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Review article

Accelerometer measured physical activity and sedentary time in individuals with multiple sclerosis versus age matched controls: A systematic review and meta-analysis

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ABSTRACT

Background: People with Multiple Sclerosis (PwMS) find it more difficult to engage in physical activity (PA) than healthy controls. Accelerometers can be used to measure sedentary time and free-living physical activity, understanding the differences between PwMS and controls can help inform changes such as interventions to promote a more active lifestyle. This in turn will help prevent secondary conditions and reduce symptom progression.
Objective: To conduct a systematic review and meta-analysis on accelerometer measured sedentary behavior and physical activity between PwMS and healthy controls.
Methods: A systematic search of five databases (PubMed, Web of Science, Ovid, Science Direct and CINAHIL) from inception until 22nd November 2019. Inclusion criteria was (1) included a group of participants with a definite diagnosis of multiple sclerosis of any type; (2) have 3 or more days of PA monitoring using accelerometers during free living conditions; (3) include age matched healthy controls; (4) assess adults over the age of 18; (5) reported data had to have been reported in a manner suitable for quantitative pooling including: percent of time spent sedentary, minutes per day of sedentary, light, moderate, vigorous activity (moderate and vigorous totaled together), steps per day or counts per day.
Results: Initial search produced 9021 papers, after applying inclusion criteria 21 eligible papers were included in the study. One paper was a longitudinal study from which only baseline data was included. One paper was a reliability and validity study, with data for PwMS versus controls in the validity section. All other papers are cross sectional, with one being a pilot study and another a random control study. One paper used two devices in unison, only one set of data is included in the statistics. Outcome data was available for 1098 participants, 579 PwMS and 519 healthy controls. Significant differences were seen in all categories tested: (1) sedentary time (min/day), standard mean difference -0.286, P = 0.044, n = 4 studies; (2) relative sedentary time (%/day), standard mean difference -0.646, P = 0.000, n = 5 studies; (3) LPA (min/day), standard mean difference 0.337, P = 0.039, n = 5 studies; (4) relative LPA (%/day), standard mean difference 0.211, P = 0.152, n = studies; (5) MVPA (min/day), standard mean difference 0.801, P = 0.000, n = 8 studies; (6) relative MVPA (%/day), mean difference 0.914, P = 0.000, n = 5 studies; (7) step count, standard mean difference 0.894, P = 0.000, n = 8 studies; (8) activity count, standard mean difference 0.693, P = 0.000, n = 13 studies.
Conclusion: PwMS are more sedentary and engage in less LPA, MVPA, steps per day and accelerometer counts per day than healthy controls when measured using accelerometers during free-living conditions.

1. Introduction

Multiple sclerosis (MS) is an autoimmune disease characterized by chronic inflammation, oligodendrocyte destruction and demyelination causing lesions throughout the central nervous system (CNS), from which the condition derives its name ('many scars') (Reipert, 2004).

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These lesions' cause irreparable damage and impair the function of both somatic and autonomic branches of the CNS (Lensch and Jost, 2011). However, the diffuse nature of damage to the CNS means that there is no consistent pattern as to which systems are affected, and consequently symptoms are frequently idiosyncratic, with wide variations in the type of impairments, the degree of impairment and, the rate of decline over time (Murray, 2009). Nevertheless, while the symptoms experienced by people with MS (PwMS) are heterogenous, common symptoms of the condition include muscle spasticity, tremor, impaired motor control, numbness, pain, fatigue, cognitive dysfunction, and depression.

Several of these symptoms make it difficult for individuals with MS to participate in physical activity (PA). Fatigue, will frequently leave PwMS with little energy to engage in PA (Kalron et al., 2019; Kratz et al., 2019) while the effects of spasticity, muscle tremor and impaired motor control can cause significant impairments in mobility (Kalron et al., 2018; Klaren et al., 2015; Sebastião et al., 2017; Williams et al., 2014) which may deteriorate further as the disease progresses (Sandroff et al., 2015). Moreover, psychological factors such as depression, and impaired cognitive function may make managing daily tasks difficult, and prevent engagement with more active lifestyles (Sadeghi Bahmani et al., 2017). Overall, these factors contribute to an increase in time spent being sedentary and reduced time engaged in moderate or vigorous intensity PA (MVPA) resulting in an elevated risk of secondary comorbidities including cardiovascular disease (CVD), stroke and type 2 diabetes (Wens et al., 2013). Correspondingly, previous work has suggested that the majority of PwMS do not engage in adequate PA, especially MVPA (Klaren et al., 2013; Motl et al., 2015, 2005, p. 05) despite evidence indicating that it can improve fatigue, balance, quality of life, and slow disease progression (Ensari et al., 2014; Motl et al., 2012; Pilutti et al., 2013b; Sebastião et al., 2017).

Early work assessing levels of PA in PwMS used questionnaire and self-reported measures of PA, while more recently, objective assessment using accelerometers has become the dominant technique. Indeed, accelerometry has been validated as a measure of walking performance (Klaren et al., 2016; Motl et al., 2013) and physical activity (Busse et al., 2004; Motl et al., 2006) for people with MS, and population specific cut-points for different levels of physical activity have been developed (Sandroff et al., 2004, 2014b). While previous reviews have suggested that PwMS fail to get sufficient PA, there are some important limitations to note. An early review by Motl et al. (2005), combined self-reported and objective assessments of PA commenting on effect size when comparing between PwMS and controls, preventing effective pooling of accelerometer only outcomes as the data was not available. Additionally, there are concerns over the accuracy of self-reported measures. Participants have been found to over report their activity levels, especially those with lower levels of fitness (Sallis and Saelens, 2000; Shook et al., 2016). Additionally factors such as social desirability (the tendency to keep to cultural 'norms') and social approval (the need to obtain a 'good' test score (Hebert et al., 1997)) mean that self-reported measures seldom capture even 50% of the variance in physical activity (Durante and Ainsworth, 1996). Additionally, the increase in studies using objective measures since then, means that an updated review using only objective measures is warranted. More recently a meta-analysis by Casey et al. (2017) assessed objective measures of PA in people with MS and while comprehensive, they chose to compare their data to NAHNES activity data rather than to non-MS control groups. Since the NAHNES data is specific to the US it is not clear if its use as a control variable is appropriate for studies in other locations. Moreover, there have been some criticisms of the validity and reliability of some NAHNES data sets, primarily under reporting of data sets including body mass index (BMI) and total energy expenditure (TEE) among other variables (Archer et al., 2013). Similarly, Block et al. (2016) assessed remote activity monitoring in a variety of neurological conditions using a variety of activity monitoring devices, including accelerometers, step-counters, and making conclusions about objectively measured PA in PwMS difficult. Moreover, because of these different methods of data collection they were unable to undertake statistical pooling of PA outcomes.

Consequently, there are no current reviews that have compared physical activity levels, sedentary time or step and activity counts of people with MS to healthy controls within the same study, which have used accelerometry. Therefore, the aim of this review is to systematically review the literature regarding objective assessment of sedentary time, MVPA, LPA, step and activity counts in PwMS compared to healthy, matched controls, and to provide quantitative data pooling to determine if differences exist in time spent in different PA domains between PwMS and healthy controls.

2. Methods

This systematic review and meta-analysis followed the reporting guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement by Moher et al. (2009) a systematic search processes, evaluation, analysis, and reporting was conducted.

2.1. Search strategy

An electronic database search was conducted to procure English language papers comparing accelerometer data from people with multiple sclerosis and controls. Five databases (PubMed, Web of Science, Ovid, Science Direct and CINAHIL) were searched from inception until 22nd November 2019. The search included the keywords: ("multiple sclerosis AND Actigraph OR accelerometer"), ("multiple sclerosis AND physical activity OR sedentary behaviour"), ("multiple sclerosis AND MVPA"), ("multiple sclerosis AND light physical activity"), (multiple sclerosis AND step count"), ("multiple sclerosis AND sedentary time"). Light physical activity was used instead of the abbreviation LPA as this incurred search results relating to lysophosphatidic acid. A second search to find journals relating to sedentary time was also conducted after realizing that sedentary behavior is a term relating to posture, although it has been used frequently in the past to denote sedentary time which is studied in this review. A specific search for Actigraph accelerometers was applied as they are the most frequently utilized monitors on the market for objective physical activity measurements in MS populations (Sandroff et al., 2014a). A manual search of previously published relevant meta-analysis and systematic reviews was also conducted, as was a review of the reference lists of studies included in this review.

