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REVIEW

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Physical activity in children and adolescents with cystic fibrosis: A systematic review and meta-analysis

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Abstract

Background: Exercise and physical activity (PA) are essential components of the care of cystic fibrosis (CF) patients. Lower PA levels have been associated with worse pulmonary function, aerobic fitness, glycemic control, and bone mineral density. Most people with CF do not engage in the recommended amounts of PA.

Objective: To determine the level of PA in children and adolescents with CF.

Methods: A systematic review with meta-analysis was conducted without language restrictions in five databases. Were included studies that analyzed PA measured by objective and subjective instruments in children and adolescents with CF. Two independent reviewers analyzed the studies, extracted the data, and assessed the quality of evidence. The risk of bias of the included studies was assessed with the National Heart, Lung, and Blood Institute's risk-of-bias tool.

Results: Of the 1535 reports returned by the initial search, 20 articles reporting on 785 patients were included in the data synthesis. The forest plot showed that the CF group had a similar moderate-to-vigorous PA (MVPA) (mean difference, −7.79; 95% CI, −15.65 to 0.08 min/d; $P = .05$) and sedentary time (mean difference, −50.81; 95% CI, −109.96 to 8.35 min/d; $P = .09$) to the control group.

Conclusion: Children and adolescents with CF have a similar MVPA and sedentary time compared to controls. There are many options, subjective and objective, for assessing PA in this population. Optimal tool selection should guarantee more valid results.

KEYWORDS

adolescents, children, cystic fibrosis, physical activity, systematic review

1 | INTRODUCTION

Cystic fibrosis (CF) is an autosomal recessive disease involving mucus and sweat-producing cells and affecting multiple organs, with the lungs most severely affected. CF leads to death in 90% of patients.[1] There are about 70 000 cases worldwide, and approximately 1000 new cases are diagnosed each year.[2] People with CF have complications in different systems, but the most common are in the respiratory and digestive systems.[2]

Physical activity (PA) is defined as "any bodily movement produced by the contraction of skeletal muscles that results in a substantial increase in caloric requirements over resting energy expenditure."[3] This includes movement related to activities of daily living (ADL), work, and physical exercise.[4] The evaluation of PA is one

of the most relevant variables that must be considered in both healthy people and people with diseases since it allows changes to be established after intervention.[5]

Exercise and PA are essential components in the care of patients with CF.[6] Lower PA levels have been associated with worse pulmonary function, aerobic fitness,[7] glycemic control,[8] and bone mineral density.[9] While the term "exercise" infers prescribed structured activity with a specified intensity and duration, PA emphasizes activity that is incorporated into daily life and encompasses a broader range of options for being active.[10]

A high level of PA may lead to improved airway clearance by increasing transepithelial fluid transport, vibration, and ventilation and consequently may reduce or even prevent lung function decline in CF patients.[11-13] Importantly, moderate to vigorous PA (MVPA), recommended by the WHO, produces the most beneficial effects and is associated with less decline in lung function and improved quality of life.[11,14] Understanding that PA is an independent variable in physical capacity, we should promote more intense exercises for children with CF that stimulate better aerobic capacity and lead to greater survival.[15,16]

Unfortunately, the majority of young people with CF do not engage in the recommended amounts of PA.[17] PA among youth with CF decreases during adolescence.[18] Although the reasons for physical inactivity in the CF population are not entirely known, it is thought that young people with CF face numerous barriers to PA participation, such as low self-efficacy and competing time demands.[19]

There are different ways of evaluating PA: subjective, such as using diaries or questionnaires, and objective, such as using accelerometers or indirect calorimetry.[5] The choice of the methods of assessment depends on the availability of the instruments, and the aim of clinical assessment. Our aim was to determine the level of PA in children and adolescents with CF.

2 | METHODS

2.1 | Protocols and registration

We performed a systematic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[20] The review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42020188603).

2.2 | Inclusion criteria

We included RCTs or observational studies (cross-sectional, longitudinal, case–control, and cohort) in children and adolescents of either gender with a medical diagnosis of CF. The included studies aimed to determine the levels of PA in patients with CF. Additionally, the studies should have reported the MVPA, steps/d, sedentary time, activity time, or a similar measure through the subjective or objective instrument. We excluded all articles that did not follow the international guidelines for diagnosis of CF or combined different diseases without sub-analysis.[21] The main outcome is PA assessed as MVPA, steps/d, and sedentary time.

2.3 | Search strategies and data resources

We reviewed the Embase, PubMed/MEDLINE, Web of Science, CINAHL, and Cochrane Register of Clinical Trials (CENTRAL) databases on 23 May 2020 and performed manual searches with the followings terms: (a) for condition: cystic fibrosis OR mucoviscidosis; (b) physical activity OR daily activity OR moderate-to-vigorous physical activity OR MVPA OR steps OR pedometer OR accelerometer OR METs OR sedentary; (c) for population: children OR adolescents OR pediatrics OR pediatrics OR infants. We imposed no language or publication restrictions (Supporting Information file 1).

