-analysis identified several gaps in the current literature and provides a basis for future research. Specifically, we were unable to explore whether physical activity and sedentary levels assessed with subjective versus objective tools differed in people with epilepsy. Previous research in other populations has suggested there is often a discrepancy in the data

acquired from physical activity and sedentary behavior in self-report and objective measures [48-51]. Given that people with epilepsy often experience varying degrees of cognitive impairment [52], which has been implicated in affecting accurate physical activity recall in other populations [48], our data could be an under- or over-representation of physical activity and sedentary behavior levels. Similarly, depression and anxiety are common in people with epilepsy [1, 2]. Both co-morbid conditions can influence cognition and may lead to recall bias [53, 54]. Given this, future research should explore first whether the current physical activity questionnaires accurately collect data on physical activity and sedentary behavior in people with epilepsy or whether over- or underestimates of physical activity participation and sedentary behavior occur systematically in this at-risk group. A priority should be objective assessment of physical activity and sedentary behavior with accelerometers.

Several limitations of this meta-analysis should be noted. Firstly, all but one of the included studies relied on data drawn from subjective rather than from objective assessment methods. Secondly, in the main analyses, we encountered high levels of heterogeneity. Whilst such heterogeneity is expected when combining observational data, this is a consideration when these main analyses are reviewed in isolation. However, we follow the MOOSE guidelines [26] to try address this heterogeneity, but due to limited data were not able to explain some portion of the heterogeneity with subgroup and meta-regression analyses. For example, there was inadequate information on other lifestyle factors (such as smoking), epilepsy characteristics, side effects of antiepileptic medication, and physical and psychiatric co-morbidities, thus precluding rigorous meta-analytical or meta-regression analyses. Future research is required to understand the impact of these variables on physical activity and sedentary behavior in this population. It is also important that future research should seek to investigate physical activity and sedentary behavior levels in this vulnerable population and compare it with well-matched (age, gender and BMI) healthy controls. Further research is needed in children and adolescents, adults and middle-aged and old age people with epilepsy in order to be able to define age-appropriate recommendations. Nevertheless, allowing for these caveats, the current results clearly demonstrate that adults with epilepsy are less likely to comply with international physical activity recommendations and are more likely to be physically inactive. Public health campaigns specifically targeting the prevention of physical inactivity by promoting physical activity participation in people with epilepsy are warranted.

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Conflict of interest

The authors declare that they have no conflicts of interest to report.

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Figure 1. Flow diagram of the included and excluded studies