2.2. Inclusion criteria

To be included studies had to: (1) included a group of participants with a definite diagnosis of multiple sclerosis of any type; (2) have 3 or more days of monitoring free living conditions with an accelerometer; (3) include age matched healthy controls; (4) assess adults over the age of 18; (5) reported data had to have been reported in a manner suitable for quantitative pooling including: percent of time spent sedentary, minutes per day of sedentary, light, moderate, vigorous activity (moderate and vigorous totaled together), steps per day or counts per day.

2.3. Study selection

All papers were transferred to a reference manager (Zotero: V 5.0.60, Fairfax, VA, USA). Articles were screened for duplicates. The remaining papers were screened using title, then abstracts. Subsequently, remaining papers were then analyzed by reading the full text identifying relevant studies. Abstract only papers, conference papers and posters were excluded. If there were no results reported of an original study i.e. reviews, secondary analysis or study protocols, they were eliminated. Papers were further excluded if they did not provide accelerometer data, only correlations and other statistical measures.

2.4. Data extraction

Data was extracted and entered in a spreadsheet (Microsoft® Excel 2016, Microsoft Corporation, Redmond, WA, USA). The following fields were collected: MS type, years diagnosed, gender, age, disease severity (using Expanded Disability Status Scale (EDSS) or Patient Determined Disease Steps (PDDS)), intervention duration, objectives, findings, other outcomes, biometric outcomes, and the presence of other cardio metabolic diseases. Accelerometer fields included: outcomes, make/model, cut points used, calibration, position worn, valid days for collection, duration, wear time criteria, and wear time. Accelerometer outcomes were further examined, data procured from the different studies included: percent of time spent sedentary, minutes per day sedentary, light physical activity, moderate PA, vigorous PA, MVPA, steps per day and counts per day.

Studies that provided percent of wear time for the different categories of physical activity were equated to minutes per day by using the percentage from the average daily wear time (min) provided for each group. All other data was converted to give a value per day, weekly data was divided by seven, hourly data was multiplied by hours per day the device was worn. The quality of each study was evaluated using a 20 question appraisal of cross sectional studies form (AXIS) provided by the British Medical Journal (BMJ) (Downes et al., 2016).

2.5. Statistical analyses

Meta-analyses were executed using Comprehensive Meta-Analysis (Biostat, V 2.2.064, Englewood, NJ, USA). Pooled data using a random-effects model were used to investigate differences between healthy controls and PwMS. Due to the likely differences in device, wear time, and calibration protocols, studies were assessed using standardized mean differences (SMD) rather than differences in means. Mean, standard deviation and sample size for PwMS and healthy controls for each variable of interest were used to determine overall effect size using a random effects model.

3. Results

3.1. Search results

The search criteria and review process are outlined in Fig. 1. The initial search using the five databases produced 9021 papers. One paper

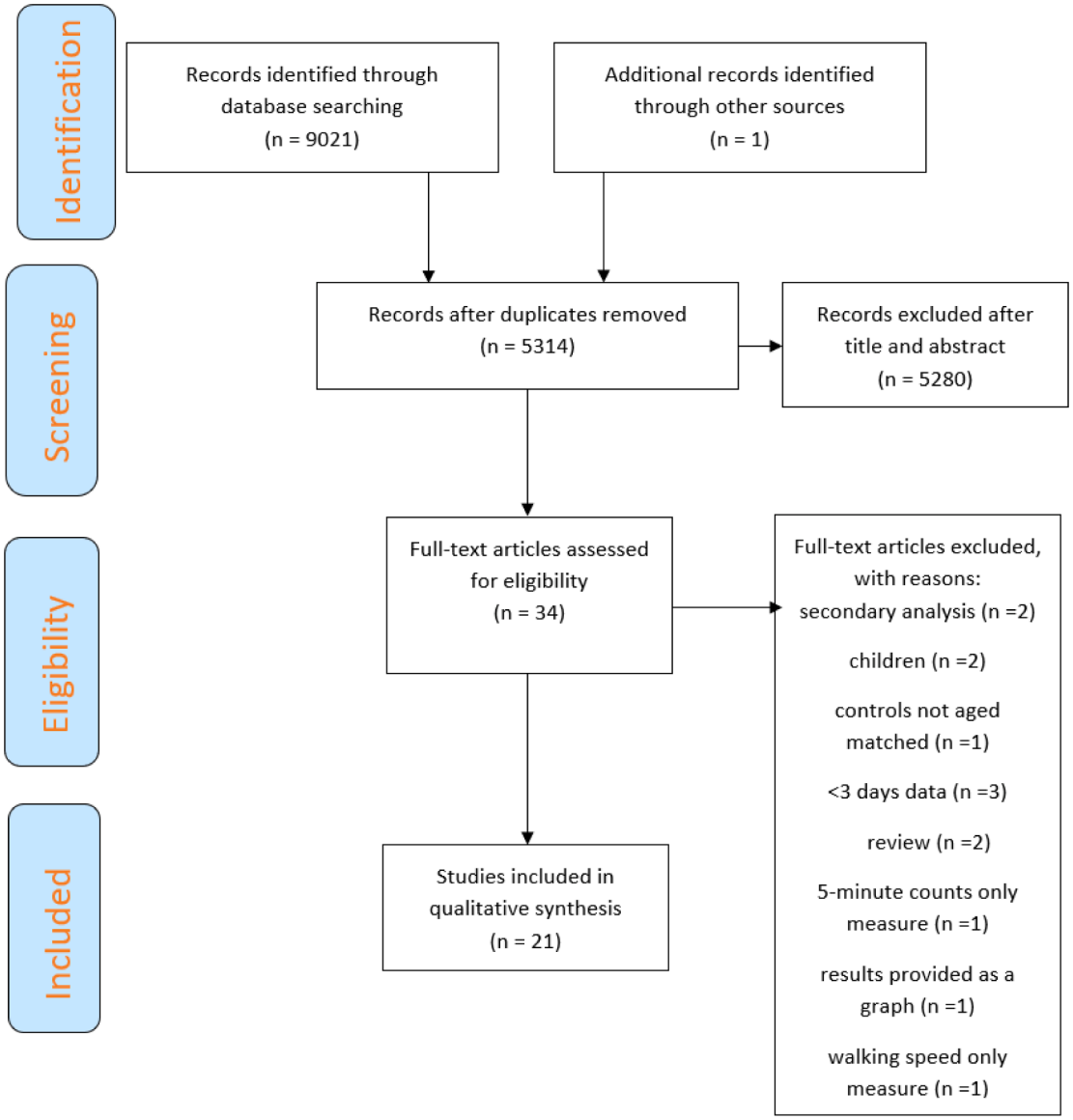

Fig. 1. The PRISMA flow diagram with numbers of included and excluded articles at each step of the review process.

was extracted after reviewing similar systematic review and meta-analysis. After removal of duplicates 5314 papers remained. Initial filtering for inclusion and exclusion criteria via title and abstract resulted in the removal of 5280 papers. Full papers of the remaining 34 articles were assessed with a further 13 removed (two reviews, two secondary analysis, two included children, one did not age match controls, three provided less than three days of data, three papers displayed or collected results in a different format; one only shared five-minute counts, one measured walking speed, and one provided no written results only a graph). Subsequently, 21 eligible papers were included in the study.

One paper was a longitudinal study with accelerometer data collected in baseline and week eight. Only the baseline data was extracted for use in this study due to the statistical powers of analyzing the number of participants, also, to ensure the behavioral change of the study did not reflect on the study as all other papers used baseline data (Hale et al., 2008). One paper was a reliability and validity study, with data for PwMS versus controls in the validity section (Busse et al., 2004). All other papers are cross sectional, (Blikman et al., 2015; Bollaert and Motl, 2019; Chung et al., 2016; Engelhard et al., 2018; Fakolade et al., 2018; Fjeldstad et al., 2015; Freund et al., 2016; Ickmans et al., 2014; Kent-Braun et al., 1997; Klassen et al., 2008; Kos et al., 2007; Krüger et al., 2017; Ranadive et al., 2012; Sandroff et al., 2015, 2012; Scott et al., 2011; Ward et al., 2013; Weikert et al., 2010), Sandroff and Motl (2013) used two devices in unison (Actigraph 7164 and GT3X), only data collected using the 7164 are included in the statistics due to the GT3X being calculated as one axis making comparison to the three axis mode in all other studies using the GT3X model collected in this review balanced.