The terms selected were combined using Boolean logical operators (OR, AND, NOT). Also, we did a manual search of the references included in the selected articles. All references were analyzed in Rayyan web software.[22]

2.4 | Reviewing procedure and data extraction

The article review was performed independently by investigators experienced in meta-analysis and trained in literature review. First, two investigators (RTC/LVC) reviewed the titles and abstracts of all references. Studies deemed not relevant based on the review of the title and abstract were excluded. A third reviewer (RAD) resolved any disagreements. Second, the two investigators (RTC/LVC) read the articles selected in the first step in the full-text versions and checked the eligibility criteria again. The third reviewer (RAD) resolved any disagreements. Additional unpublished data were obtained from the study authors where possible.

2.5 | Methodological quality assessment

The assessment of the methodological quality of the primary articles was carried out using the quality assessment tools from the National Heart, Lung, and Blood Institute (NHLBI).[23] Each tool contains criteria for evaluating internal validity and risk of bias. The criteria were evaluated as "yes," "no," or "other" (not reported, not applicable, or not determinable), and an overall rating was provided for each study based on the items rated with an affirmative answer: ≥75% = good, 50 to 75% = fair, <50% = poor.

By mutual agreement, it was determined that in the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, the following items were considered "not applicable" for the articles with a cross-sectional design: 3, "Was the participation rate of eligible persons at least 50%?"; 6, "For the analysis in this paper, were the exposure(s) of interest measured before the

outcome(s) being measured?"; 7, "Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?"; 10, "Was the exposure(s) assessed more than once over time?"; and 13, "Was loss to follow-up after baseline 20% or less?". Therefore, in this tool, a total of nine items were counted evaluable for this design. Two authors carried out this evaluation independently (RAD/HP), and the discrepancies were resolved by consensus. For discrepancies that could not be resolved, a third author (JV) was consulted.

2.6 | Data synthesis and analysis

We reported summaries of the association between the outcomes for each study in terms of mean differences. We compared absolute values. We obtained combined measures of effect for each primary outcome through meta-analysis under a random-effect model due to the expected heterogeneity between studies.[24] Statistical heterogeneity was measured through the I^2 statistic and classified as low (I^2 < 25%), moderate (I^2 25%–50%), or high (I^2 > 50%).[25]

3 | RESULTS

3.1 | Study selection

The flow chart of the study selection is shown in Figure 1. In the initial search of the selected databases, 1535 potential studies were identified. Of the 66 studies assessed as full-text, we excluded 30 studies for being abstract for meetings, five for having the wrong study design, four for having the wrong population, three for protocol, two for incomplete data, one for duplicate data, and one for