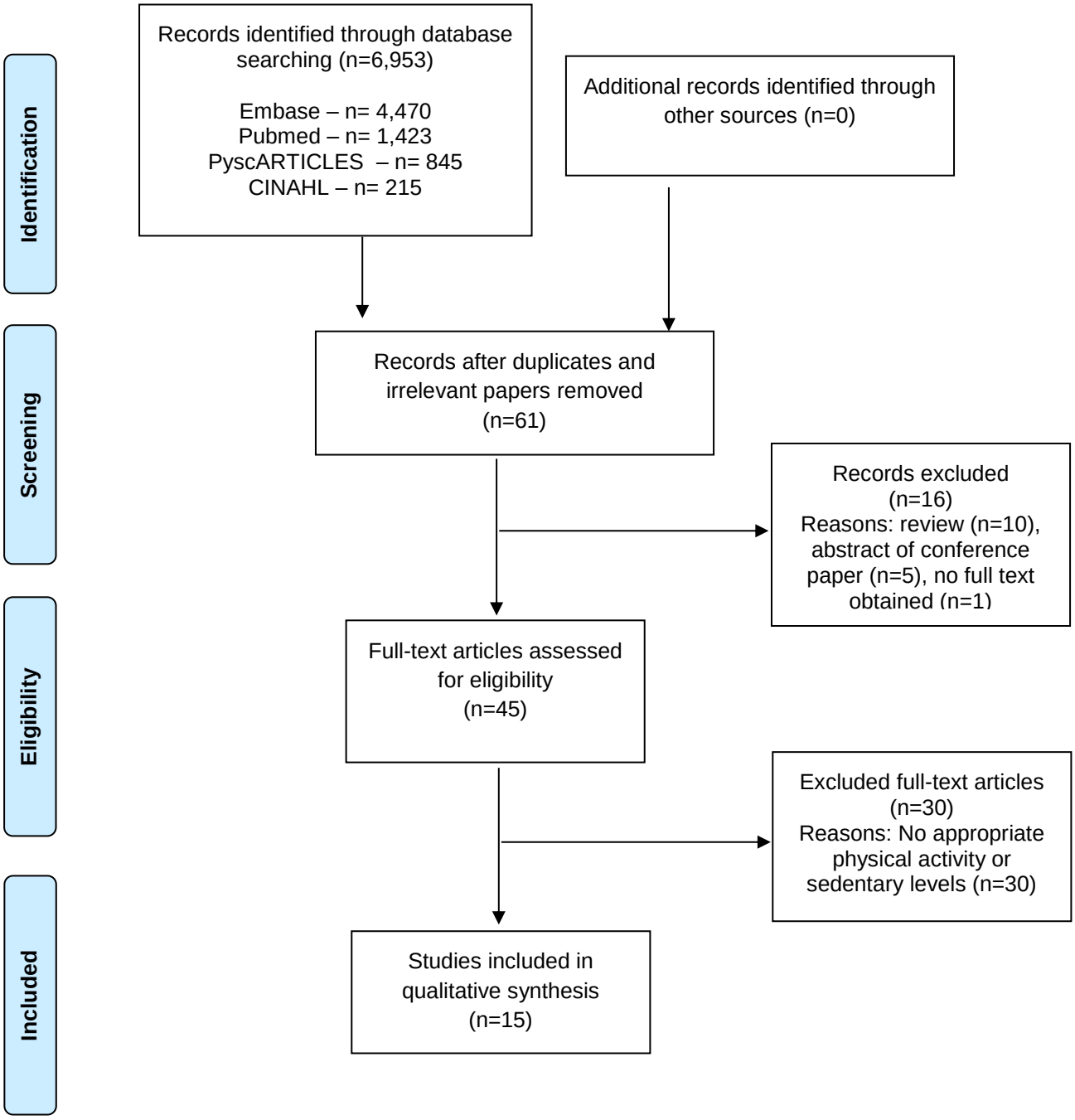

Table 1. Demographical and clinical data of the included studies

Author	Age group	Assessment	Sample size	Mean age (years)	Gender (% male)	% active epilepsy	% antiepileptic drugs	% physical co-morbidity	% mental co-morbidity	% smoking
Dustin 2019	2	2	30	47	37					
Pohl 2019	1	2	35	10	37					
Rauchenzauner 2017	1	1	48	11	35	0				
Tedrus 2017	2	1	67	45	45		46		31	
Volpato 2017	2	1	38	43	37					
Roberts 2015 [2001]	2	1	845	42	49					
Roberts 2015 [2003]	2	1	845	44	51					
Roberts 2015 [2005]	2	1	845	43	47					
Roberts 2015 [2010-2011]	2	1	845	44	45					
Cui 2015 [active]	2	1	277		46	100				20
Cui 2015 [inactive]	2	1	198		46	0				24
Cui 2015 [history]	2	1	480		46	0				22
Whitney 2013	1	2	8	12						
Han 2011	2	1	178	36	56			13		
Chong 2010 [active]	2	1	66		56	100	91	48		33
Chong 2010 [inactive]	2	1	59		41	0	0	32.5		29
Hindell 2010	2	1	2555	43	49					
Elliot 2008	2	1	97		37					
Ferguson 2008 [active]	2	1	207			1				37
Ferguson 2008 [inactive]	2	1	172			0				38
Wong 2006	1	1	79	11.2	54					

Age group (1= children and adolescents and 2= adults); assessment method (1= subjective and 2= objective).

Table 2. Physical activity and sedentary outcomes of the included studies in people with epilepsy (vs matched general population controls)

Author	Steps per day (n)	Complying with guidelines (%)	Screen time (hours per week)	Sedentary time (hours per day)	Inactive (%)
Dustin 2019	5107 ± 3434				
Pohl 2019	9692 ± 2932 (vs 10772 ± 3351)	6 (vs 24)			
Rauchenzauner 2017			11.6 ± 7.6 (vs 10.2 ± 8.1)		
Tedrus 2017		67			
Volpato 2017		71 (vs 80)			
Roberts 2015 [2001]					17 (vs 11)
Roberts 2015 [2003]					15 (vs 8)
Roberts 2015 [2005]					11 (vs 7.5)
Roberts 2015 [2010-2011]					8.5 (vs 8)
Cui 2015 [active]		35 (vs 46)			
Cui 2015 [inactive]		44 (vs 46)			
Cui 2015 [history]		46 (vs 46)			
Whitney 2013	6865 ± 5275				
Han 2011					58
Chong 2010 [active]		40 (vs 53)			
Chong 2010 [inactive]		47 (vs 53)			
Hindell 2010					60 (vs 50)
Elliot 2008					42 (vs 24)
Ferguson 2008 [active]		27 (vs 46)			
Ferguson 2008 [inactive]		38 (vs 46)			

Wong 2006				3.7±1.6 (vs 3.8±1.7)	
Arida 2003					85

Complying with guidelines= expressed as percentage complying with at least 150min of physical activity at moderate intensity per week: inactive = according to the criteria used by the study.

Table 3. Meta-analytic results of physical activity levels in people living with epilepsy

Analysis	N analyses	N participants	Meta-analysis			I^2
			Point estimate	95%CI		
Steps (number/day)	3	73	7,268	3,696	10,840	94%
Complying with guidelines (%)	9	1,564	44.4	37.3	51.8	87%
Inactive (%)	8	6,310	32.8	15.6	56.4	99%