3.2. Demographic information

Twenty-one papers included in the analysis had a total of 1098 participants, including 519 controls (73.5% female) and 579 people with a definite diagnosis of multiple sclerosis (76.7% female). The mean age of controls was 46.6 ± 10.79 years versus 47.9 ± 9.48 years for PwMS. 15 papers included figures on years since diagnosis, with a resulting mean was 10.9 ± 6.8 years (Blikman et al., 2015; Bollaert and Motl, 2019; Chung et al., 2016; Engelhard et al., 2018; Fakolade et al., 2018; Fjeldstad et al., 2015; Freund et al., 2016; Ickmans et al., 2014; Kent-Braun et al., 1997; Ranadive et al., 2012; Sandroff et al., 2015, 2012; Sandroff and Motl, 2013; Ward et al., 2013; Weikert et al., 2010). One paper recruited people classified as relapse remittent (Fjeldstad et al., 2015), one specifically primary progressive multiple sclerosis (Scott et al., 2011), 13 others included a mix of multiple sclerosis classifications (Blikman et al., 2015; Bollaert and Motl, 2019; Chung et al., 2016; Engelhard et al., 2018; Fakolade et al., 2018; Freund et al., 2016; Krüger et al., 2017; Ranadive et al., 2012; Sandroff et al., 2015, 2012; Sandroff and Motl, 2013; Ward et al., 2013; Weikert et al., 2010). Fourteen papers specified the number of relapse remittent cases and the combined average was 75.1% (Blikman et al., 2015; Bollaert and Motl, 2019; Chung et al., 2016; Engelhard et al., 2018; Fakolade et al., 2018; Fjeldstad et al., 2015; Freund et al., 2016; Krüger et al., 2017; Sandroff et al., 2015, 2012; Sandroff and Motl, 2013; Scott et al., 2011; Ward et al., 2013; Weikert et al., 2010). Eleven papers reported BMI (Blikman et al., 2015; Bollaert and Motl, 2019; Fakolade et al., 2018; Freund et al., 2016; Ickmans et al., 2014; Klassen et al., 2008; Krüger et al., 2017; Ranadive et al., 2012; Scott et al., 2011; Ward et al., 2013), with a further seven reporting height and weight (Fjeldstad et al., 2015; Hale et al., 2008; Kent-Braun et al., 1997; Sandroff et al., 2015, 2012; Sandroff and Motl, 2013; Weikert et al., 2010), which was converted to provide BMI figures. The combined BMI average of the 18 papers was 25.49 for controls and 26.09 for PwMS. Thirteen studies reported on EDSS with five providing an average (Chung et al., 2016; Fjeldstad et al., 2015; Freund et al., 2016; Ickmans et al., 2014; Ward et al., 2013), one provided a range (Engelhard et al., 2018), and seven a median (Blikman et al., 2015; Bollaert and Motl, 2019; Busse et al., 2004; Kent-Braun et al., 1997; Kos et al., 2007; Krüger et al., 2017; Scott et al., 2011). Seven papers provided a PDDS score 3 providing a mean (Sandroff et al., 2012; Sandroff and Motl, 2013; Ward et al., 2013), and four a median value (Fakolade et al., 2018; Ranadive et al., 2012; Sandroff et al., 2015; Weikert et al., 2010). All participants were ambulatory with some requiring an assistive device i.e. a cane or walking frame. Demographic information shown in Tables 1 and 2.

3.3. Accelerometers

The Actigraph 7164 was used in six studies (Kos et al., 2007; Ranadive et al., 2012; Sandroff et al., 2012; Sandroff and Motl, 2013; Ward et al., 2013; Weikert et al., 2010). The G1TM was used in three studies (Chung et al., 2016; Fjeldstad et al., 2015; Scott et al., 2011). The GT3X in four studies (Blikman et al., 2015; Bollaert and Motl, 2019; Engelhard et al., 2018; Sandroff et al., 2015). One study used both the 7164 and the GT3X device simultaneously, however for the purposes of the current analysis the results used in this analysis were of the 7164 (Sandroff et al., 2013; Motl et al., 2013). TriTrac RD3 model was used in one study (Kent-Braun et al., 1997). The updated TriTrac version the RT3 used in two studies (Hale et al., 2008; Klassen et al., 2008). Other accelerometers used are the Actical in two studies (Fakolade et al., 2018; Ickmans et al., 2014). The SWA Mini was used in one study (Krüger et al., 2017). The Stepwatch, Step Activity Monitor (SAM) which is a pedometer which uses accelerometry, therefore is included in this review was used in two studies (Busse et al., 2004; Freund et al., 2016).

In terms of accelerometer placement, one study placed the device on the central back (Hale et al., 2008). 10 studies had participants wear the device at the waist, four did not indicate a specific placement (Blikman et al., 2015; Chung et al., 2016; Kent-Braun et al., 1997; Klassen et al., 2008). The most popular placement throughout the studies specified the non-dominant hip at the waist position (Sandroff et al., 2015, 2012; Sandroff and Motl, 2013; Ward et al., 2013; Weikert et al., 2010). A final study specified the waist and a hip placement but no specific side (Fjeldstad et al., 2015). Scott et al. (2011) specified a right hip placement and two studies stated the non-dominant hip with no mention of a waist placement (Engelhard et al., 2018; Fakolade et al., 2018). One study used the right ankle as placement for the device (Busse et al., 2004). Three studies used arm placement for their devices, Ickmans et al., (2014) and Kos et al., (2007) used the non-dominant wrist, and Krüger et al. (2017) used the right tricep. Three studies did not provided placement position (Bollaert and Motl, 2019; Freund et al., 2016; Ranadive et al., 2012).

The most common epoch used by 13 papers was 60 s (Engelhard et al., 2018; Fjeldstad et al., 2015; Freund et al., 2016; Hale et al., 2008; Ickmans et al., 2014; Kent-Braun et al., 1997; Klassen et al., 2008; Krüger et al., 2017; Ranadive et al., 2012; Sandroff et al., 2015, 2012; Sandroff and Motl, 2013; Scott et al., 2011). Blikman et al. (2015) specified ten second epochs and Kos et al., (2007) used the extremely low value of one second for their epoch. Six studies did not provide data on epoch length (Bollaert and Motl, 2019; Busse et al., 2004; Chung et al., 2016; Fakolade et al., 2018; Ward et al., 2013; Weikert et al., 2010). Sampling frequency was poorly reported, only four papers specifying a value, Blikman et al. (2015) and Sandroff et al. (2015) used 30 Hz and Sandroff and Motl (2013) and Sandroff et al. (2012) used 10 Hz.

In terms of the monitoring period, in which the participants wore their accelerometers, Kos et al. (2007) used three days wear time, Klassen et al. (2008) had four days, Sandroff and Motl (2013) chose six days and the remaining papers used the more standardized seven-day period of data collection (Blikman et al., 2015; Bollaert and Motl, 2019; Busse et al., 2004; Chung et al., 2016; Engelhard et al., 2018; Fakolade et al., 2018; Fjeldstad et al., 2015; Freund et al., 2016; Hale et al., 2008; Ickmans et al., 2014; Kent-Braun et al., 1997; Krüger et al., 2017; Ranadive et al., 2012; Sandroff et al., 2015, 2012; Scott et al.,

Table 1
Demographic information and study quality.