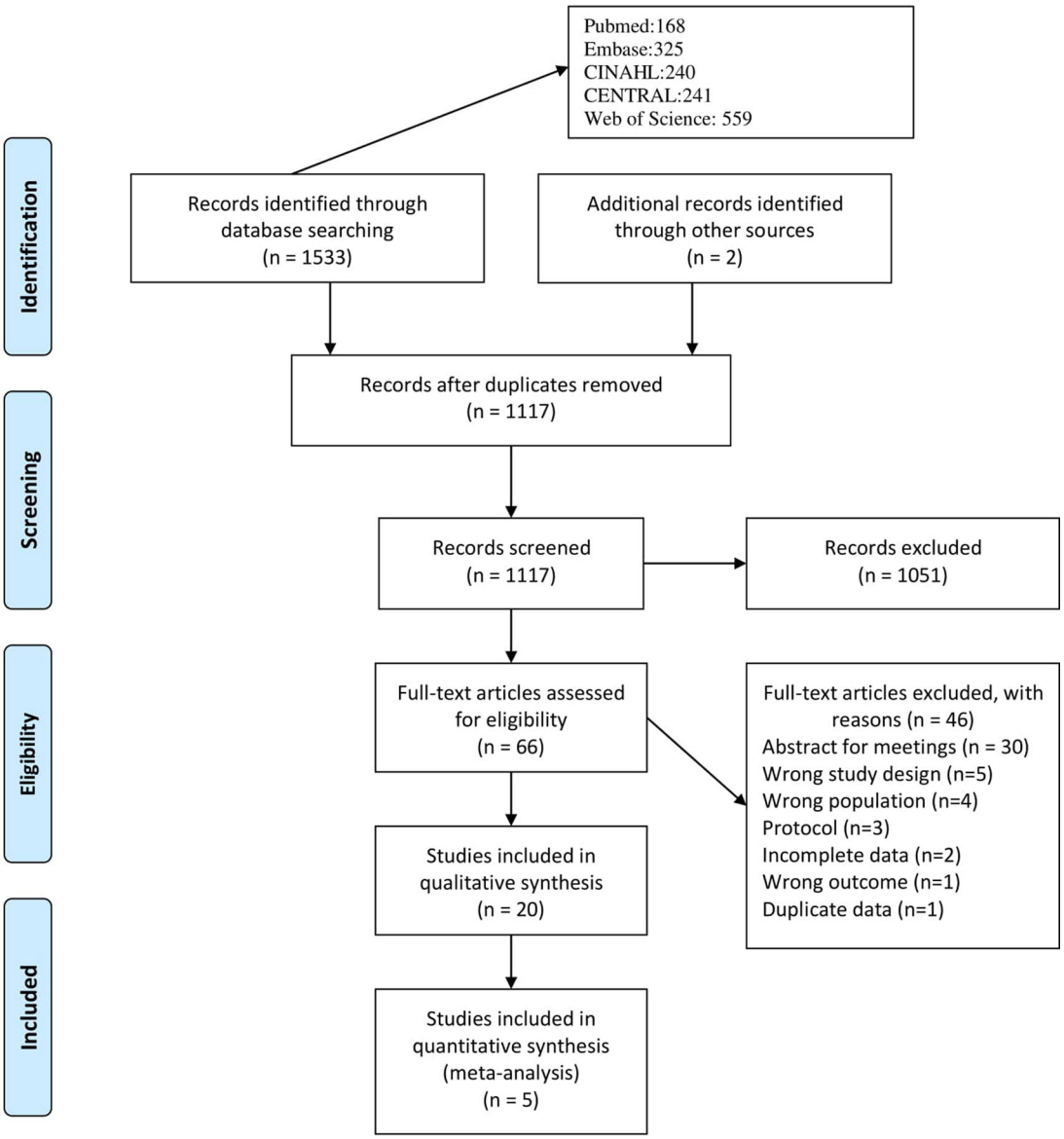

FIGURE 1 PRISMA flowchart of the selection of studies [Color figure can be viewed at wileyonlinelibrary.com]

having the wrong outcome. Finally, 20 studies fulfilled the criteria for eligibility and were included in the review.

3.2 | Characteristics of included studies

Twelve studies were performed in North America,[11,17,26-35] and eight in Europe.[36-43] The designs were as follows: fourteen cross-sectional,[27,28,31-40,42,43] two longitudinal,[29,30] and four of other designs.[11,17,26,41]

3.3 | Participants

In total, 785 participants were enrolled in the included studies. The sample size varied from 6[34,40] to 212[11] across studies.

3.4 | Methodological quality assessment

From the cohort and cross-sectional selected articles, only two (12.5%) met 75% of the affirmative answers, earning a "good" rating. Twelve (75%) affirmed 50% to 75%, qualifying as "fair," and two articles (12.5%) were rated as "poor." Regarding this study design, the greater risk of bias was mainly due to the justification of the sample size, the analysis of differentiated by exposure levels, and a lack of blinded result evaluations. Regarding the evaluation of quality assessment in the controlled intervention studies, both articles obtained a fair rating. For studies with no control group, the articles met the items with affirmative answers between 58.3% and 75.0%. The results of the quality assessment of the individual studies according to the NHLBI quality assessment tool are presented in Supporting Information file 2.

3.5 | Subjective measures

Nine studies used questionnaires,[11,28-31,33,34,36,37] and one study used a diary[32] to measure PA. The instruments used were the Habitual Activity Estimation Scale (HAES),[11,28,30] the original and modified versions of the Modifiable Activity Questionnaire (MAQ),[31,33,37] the interviewer-administered checklist,[29] the 30-day PA recall (PAR),[29] the physical activity questionnaire (PAQ),[34] the one representative week questionnaire,[36] and the Modified Bouchard Activity Diary.[32] Only four of these studies compared CF children and adolescents with healthy controls[31-33,37]; three authors did not find differences in PA outcomes between the groups,[32,33,37] and only one found less activity in metabolic equivalents (METs) hour/week in CF children [31] (Table 1).

3.6 | Objective measures

Eleven studies used objective instruments.[17,26,27,35,37-43] Nine studies used accelerometers[17,27,37-43] (Table 2), two studies used indirect calorimetry,[26,43] one study used doubly labeled water,[35] and one study used the flex heart rate method[26] (Table 3). Seven studies compared CF children with healthy controls.[26,35,37,39-42] Four authors did not find differences,[37,40-42] and three authors found lower PA levels in CF patients.[26,35,39]

3.7 | Time of use of objective instruments

The time required as a minimum in the studies that used the accelerometer was 7 days,[41,43] 5 days,[38] 4 days,[17,39,40] and 3 days.[37,42]

3.8 | Differences by gender

Seven studies reported analyses by gender.[11,28-30,32,36,37] Four authors did not find differences in PA between genders.[28,30,36,37] Two authors found differences in favor of males.[11,29] Selvadurai et al[32] did not find differences in habitual activity between prepubescent boys and girls with CF. However the pubescent boys with CF were significantly more active than girls with the same degree of disease severity.