Author / Year	BMJ AXIS Score (x/20)	Sample Size	MS Sample Size	Control Sample Size	MS BMI (kg/m2) ± S.D	Control BMI (kg/m2) ± S.D	MS Sex (% female)	Control Sex (% female)	MS Age (years) ± S.D	Control Age (years) ± S.D
Weikert et al. (2010)	17	66	33	33	27.9*	26.3*	82	82	47.5 ± 10.6	47.7 ± 11.3
Klassen et al. (2008)	16	36	27	9	24.7 ± 3.8	24.6 ± 3.8	70	89	47.7 ± 6.97	41.6 ± 4.4
Ward et al. (2013)	17	51	25	26	27.5 ± 5	26.6 ± 5.3	100	100	48.1 ± 9.7	48.2 ± 10.1
Sandroff and Motl (2013)	19	82	41	41	26.7*	26.3*	87.8	87.8	47.4 ± 8.8	47.4 ± 9.1
Fakolade et al. (2018)	19	28	14	14	28.5 ± 8.5	27.6 ± 4.9	71.4	28.6	52 ± 11.7	54.1 ± 13.5
Blikman et al. (2015)	19	46	23	23	24.8 ± 4.3	23.4 ± 2.6	78.3	78.3	45.7 ± 10.2	45.7 ± 10.2
Hale et al. (2008)	19	20	11	9	25.4*	24.8*	72.7	89	50.7 ± 11.8	51 ± 18.1
Bollaert and Motl (2019)	18	80	40	40	28.5 ± 6.9	27.1 ± 5	62.5	62.5	65.3 ± 4.3	66.5 ± 6.7
Engelhard et al. (2018)	19	126	88	38	NR	NR	84	71.1	44 ± 8.82	35.05 ± 12.38
Ickmans et al. (2014)	19	51	19	32	24 ± 3.52	25.3 ± 5.11	68.4	68.8	39.74 ± 10.67	39.34 ± 13.85
Sandroff et al. (2015)	19	62	31	31	25.7*	24.4*	87.1	87.1	43.4 ± 7.7	42.4 ± 7.5
Krüger et al. (2017)	17	56	26	30	26 ± 3.5	25.3 ± 3.9	61.5	66.7	50.9 ± 5.2	49.7 ± 8.3
Fjeldstad et al. (2015)	19	25	13	12	26.1*	23.3*	69	42	47.6 ± 10.81	45.5 ± 18.71
Sandroff et al. (2012)	20	154	77	77	26.8*	26.4*	85	85	47.3 ± 9.7	47 ± 10.5
Chung et al. (2016)	19	24	10	14	27 ± 4.5	25.7 ± 4.4	90	78.6	45 ± 8	46 ± 7
Ranadive et al. (2012)	19	66	33	33	27 ± 7.18	26.4 ± 6.49	81.8	81.8	47 ± 10.51	47 ± 11.31
Scott et al. (2011)	19	29	15	14	27.7 ± 6.1	26.5 ± 4	53.3	42.9	53.7 ± 10.5	54.6 ± 9.6
Kent-Braun et al. (1997)	16	17	9	8	21.7*	26.4*	66.7	50	47 ± 6	42 ± 5.66
Kos et al. (2007)	18	29	19	10	NR	NR	47	60	47.2 ± 12.1	39.6 ± 12.3
Busse et al. (2004)	15	20	10	10	NR	NR	100	100	37.9 ± 10.1	37.5 ± 12.6
Freund et al. (2016)	17	30	15	15	23.7 ± 3.54	22.4 ± 3.12	93	93	51.13 ± 14.82	51.07 ± 13.46

MS – Multiple Sclerosis, NR – Not reported,
* BMI calculated from height and weight figures so no standard deviation available.

Table 2
Multiple sclerosis information.

Author / Year	Diagnosed (years) ± S.D	MS Subtype	Relapse Remittent (%)	EDSS Median	EDSS Mean	PDDS Median	PDDS Mean
Weikert et al. (2010)	9.2 ± 6.7	all	85			2	
Klassen et al. (2008)	NR	NR	NR		2.6		
Ward et al. (2013)	9.8 ± 7.2	all	84				1.9
Sandroff and Motl (2013)	11 ± 7.9	all	90.2				1
Fakolade et al. (2018)	13.2 ± 8.2	all	42.9			5	
Blikman et al. (2015)	9.3 ± 7.1	RR/SP	87	2			
Hale et al. (2008)	NR	NR	NR				
Bollaert and Motl (2019)	21.5 ± 8.6	all	67.5	4			
Engelhard et al. (2018)	12.67 ± 5.81	all	83				
Ickmans et al. (2014)	6.96 ± 5.71	NR	NR		1.64		
Sandroff et al. (2015)	8.6 ± 6.3	all	93.5			2	
Krüger et al. (2017)	NR	all	69.2	4			
Fjeldstad et al. (2015)	7.5 ± 3.61	RR	100		2.5		
Sandroff et al. (2012)	10.1 ± 7.3	all	86				1
Chung et al. (2016)	12 ± 8	RR/PP	90		4.6		
Ranadive et al. (2012)	9.2 ± 6.7	all	NR			2	
Scott et al. (2011)	NR	PP	0	5			
Kent-Braun et al. (1997)	11 ± 6	NR	NR	4			
Kos et al. (2007)	NR	NR	NR	5.5			
Busse et al. (2004)	NR	NR	NR	4			
Freund et al. (2016)	11.4*	all	73.3		4.13		

MS – Multiple Sclerosis, RR – Relapse Remittent, SP – Secondary Progressive, PP – Primary Progressive, all – all Multiple Sclerosis subtypes.
* No standard deviation available.

2011; Ward et al., 2013; Weikert et al., 2010). Twelve papers included information on minimum valid days of accelerometer data need for inclusion. Four papers accepted a minimum of three days, which is the lowest end of the scale (Fakolade et al., 2018; Kos et al., 2007; Sandroff et al., 2015; Weikert et al., 2010). Bollaert and Motl (2019) adopted a four-day period of validation, Blikman et al. (2015) and Chung et al. (2016) selected a five-day period. At the highest end of the scale Engelhard et al. (2018) stated a six-day minimum and four papers expected data for all seven days of testing at the highest end of the wear time scale (Busse et al., 2004; Ickmans et al., 2014; Krüger et al., 2017; Scott et al., 2011). Several studies did adopt, state, or reach, the criteria of a valid day as ≥10 h wear time without periods exceeding 60 min of continuous zeroes per day, with at least 3 valid days of wear time as the inclusion criteria in their subsequent analyses (Engelhard et al., 2018; Fakolade et al., 2018; Fjeldstad et al., 2015; Sandroff et al., 2015; Sandroff and Motl, 2013; Weikert et al., 2010). This approach is considered acceptable for generating a reliable estimate of usual physical activity in persons with MS (Colley et al., 2010; Motl et al., 2007). Two further papers explicitly mentioned wear time criteria, Blikman et al. (2015) required ≥660min/day (9 h) with periods of 180min continuous 0 excluded, for 5 days and Scott et al. (2011) aired on the more conservative side with an inclusion criteria of ≥8 h per day for all 7 days of monitoring. Furthermore, from the results and reasons for exclusion it appears that other studies did achieve the validated monitoring period although they did not expressly state it in their requirements (Bollaert and Motl, 2019; Busse et al., 2004; Kos et al., 2007; Krüger et al., 2017). Without knowing wear time it is difficult to determine if the rest of the papers met this goal (Chung et al., 2016; Freund et al., 2016; Hale et al., 2008; Ickmans et al., 2014; Kent-Braun et al., 1997; Klassen et al., 2008; Ranadive et al., 2012; Sandroff et al., 2012; Ward et al., 2013). In order to accommodate as many papers as possible into this study and due to a lack of information there is no specified wear time in terms of hours that validate a day or minimum number of days data required, only a requirement for the device to be sent out to participants for a minimum of three days Information shown in Table 3.

3.4. Sedentary time

Four studies out of 21 studies provided data on sedentary time with a pooled sample of 205 participants (96 PwMS and 109 controls) (Blikman et al., 2015; Bollaert and Motl, 2019; Fakolade et al., 2018; Ickmans et al., 2014). The average time spent sedentary was 532.13 ± 89.67 min for people with MS and 506.37 ± 81.55 min for controls. This equates to PwMS being sedentary for 25.042 min per day more than their sedentary counterparts. To account for differences in wear time, comparisons were assessed as standardized mean difference (SMD). This equated to an SMD of -0.286 ($p = 0.044$; Fig. 2).

Five studies showed relative sedentary time, totaling 235 participants (111 PwMS and 124 controls) (Blikman et al., 2015; Bollaert and Motl, 2019; Fakolade et al., 2018; Freund et al., 2016; Ickmans et al., 2014). Relative sedentary time measured as a percent of wear time is 66.88 ± 9.62 % for PwMS and 61.42 ± 7.66 % for controls. People with MS in this study spend 5.46% more of their day sedentary compared to controls resulting in a SMD of -0.646 ($p < 0.001$; Fig. 3).

3.5. Light physical activity

Five studies out of 21 provided data on LPA, including 261 participants of whom 122 had MS and 139 were controls (Blikman et al., 2015; Bollaert and Motl, 2019; Fakolade et al., 2018; Ickmans et al., 2014; Krüger et al., 2017). The average time spent performing light physical

Table 3
Accelerometer information.