3.9 | Outcome measures

The assessed outcomes were as follows: ten studies assessed the activity levels classified by METs intensity as MVPA, VPA, sedentary time, or similar[17,27,28,30,33,37,39-42]; six reported PA duration[11,27,31,33,36,37]; four studies reported in METs,[29,31,33,37] three studies reported in resting energy expenditure (REE) or total energy expenditure TEE[26,35,43]; two reported in accelerometer counts[32,38]; one reported in a score of a questionnaire[34]; and one reported in joules.[32]

3.10 | Main findings

3.10.1 | Primary outcomes

MVPA

Four studies examined PA according to MVPA.[37,39,41,42] These studies compared 102 children and adolescents with CF to 178 healthy controls. For the quantitative synthesis, we excluded the study of Kilbride et al[37] for not using min/day as the unit. In the selected articles, the heterogeneity of the comparison was low ($I^2 = 0\%$). The forest plot showed that both groups had similar values (mean difference, −7.79; 95% CI −15.65 to 0.08 min/d; $P = .05$) (Figure 2).

Sedentary time

Four studies examined the sedentary time in min/day.[39-42] These studies compared 92 participants with CF to 107 healthy controls. The analysis found no significant differences. The forest plot showed that both groups had similar values (mean difference, −50.81; 95% CI from −109.96 to 8.35; $P = .09$). The heterogeneity of the comparison was high ($I^2 = 86\%$) (Figure 3).

TABLE 1 Description of included studies of questionnaires

Author, country	Design	Participants	Age, y	FEV1, %	Assessment	Results	Conclusion
Boucher et al, 1997 Canada	Cross- sectional	n = 36 (15 M/21 F)	11.6 ± 3.45	85.7 ± 20.0	HAES Each subject was asked to describe a typical day during the preceding month.	Activity level: 32.4% ± 12% Patients with significant airflow limitation (n = 11), the PA level correlated with BMP (r = 0.675; P = .023)	Decreased nutritional status in patients with airflow limitation, was associated with a lower amount of time active.
Nixon et al, 2000 USA	Cross-sectional	CF n = 30 (14 M/16 F) Control n = 30 (17 M/13 F)	CF 10.8 ± 2.9 Control 11.4 ± 2.2	CF 96 ± 24 Control Not reported	Kriska's MAQ	CF 8.6 ± 6.4 Total h/wk 43.4 ± 32.6 MET-h/wk 2.0 ± 2.5 VPA-h/wk Control 8.5 ± 5.6 Total h/wk 49.7 ± 31.3 MET-h/wk 3.7 ± 2.8 VPA-h/wk	Total and MET-hours of PA did not differ between groups
Selvadurai et al, 2004 Canada	Cross-sectional	CF n = 148 (73 M/75 F) Control n = 148 (73 M/75 F)	CF 12.7 ± 1.2 Control 12.7 ± 1.1	CF Not reported Control not reported	Modified Bouchard Activity Diary. Children completed the diaries for two weeks.	CF Total: 12.2 ± 19.5 (MJ/d) Control Total: 11.9 ± 20.7 (MJ/d)	There were no significant differences in habitual activity between prepubescent children with CF and controls
Baker et al, 2006 USA	Longitudinal quasi-experimental	CF n = 16 (8 M /8 F)	CF 14.1 ± 2.0	CF 79.9 ± 16.5	Interviewer - administered checklist (MET)	MET-hour score 675.97	Adolescents with mild to moderate chronic lung disease can safely and significantly increase their time, intensity, and duration in vigorous PA for six weeks.
Swisher et al, 2007 USA	Cross-sectional	CF n = 31 (14 M/17 F) Control n = 24 (14 M/10 F)	CF 11.9 ± 4.0 Control 9.6 ± 3.5	CF 77.5 ± 25.9 Control 93.9 ± 14.1	MAQ-A	CF Activity (h/wk): 7.8 ± 6.0 (1.4-25.8) Activity (MET-h/wk): 31.4 ± 26.1 (5.2-107.0) Control Activity (h/wk): 10.2 ± 8.4 (0.2-30.3) Activity (MET-h/wk): 52.0 ± 39.9 (0.7-136.2)	The results suggest increasing habitual activity levels might improve exercise capacity in children with CF independent of lung function.