Author / Year	Accelerometer	Placement	Duration (days)	Minimum Duration (days)	MS specific cut point	Epoch (seconds)	Frequency (hertz)	Axis
Weikert et al. (2010)	Actigraph 7164	Waist, non-dominant hip	7	3	NR	NR	NR	VA
Klassen et al. (2008)	TriTrac RT3	Waist	4	NR	NR	60	NR	VM
Ward et al. (2013)	Actigraph 7164	Waist, non-dominant hip	7	NR	NR	NR	NR	VA
Sandroff and Motl (2013)	Actigraph 7164	Waist, non-dominant hip	6	NR	NR	60	10	VA
Fakolade et al. (2018)	Actical	Non-dominant hip	7	3	NO	NR	NR	2D
Blikman et al. (2015)	Actigraph GT3X	Waist	7	5	NO	10	30	VM
Hale et al. (2008)	TriTrac RT3	Central back	7	NR	NR	60	NR	VM
Bollaert and Motl (2019)	Actigraph GT3X	NR	7	4	YES	NR	NR	VM
Engelhard et al. (2018)	Actigraph GT3X	Non-dominant hip	7	6	*YES	60	NR	VM
Ickmans et al. (2014)	Actical	Non-dominant wrist	7	7	NO	60	NR	2D
Sandroff et al. (2015)	Actigraph GT3X	Waist, non-dominant hip	7	3	YES	60	30	VM
Krüger et al. (2017)	Swa Mini	Left tricep	7	7	NO	60	NR	2D
Fjeldstad et al. (2015)	Actigraph G1TM	Waist, hip	7	NR	NR	60	NR	2D
Sandroff et al. (2012)	Actigraph 7164	Waist, non-dominant hip	7	NR	YES	60	10	VA
Chung et al. (2016)	Actigraph G1TM	Waist	7	5	NR	NR	NR	2D
Ranadive et al. (2012)	Actigraph 7164	NR	7	NR	NR	60	NR	VA
Scott et al. (2011)	Actigraph G1TM	Right hip	7	7	NR	60	NR	2D
Kent-Braun et al. (1997)	TriTrac RD3	Waist	7	NR	NR	60	NR	VM
Kos et al. (2007)	Actigraph 7164	Non-dominant wrist	3	3	NR	1	NR	VA
Busse et al. (2004)	Stepwatch (SAM)	Right ankle	7	7	NR	NR	NR	2D
Freund et al. (2016)	Stepwatch (SAM)	NR	7	NR	NR	60	NR	2D

* MS specific cut points were used but were determined from Multiple Sclerosis Walking Scale – 12, not activity counts. VA- vertical axis, 2D- motion detected in 2 axes, VM – vector magnitude, motion detected in all 3 axes.

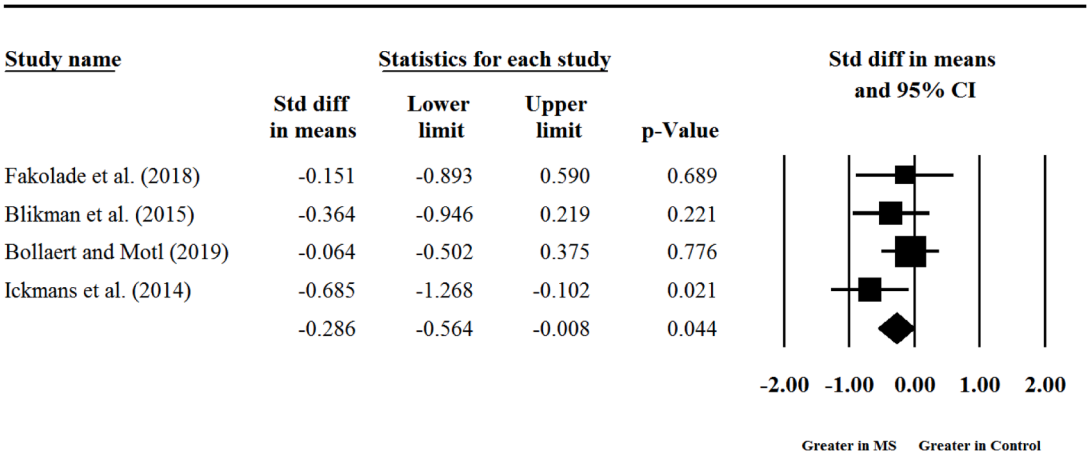

Fig. 2. Forest plot of the comparison of sedentary intensity physical activity in minutes per day between people with multiple sclerosis and healthy participants. Sample size PwMS and Control; Standard Difference in means; Lower limit; Upper limit; p-Value; Standard difference in means and CI: 95% Confidence interval.

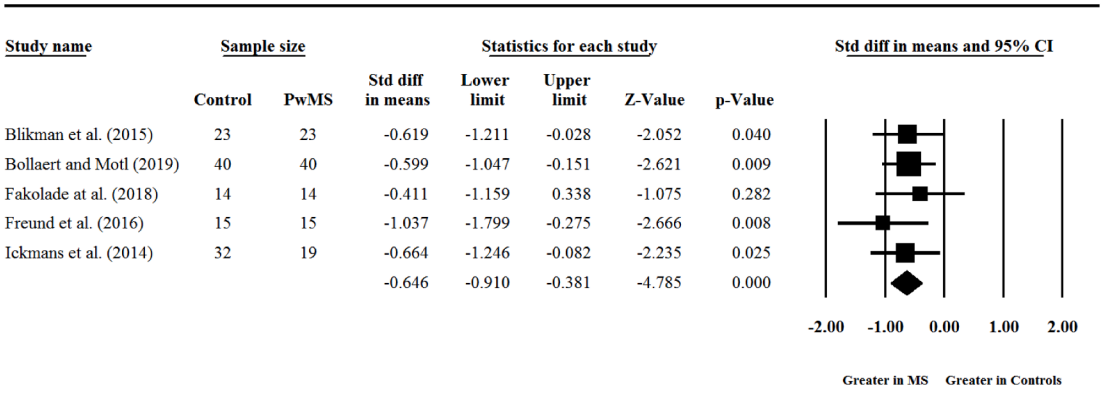

Fig. 3. Forest plot of the comparison of relative mean sedentary intensity physical activity percentage between people with multiple sclerosis and healthy participants. Sample size PwMS and Control; Standard Difference in means; Lower limit; Upper limit; p-Value; Standard difference in means and CI: 95% Confidence interval.

activity was 230.73 ± 67.68 min for people with MS and 255.11 ± 58.19 min for healthy controls, with a difference of 24.38 min. The equated to an SMD of 0.337 (p = 0.039 Fig. 4).

Relative light physical activity 26.6 ± 8 percent of daily wear time of the accelerometer for PwMS and 28.4 ± 6.27 percent for controls. People with MS in this study spend 1.8% of their day doing LPA compared to controls with a SMD of 0.211, p-value 0.152, as shown in Fig. 5. Krüger et al. (2017) was the only study to indicate that people with MS were more active at this threshold.

3.6. Moderate to vigorous physical activity

Eight studies out of 21 provided data on MVPA minutes per day, 603 participants of whom 318 had MS and 285 were controls (Blikman et al., 2015; Bollaert and Motl, 2019; Engelhard et al., 2018; Fakolade et al., 2018; Ickmans et al., 2014; Krüger et al., 2017; Sandroff et al., 2015,

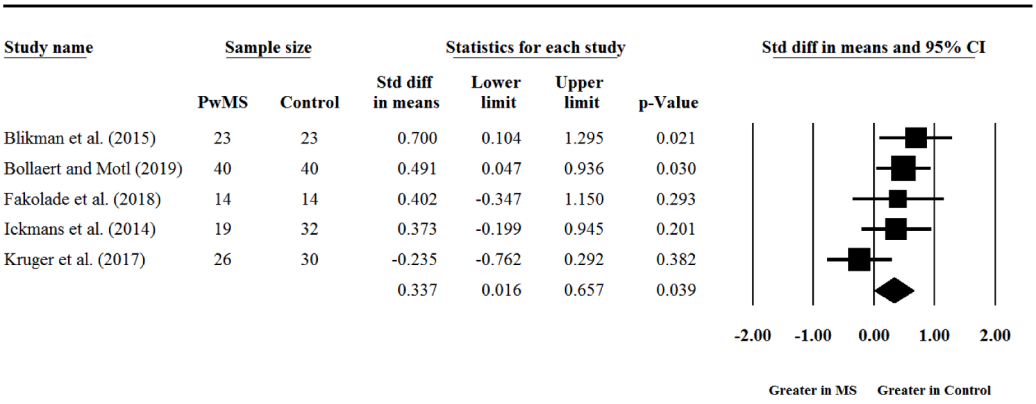

Fig. 4. Forest plot of the comparison of light intensity physical activity in minutes per day between people with multiple sclerosis and healthy participants. Sample size PwMS and Control; Standard Difference in means; Lower limit; Upper limit; p-Value; Standard difference in means and CI: 95% Confidence interval.