(Continues)

TABLE 1 (Continued)

Author, country	Design	Participants	Age, y	FEV1, %	Assessment	Results	Conclusion
Paranjape et al, 2011 USA	Longitudinal quasi-experimental	CF n = 78 (45 M/33 F)	CF 10 (6-16)	CF 100 (52-132)	HAES The habitual activity was expressed as the percentage of time when the study subject was awake and engaged in MVPA and recorded for a typical weekday and weekend.	Weekday activity 55.7% (6.0-93.7) Weekend activity 63.2% (0.0-95.8)	A 2-month, at-home exercise regimen is beneficial for pediatric CF patients. The HAES questionnaire has practical applications in the outpatient setting for measuring habitual activity that is well tolerated by the patients and easily implemented.
Swisher et al, 2010 USA	Cross- sectional	n = 6	Not reported	Not reported	PAQ 7-d recall instrument	3.0 ± 0.73 points	This study suggests that an individualized approach to training in CF kids and adolescents may improve PA levels.
Kilbride et al, 2012 Ireland	Cross-sectional	CF n = 16 (9 M/7 F) Control n = 99 (47 M/52 F)	CF 11.0 ± 0.9 Control 11.1 ± 0.7	CF 77.5 ± 25.9 Control 93.9 ± 14.1	A modification of the MAQ	CF PA (MET-h/d) 4.5 ± 13.6 Control PA (MET-h/d) 5.8 ± 41.4	Boys and girls with CF were equally active as their corresponding controls.
Hafen et al, 2013 Switzerland	Cross- sectional	n = 22 (13 M/9 F)	11 ± 2.27	>70 (n = 20, 91%) 60-69 (n = 2, 9%)	"One representative-week" questionnaire Activities at school, within a club, personal trainer and activities executed on its own respectively within the family were addressed.	PA hours 9.7	PA, as part of respiratory therapy, maybe a way to reinforce the treatment: all the more if it is encouraged from a young age and with the aim of maintaining social interactions.
Schneiderman et al, 2014 Canada	Cohort Study	CF n = 212 (104 M/108 F)	CF 12.0 ± 2.82	CF 85.5 ± 17.3	HAES At each quarterly clinic visit, the patients completed the HAES	HPA h/d 5.47 ± 2.80 HPA h/d (M):5.90 ± 2.87 HPA h/d (F):5.06 ± 2.69	Males with CF had a significantly higher pulmonary function and activity levels than females with CF

Abbreviations: BMP, body mass percentile; CF, cystic fibrosis; FEV1, forced expiratory volume at the first second; HAES, Habitual Activity Estimation Scale; HPA, habitual physical activity; MAQ, Modifiable Activity Questionnaire; MAQ-A, Modifiable Activity Questionnaire for Adolescents; MET, metabolic equivalent of task; MJ, megajoules; PA, physical activity; PAQ, physical activity questionnaire; VPA, vigorous physical activity; yrs: years.

TABLE 2 Description of included studies of accelerometers

Author (country)	Design	Participants	Age, y	FEV1, %	Assessment	Results	Conclusion
Selvadurai et al, 2004 Canada	Cross-sectional	CF n = 148 (73 M/75 F) Control n = 148 (73 M/75 F)	CF 12.7 ± 1.2 Control 12.7 ± 1.1	CF Not reported Control Not reported	Accelerometer WAM 7164 Children wore the accelerometer for 14 days	CF Counts 9428 ± 286 Control Counts 9375 ± 277	PA assessed by the accelerometer is similar between CF children and healthy controls
Kilbride et al, 2012 Ireland	Cross-sectional	CF n = 16 9 M/7 F) Control n = 99 (47 M/52 F)	CF 11 ± 0.3 Control 11.1 ± 0.1	CF 83 ± 3.5 Control 91 ± 1.2	Accelerometer RT3 research tracker The accelerometer was worn for three consecutive days.	CF PA (h/d) 0.7 ± 0.2 PA (MET h/d) 4.4 ± 1.0 MVPA 15 ± 1.5% Control PA (h/d) 0.9 ± 0.1 PA (MET h/d) 5.8 ± 0.5 MVPA 18.8 ± 2.0%	The PA levels in this group of children with CF were relatively well preserved despite a significant deterioration in lung function.
Groeneveld et al, 2012 Spain	Cross-sectional	n = 28 (14 M/14 F)	11.6 ± 3.1	85.3 ± 20.9	Accelerometer ActiGraph 7164 Participants were instructed to wear the accelerometer on their lower back during all waking hours. At least 5 days of recording including two weekend days, with a minimum of 10 h/d.	CF 549.7 ± 189 counts/min	No significant associations between Physical Activity and HRQOL were found with the multiple linear regression model
Aznar et al, 2014 Spain	Cross-sectional	CF n = 47 (24 M/23 F) Control n = 39 (23 M/16 F)	CF 12.0 ± 3.0 Control 12.0 ± 2.0	CF Not reported Control Not reported	Accelerometer ActiGraph GT3X by 7 days. Children wore the accelerometer on their right hip during the day, at least 4 days' monitoring including one weekend day, and a minimum of 10 h of complete accelerometry data per day	CF MVPA 44 ± 28 (min/d) Sedentary time 362 ± 67 (min/d) Control MVPA 54 ± 15 (min/d) Sedentary time 484 ± 85 (min/d)	2.1% of children with CF achieved PA guidelines. Compared to controls, they performed a higher quantity of PA but were of insufficient intensity.

(Continues)

TABLE 2 (Continued)

Author (country)	Design	Participants	Age, y	FEV1, %	Assessment	Results	Conclusion
Walker et al, 2015 Netherlands	Cross-Sectional	CF n = 6 (4 M/2 F) Control n = 29 (21 M/8 F)	CF 15 ± 2.5 Control 13.8 ± 2.5	CF Not reported Control Not reported	Accelerometer ActiGraph GT1M and GT3X.Children wore the accelerometer over their right hip during all waking hours. Wear time for at least 10 h per day and at least 4 of 7 days.	CF Sedentary time 9.5 ± 1.1 h/d 46.0 ± 2.2 min/h Control Sedentary time 10.2 ± 1.6 h/d 44.3 ± 4.5 min/h	Children with CF expend similar sedentary time than healthy controls
Stephens et al, 2016 Canada	Cross-sectional	n = 12 (9 M/3 F)	CF 14 ± 2.1	Not reported	Accelerometer Actical Koninklijke Philips Electronics. Participants were instructed to wear the accelerometer on their right hip seven consecutive days during walking hours.	PA (min/d) Sedentary 470 ± 68 Light 217 ± 46 Moderate 23 ± 9 Vigorous 9 ± 7 MVPA 34 ± 4	The CF group has less MVPA than recommended by the International CF guidelines, and no differences between children with rheumatologic conditions
Moola et al, 2017 Canada	RCT	n = 13 (5 M/8 F)	11.6 ± 3.2	95.4 ± 14.2	Accelerometer (no model specified) The participants had to wear the accelerometer for at least 4 days. This included at least 3 weekdays and one weekend day. They were instructed to put the accelerometer every day for 1 week.	MVPA 45.3 ± 9.1 (min/d) Sedentary time 580.8 ± 91.5 (min/d)	This group has fewer minutes of MVPA than the recommendations for PA in children (i.e., ≥60 min/d of moderate-to-vigorous PA (MVPA))
Mackintosh et al, 2018 United Kingdom	Cross-sectional	CF n = 18 (10 M/8 F) Control n = 18 (10 M/8 F)	CF 12.4 ± 2.8 Control 12.5 ± 2.7	CF 80 ± 9 Control 89 ± 17	Accelerometer ActiGraph GT3X by seven days. A valid day was defined as ≥ 9 hours day. Children were required to have worn the accelerometer for at least 3 days.	CF MVPA 55.3 ± 38 (min/d) Sedentary time 539 ± 65 min/d Control MVPA 56.1 ± 27.9 min/d Sedentary time 551 ± 87 min/d	Both children with CF and healthy children demonstrated similar PA levels and patterns of accumulation across the intensity spectrum, with higher levels of PA during weekdays in both groups

TABLE 2 (Continued)

Author (country)	Design	Participants	Age, y	FEV1, %	Assessment	Results	Conclusion
Mackintosh et al, 2019 United Kingdom	Cohort study	CF n = 21 Control n = 22	CF 12.1 ± 2.6 Control 1.7 ± 2.7	CF 80 ± 10 Control 92 ± 14	Accelerometer ActiGraph GT3X by seven days. Participants were instructed to wear the accelerometer for seven consecutive days. A valid day was defined as at least 9 h of wear-time. At least three valid days of data, were included in the analyses	CF MVPA 58.9 ± 36.9 min/d Sedentary time 555.8 ± 59.9 min/d Control MVPA 62.2 ± 30.3 min/d Sedentary time 576.5 ± 69.9 min/d	Children with CF have similars levels of MVPA and sedentary time than healthy controls

Abbreviations: CF, cystic fibrosis; FEV1, forced expiratory volume at the first second; HRQOL, health related quality of life; MVPA, moderate-to-vigorous physical activity; PA, physical activity; RCT, randomized control trial.

Other outcomes

Three authors reported measures dependent on energy expenditure as REE or TEE.[26,35,43] Only two authors compared with controls.[26,35] Tomezsko et al[35] found no differences, and Johnson et al[26] showed that the energy cost of daily activities was significantly lower in CF adolescents than in the controls. No author reported the number of steps/day.