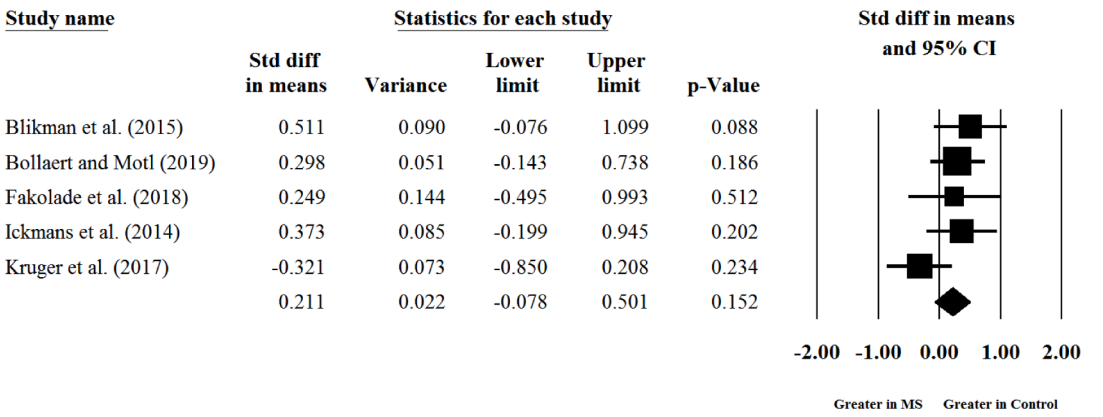

Fig. 5. Forest plot of the comparison of relative mean light intensity physical activity percentage between people with multiple sclerosis and healthy participants. Sample size PwMS and Control; Standard Difference in means; Lower limit; Upper limit; p-Value; Standard difference in means and CI: 95% Confidence interval.

2012). The average time spent performing moderate to vigorous physical activity was 35.99 ± 21.59 min of daily accelerometer wear time for people with MS and 56.42 ± 27.07 min for the control group. Fig. 6 indicates controls being active at this level for an average of 20.43 min more than people with MS with a SMD of 0.801, ($p < 0.001$).

Five studies out of 21 provided data on relative MVPA, 261 participants of whom 122 had MS and 139 controls (Blikman et al., 2015; Bollaert and Motl, 2019; Fakolade et al., 2018; Ickmans et al., 2014; Krüger et al., 2017). The MS subgroup spent a meager 5.21 ± 2.83% of their day in MVPA compared to 7.98 ± 3.42% for controls a difference of 2.77%. The SMD denoted in Fig. 7 is 0.914 favoring controls, ($p < 0.001$).

3.7. Step count

Eight papers out of 21 included step count which was analyzed as a total steps per day and included 490 participants; 268 with MS and 222 controls (Busse et al., 2004; Engelhard et al., 2018; Fakolade et al., 2018; Fjeldstad et al., 2015; Freund et al., 2016; Krüger et al., 2017; Sandroff et al., 2012; Ward et al., 2013). It is evident from Fig. 8 Forrest plot that controls engage in more physical activity calculating to a elevated total sum of step counts under all investigations. Mean step count per day for PwMS is 5896.39 ± 2876.36 and controls 8778.46 ± 2955.56, a difference of 2882 steps per day (SMD 0.959 $p < 0.001$).

3.8. Activity count

Thirteen of the 21 studies reported activity counts, including 645 people, 330 with MS and 315 controls (Blikman et al., 2015; Chung et al., 2016; Fjeldstad et al., 2015; Hale et al., 2008; Ickmans et al., 2014; Kent-Braun et al., 1997; Klassen et al., 2008; Kos et al., 2007; Ranadive et al., 2012; Sandroff et al., 2012; Sandroff and Motl, 2013; Scott et al., 2011; Weikert et al., 2010). Data pooling demonstrates a significant difference between groups with greater activity counts in controls, $p < 0.001$. The 0.693 standard difference in mean equates to average daily activity counts of 204216.42 ± 121156.36 for MS and 280700.9 ± 167429.91 for controls, a difference of 76484.48 counts per day Fig. 9.

4. Discussion

The aim of this review was to assess objective measures of PA in PwMS compared to healthy controls using objectively measured data from accelerometers. The main findings are that (1) PwMS are significantly more sedentary than comparable healthy controls, (2) PwMS also spend fewer mins/day engaging in light physical activity, and (3) they engage in less MVPA whether assessed in mins.day^{-1} or % of daily activity, (4) These differences are also reflected in reduced step and activity counts for PwMS compared to healthy controls. Taken together the data indicates that people with MS are more sedentary and less active, particularly in the moderate to vigorous intensity domain than matched

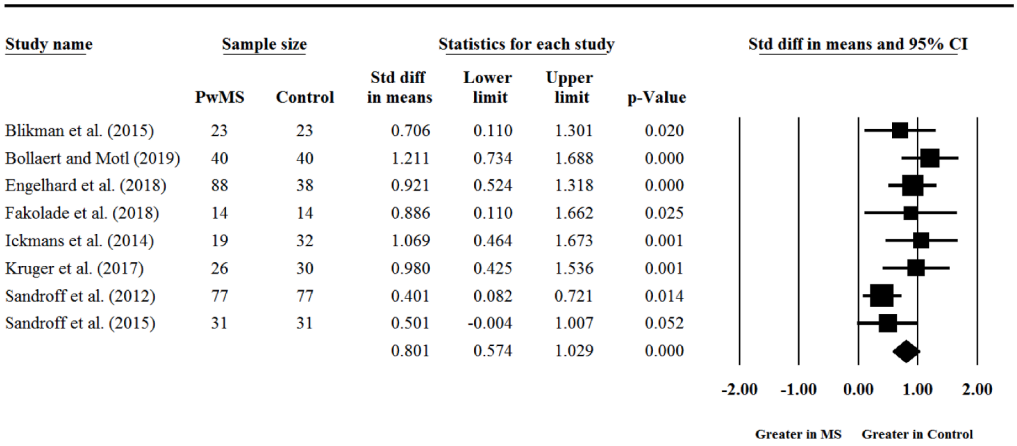

Fig. 6. Forest plot of the comparison of moderate to vigorous intensity physical activity in minutes per day between people with multiple sclerosis and healthy participants. Sample size PwMS and Control; Standard Difference in means; Lower limit; Upper limit; p-Value; Standard difference in means and CI: 95% Confidence interval.

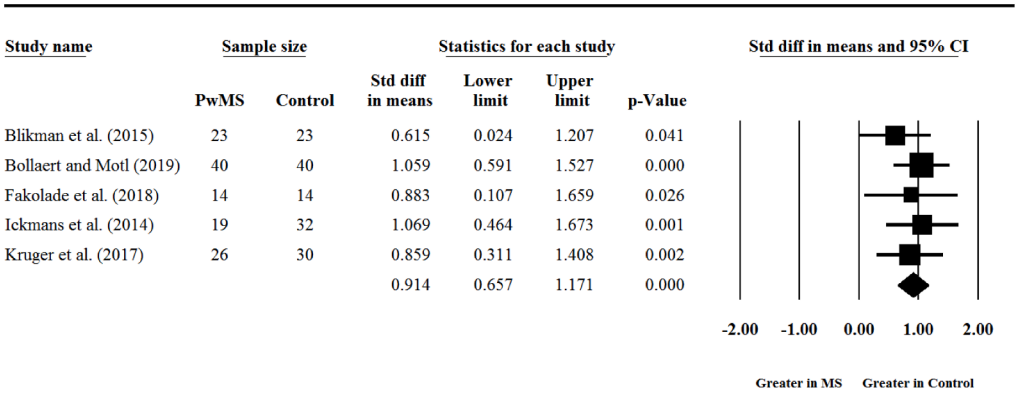

Fig. 7. Forest plot of the comparison of relative mean moderate to vigorous intensity physical activity between people with multiple sclerosis and healthy participants. Sample size PwMS and Control; Standard Difference in means; Lower limit; Upper limit; p-Value; Standard difference in means and CI: 95% Confidence interval.