4 | DISCUSSION

Our results suggest that children and adolescents with CF have MVPA and sedentary times similar to those of healthy controls. The main instruments used were questionnaires and accelerometers.

The World Health Organization recommends a minimum of 60 min/d of MVPA to maintain cardiovascular health in children and adolescents from 5 to 17 years, with a minimum of 30 min/d of at least moderate intensity to obtain some benefits.[44,45] In our results, the majority of studies report insufficient levels of MVPA[17,37,39,41-43]; however, this insufficiency is concordant with the general population. These results may be important because it is accepted that high levels of MVPA have a long-term protective effect on health.[46]

Healthy girls tend to have less PA than healthy boys. This difference is also seen in children and adolescents with CF.[28] One reason given for this is that parents and teachers have lower expectations that girls engage in regular PA than boys. This could result in an incentive for a more inactive lifestyle for girls and promote a lifestyle that increases PA for boys.[47,48] This difference is important because a more significant decline in lung function has been noted in girls than in boys.[47]

The literature shows that high levels of PA slow lung function deterioration.[11] Schneiderman et al[11] evaluated PA in 212 children with CF over a period of 9 years, finding that lung function declines more in those children who have less PA than estimated for their age and anthropometric characteristics.

Children with CF experience early alterations in the respiratory system[49] that manifest in lung function measured through spirometry. But these alterations are not significant in PA levels or physical capacity compared to healthy children at an early age.[37,50] This may be due to the heterogeneity of the severities included in the studies, such as the fact that the ventilatory reserve allows for a delay in the systemic manifestations together with a peripheral muscular force maintained in the first years of life.[37] As children with CF grow and reach adulthood, physical capacity measured with both the six-minute walk test and peak oxygen consumption decreases, as does peripheral muscle strength.[51]

Heterogeneity was observed in the use of an accelerometer. These differences make it difficult to compare the results among studies. The international guidelines recommend the use of the accelerometer for at least 7 days for at least 10 h/d,[52] only one author accomplished this.[27] Although all accelerometers have very similar operations based on 1-, 2-, or 3-axis displacement, the reported results were not the same. Some authors reported the accelerometer counts,[32,38] and others reported MVPA.[39,41,42] This is understandable since the older accelerometers delivered the data in accelerometer counts. Eventually,

TABLE 3 Description of included studies of others instruments

Author, y, country	Design	Participants	Age, years	FEV1, %	Assessment	Results	Conclusión
Tomezsko et al, 1994 USA	Cross - sectional	CF n = 25 (12 M/13 F) Control n = 25 (14 M/11 F)	CF 7.7 ± 1.3 Control 7.6 ± 1.1	CF 89.2 ± 16.4 Control Not reported	DLW REE was measured by open-circuit indirect calorimetry; each child fasted from food and medication for 12 to 14 h before REE	CF REE (kcal/d) 1193 ± 120 TEE (kcal/d) 2012 ± 435 TEE/REE 1.68 ± 0.31 Control REE (kcal/d) 1144 ± 111 TEE (kcal/d) 1808 ± 295 TEE/REE 1.61 ± 0.21	The CF group had a 9% increase in REE, which was not related to the genotype or severity of lung disease. TEE was increased by 12% in the entire CF group
Johnson et al, 2006 USA	Controlled not randomized trial	CF n = 11 (6 M/5 F) Control n = 13 (8 M/5 F)	CF 12.7 Control 11.2	CF 103 Control 106	Indirect calorimetry and FHRM. Fasting REE was determined in the morning with a metabolic cart. TDEE was determined by FHRM. ECA was calculated as the difference between TDEE-REE	CF REE (cal/d) 1393 ECA (cal/d) 267 Control REE (cal/d) 1290 ECA (cal/d) 769	ECA in CF adolescents with normal lung function is lower when compared to healthy controls.
Takken et al, 2010 Netherlands	Cross - sectional	n = 9	13.3 ± 3.53	Not reported	Indirect Calorimetry and Actiheart (only for validation). Expired gas was collected using IC to determine resting metabolism over 20 min with the participant supine in a quiet room. Recordings were taken at 1-min intervals for the duration of the last 10 min of rest.	REE (J/kg/min) 173 ± 44.8	The authors validated the Actiheart for activity energy expenditure determination in the CF population and other children with chronic diseases

Abbreviations: DLW, double labeled water; ECA, energy cost of daily activities; FEV1, forced expiratory volume in the first second; FHRM, flex-heart rate method; MVPA, moderate and vigorous physical activity; PA, physical activity; REE, resting energy expenditure; TEE, total energy expenditure.