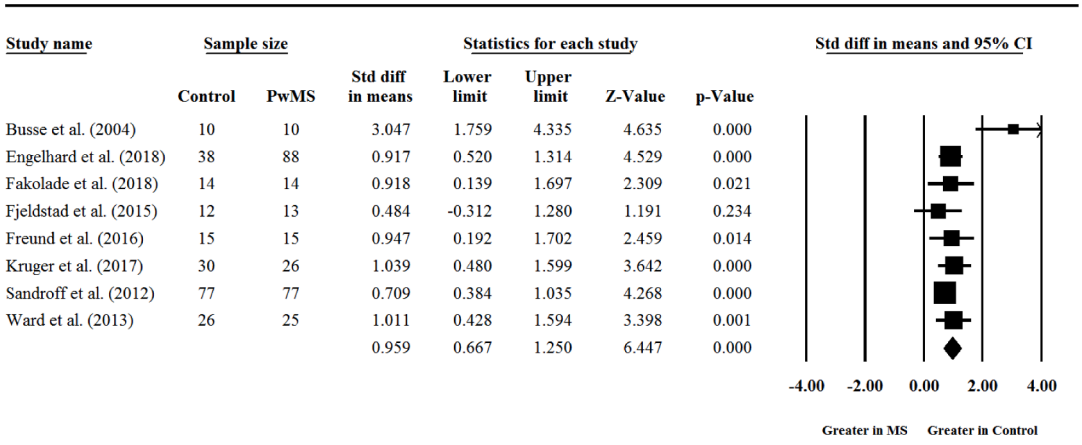

Fig. 8. Forest plot of the comparison of mean steps count per day between people with multiple sclerosis and healthy participants. Sample size PwMS and Control; Standard Difference in means; Lower limit; Upper limit; p-Value; Standard difference in means and CI: 95% Confidence interval.

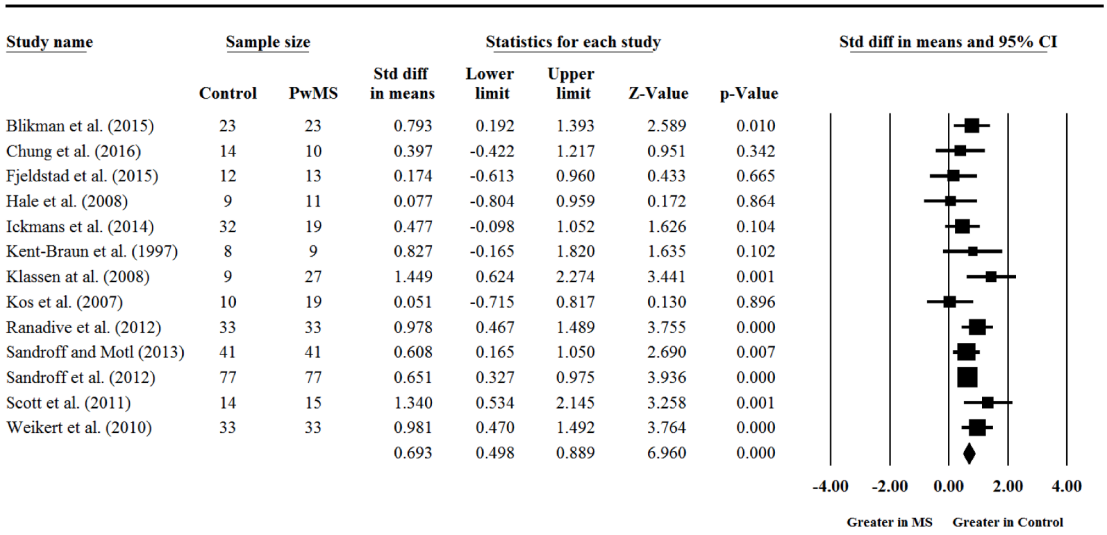

Fig. 9. Forest plot of the comparison of mean activity counts per day between people with multiple sclerosis and healthy participants. Sample size PwMS and Control; Standard Difference in means; Lower limit; Upper limit; p-Value; Standard difference in means and CI: 95% Confidence interval.

healthy controls when measured using accelerometers. The activity profiles identified in this review support concerns expressed in previous reviews (Casey et al., 2018), since there is now very strong evidence that increasing sedentary time and low time spent in MVPA directly increase the risk of a variety of comorbidities (UK Government, 2019). Moreover, these findings may provide a plausible rationale for the reported

increased risk of CVD in PwMS compared with non-diseased populations (Wens et al., 2013). Evidence collected by the world health organization (WHO) maintains that there is insufficient data linking physical activity and co-morbidities in PwMS. However, a reduction in sedentary time and increased PA for PwMS shows evidence of a strong correlation with improved function, moderate links between improvement of cognitive abilities and limited evidence of increase of quality of life (Bull et al., 2020).

4.1. Sedentary time

This is the first systematic review to compare sedentary behavior between age matched controls and people with MS within the same investigation. Our finding that PwMS engage in greater sedentary time than comparable controls provides supporting evidence inactivity may be an important contributory factor to the increased cardiovascular disease risk experienced by PwMS (Wens et al., 2013). Importantly, emerging evidence suggests that the risk created by high levels of sedentariness is attenuated but not eliminated by adding bouts of MVPA, suggesting that the risk represents a distinct pathological process (Duvivier et al., 2018). If this is the case, the evidence of this review suggests that separate strategies may be needed that both interrupt sedentary time and target reduced levels of MVPA. It is also important to note that sedentary time can be more resistant to behavior change interventions, and is extremely understudied with most interventions focused on improving MVPA, which are not suitable for people with mobility disabilities (Aminian et al., 2019; Manns et al., 2012). It is more difficult to change habits of people who are sedentary than increase intensity of physical activity for people who are moving albeit at a minimal rate, proved by the limited success of sedentary behavior interventions versus PA interventions in this systematic review (Prince et al., 2014). A systematic review assessing the effectiveness of interventions to increase physical activity and reduce sedentary behavior in PwMS reported that only subjectively measures PA improved, while there was no definitive evidence for reductions either sedentary behavior or objective PA measurement (Coulter et al., 2018).

A Previous review by Veldhuijzen van Zanten et al. (2016) on sedentary behavior in people with MS concluded sedentary behavior increases with mobility impairment and age. Sedentary behavior was calculated using a variety of methods including, accelerometers, activity monitors and the International Physical Activity Questionnaire (IPAQ) and concluded PwMS are highly sedentary. While the present study extends this by confirming that similar findings occur when sedentary time is assessed with accelerometry, the lack of available literature meant that we were unable to perform meta-regression to assess any associations with measures of impairment such as EDSS. While this review could not assess the cause of increased sedentary time in PwMS, symptoms such as fatigue and impaired mobility could act as barriers to being physically active or engaging in more structured exercise (Klaren et al., 2017). Regardless of the underlying causes, the consequence of an inactive lifestyle for people with MS is an increased likelihood of additional health concerns over time, specifically cardiovascular risk which they are more prone to than healthy counterparts (Jadidi et al., 2013; Wens et al., 2016).

4.2. MVPA

Several reviews have explored the relationship between PwMS and MVPA, but none have compared accelerometer readings to healthy controls within the same study using accelerometry. Consequently, the results of this review suggest that PwMS take part in less MVPA than age matched healthy counterparts. Previous studies have reported that people with MS do achieve less MVPA than healthy adults, although, on average they met the suggested guidelines for MVPA (Kinnett-Hopkins et al., 2017; Motl et al., 2018, 2005). Current guidelines for the UK are 150 min of moderate activity and/or 75 min of vigorous activity per week (in addition to two muscle strengthening sessions (UK Government, 2019). This is mirrored and extended by the WHO, their message is for healthy adults to achieve 150–300 min of moderate activity and/or 75-150 of vigorous activity. The goal for those with disabilities is to reduce sedentary time and work toward increasing physical activity (Bull et al., 2020). Data pooling in this review identified that on average PwMS take part in 36min.day^{-1} of MVPA, equating to 252 min. week^{-1}, and while this is less than healthy controls groups, it still exceeds the minimum recommended activity guidelines.

The implications of this finding are unclear. First, when interpreted alongside the evidence presented above that PwMS are more sedentary than healthy controls, it suggests that future interventions in PwMS may be more effective if they focus on reducing sedentary time rather than increasing MVPA. This is not to say that further increases in MVPA would not be beneficial, however, the greatest benefits from activity are seen in individuals moving from very low, to moderate levels of MVPA (Füzéki and Banzer, 2018), which does not appear to be the case in this cohort. In contrast evidence has suggested a direct relationship between reducing sedentary time and reduced cardiovascular, and cardiometabolic risk (UK Government, 2019).

One caveat, however, regards the degree to which this cohort are representative of the wider population of PwMS. In particular, the range of EDSS was relatively low, with the most individuals in the included studies being self-ambulatory. It seems plausible that individuals with greater levels of mobility impairment may find meeting the MVPA guidelines more challenging (Weikert et al., 2011). Moreover, the general characteristics of both PwMS and healthy controls also suggest that included participants may not be representative of the general population. For example, in addition to PwMS exceeding the minimum suggested thresholds for MVPA, the control groups undertook an even greater level of MVPA (395 mins.week^{-1} on average) exceeding the WHO recommendations for 'additional health benefit'(UK Government, 2019). Given that one in four adults worldwide do not meet the minimum activity threshold, the fact that both MS and healthy controls cohorts exceed this, and that healthy controls exceed the upper threshold suggests that those recruited may already have an interest in, and be engaged with practices to increase their activity levels and may not be representative of the broader general population or of PwMS.

4.3. Activity and step counts

The findings of this study are that people with multiple sclerosis accumulate fewer activity counts than healthy controls, therefore engage in less physical activity in general. A meta-analysis by Casey et al. (2017) rejected comparing activity counts between PwMS and controls from the NHANES database due to the inconsistencies between devices. However, in that study assessment of differences between groups using the same devices was not possible due to the use of database data as the comparator, and because comparing activity counts between studies is difficult due to differences in calibration and sensitivity (Casey et al., 2017). However, by comparing accelerometer counts using SMD between different groups (PwMS and healthy controls) undergoing the same intervention concurrently in the same study, the present review overcomes this limitation. This is particularly useful given that activity counts remain the most popular accelerometer derived metric reported. Bassett et al. (2015) reiterates that a single metric that correlates intensity, frequency and duration of activity is a valuable way to compare physical activity between devices and studies has worth especially in reviews. No other reviews have included comparisons of activity counts in PwMS and healthy controls, so it is difficult to compare these data with previous results. Nevertheless, when viewed alongside data on sedentary time, and MVPA, they support the view that PwMS undertake less PA than age matched healthy controls.

Similarly, the present review found reduced step counts in PwMS. This supports the view that they undertake less PA in general than their healthy counterparts, a finding that has been previously reported (Block

et al., 2016; Casey et al., 2017). However, in cohorts such as PwMS, step counts should be interpreted with caution. There are some reports that reduced accuracy at slow walking speeds which are prevalent in those with gait or mobility issues (Sandroff et al., 2014a). Nevertheless, step counts are a reliable and extensively used method of gauging physical activity in PwMS. Secondary analysis of 15 investigations has provided evidence that step count is an valid measurement of free living walking behavior and has been correlated with EDSS, timed 25 foot walk, 6 min walk and the 12 item Multiple Sclerosis Walking Scale (Motl et al., 2013).

4.4. Study quality

While most studies where of moderate or high quality, a common limitation was the use of a small sample with only one study providing justification Hale et al., (2008), although most noted the limitation. The most critical failure was missing data, especially relating to accelerometer outcomes. Device failure was reported by Ickmans et al. (2014) and Scott et al. (2011), participants were unable or unwilling to wear devices in studies by Ward et al. (2013) and Krüger et al. (2017). However, most studies provided no information on missing data or why information was excluded.

4.5. Accelerometer data reporting

Actigraph accelerometers were the most widely used accelerometer, with the most common being the older, uni-axial 7164 model. However, the more recent tri-axial instruments (including GT3X, the TriTrac RD3 model and its updated version the RT3) are more sensitive and more accurate in detecting movement in people with co-ordination, gait and balance issues as may be common in PwMS (Sandroff et al., 2014b). While this may have contributed to heterogeneity between studies, the effect is likely to be minor. Sandroff and Motl (2013) compared the Actigraph 7164 and GT3X reporting a 95.2% similarity for activity counts on the vertical axis in PwMS and 94.9% for healthy controls with the major discrepancies occurring at slow walking speeds. Two studies assessed differences in free living conditions using the Actigraph GT1M and GT3X and found when used in uniaxial mode there was a strong agreement between devices and activity counts at different levels of intensity could be compared (Kaminsky and Ozemek, 2012; Vanhelst et al., 2012).

Only three papers used MS Specific cut points, which are lower than healthy adult cut points to take into consideration disability impairments. Three studies use other methods of characterizing the distinction between activity levels. Engelhard et al. (2018) calculated cut points using the Multiple Sclerosis Walking Scale 12 which has been used extensively in MS research to study walking ability (Pilutti et al., 2013a). One paper utilized Energy Expenditure (EE) to separate the activity levels. EE is calculated by the monitor and an algorithm using age, sex and body size. It is reported as a total metabolic equivalent of task (MET) per recording time (60 sec epoch). MET cut points are used to classify physical activity classification (Krüger et al., 2017).

A final consideration when using accelerometers is epoch length, the sampling window in which the accelerometer measures count. The standard length used in thirteen studies was 60 s. One study had an epoch length of 10 s, one used 1 s and the other studies did not disclose a time. However, research for people with disabilities could focus on shorter epochs as it may be difficult for individuals with impairments to exercise at vigorous intensity for a full minute. Shorter epoch lengths have been associated with higher MVPA values (Orme et al., 2014). Future studies could examine epoch length and the proportion of light, moderate and vigorous exercise using accelerometers in PwMS.

4.6. Limitations

There are several limitations of this review which should be noted. First, while every attempt was made to include all relevant studies, only papers written in English were included and it is possible papers may have from databases indexing non-English articles may have been missed.

Seven of the 21 studies were affiliated with the same research department. While their research is highly valued, for a review such as this, it is difficult to determine if the same participants took part in multiple studies, reducing the scope of people with MS involved. This was also highlighted as a limitation in a secondary analysis of 13 studies conducted by the department focusing on MVPA levels between PwMS and a smaller sample of controls (Klaren et al., 2013). All studies were performed in the United States of America or Western Europe making generalization to the MS world population as a whole difficult. In addition, those with higher levels of disability were also underrepresented in studies.

Many of the studies investigated used accelerometer output as their secondary analysis, with the main aims of the study being different areas of PA. This may explain the exclusion of some calibration details and short discussion on the accelerometer outcomes provided. However, this allied to the small sample size of some studies also suggests that most where not adequately powered to detect changes in physical activity or sedentary behavior, underlining the importance of data pooling presented here.

5. Conclusion

This review is the first to evaluate accelerometer measure between people with MS and healthy controls studied during the same testing period. People with MS are more sedentary than healthy controls, engage in less light, moderate and vigorous activity. They perform less steps during free living activity and generate a lower activity count than healthy controls. Future studies may benefit from a greater focus on reducing sedentary time and seek to include more participants with progressive forms of MS or with higher levels of EDSS. In addition, the high levels of activity in both PwMS and HC, also suggest future studies should ensure participants are representative of the general populations they are intended to represent. More interventions should be aimed at helping those who struggle to be active without guidance and support due to mobility, emotional or cognitive issues, especially with advances in technology.

Availability of data and material

No external data sets were used in this paper.

Ethics approval

No ethical approval was administered for this research.

Consent

All data is from previous studies, so no participant consent is required.

CRediT authorship contribution statement

Eilidh Macdonald: Conceptualization, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Duncan Buchan:** Resources, Writing – review & editing, Supervision. **Luke Cerexhe:** Writing – review & editing. **Linda Renfrew:** Writing – review & editing. **Nicholas Sculthorpe:** Validation, Resources, Formal analysis, Data curation, Writing – review & editing, Supervision.

Declaration of Competing Interest

There are no conflicts of interest for any of the authors of this paper.

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