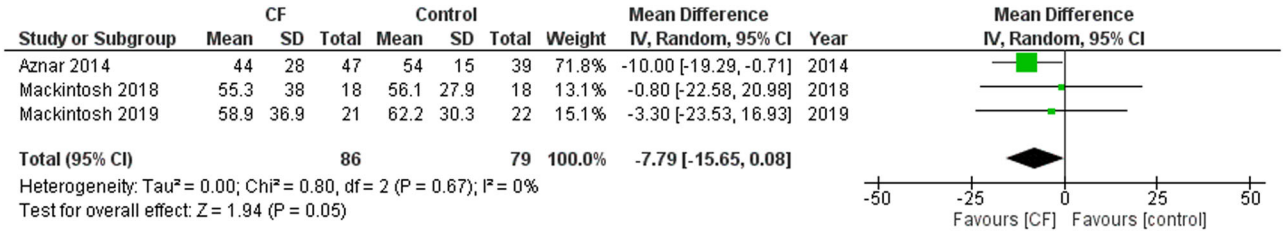

FIGURE 2 Forest plot for moderate to vigorous physical activity (MVPA) for cystic fibrosis children and adolescents and healthy pairs [Color figure can be viewed at wileyonlinelibrary.com]

software was added that allows the user to immediately extract the MVPA. However, it is unclear why the authors did not report the number of steps/day, as that is widely used as an indicator of PA and is provided by most of the accelerometers used in the selected studies.[5]

Boucher et al[28], compared the levels of PA reported by children and their parents. Activity level reported by children and adolescents 12 years of age and older was on average 24.1% ($P < .05$) higher than that reported by their parents. This underestimation may be based on expectation rather than direct observation. It might also be related to the amount of time spent together, which often decreases during adolescence. Given that perceptions of activity decrease during adolescence, the relatively high activity levels suggest that the children's reports are closer to the real activity level.[53]

The subjective evaluation of PA in CF patients can be estimated with questionnaires that are easy and inexpensive to use. A variety of questionnaires allow different aspects of PA to be evaluated, such as quantity, type, intensity, symptoms, and limitations in ADL. The most common questionnaires used were HAES and MAQ.[54,55] These tools are used to extrapolate energy expenditure and the time and intensity of the PA people report. They can be self-administered questionnaires completed by the patient or guided by trained professionals. Most importantly, these instruments must be specific, and their psychometric properties must be validated.[5] Although the questionnaires are not the most reliable tool, clinically, it may be sufficient to determine low levels of PA.

5 | POTENTIAL BIASES IN THE REVIEW PROCESS

The systematic review process was rigorous. The review was preceded by the publication of a protocol with all review methods described, and we did not change the methods. All review authors were appropriately trained and had experience in review preparation.

6 | COMPLETENESS OF EVIDENCE

We conducted a comprehensive search of the literature, including full-text publications, without language restrictions or the use of filters in the search strategy. As were included studies between 1970 and May 2020, it is unlikely that any may have been missed, given that the publications of well-designed and protocolized PA assessments began to appear in 1990.

7 | QUALITY OF EVIDENCE

This systematic review follows the standard methodology suggested for systematic reviews, and its construct is in line with the recommendations of the PRISMA statement,[20] with two independent review authors assessing the inclusion criteria for the studies, extracting data, and assessing the risk of bias of the included studies, thus reducing the risk of performance bias in the review and data extraction errors.

8 | SOURCES OF HETEROGENEITY

We found low heterogeneity in MVPA among the study results (0%). However, in the sedentary time, we found high heterogeneity (86%), probably due to the different measurement periods, three versus 7 days. Another factor that can explain the high heterogeneity is the

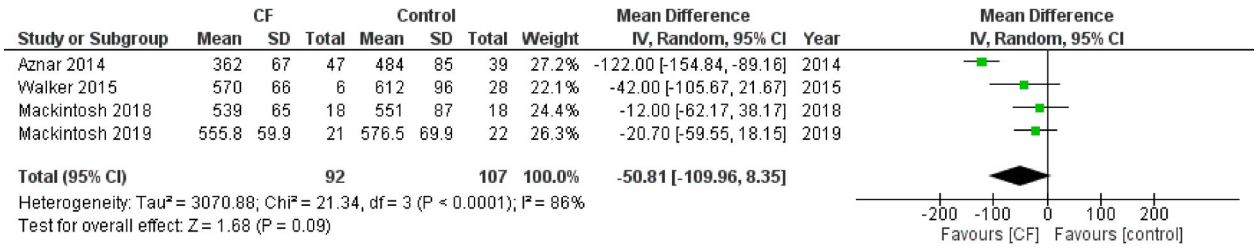

FIGURE 3 Forest plot for sedentary time for cystic fibrosis children and adolescents and healthy pairs [Color figure can be viewed at wileyonlinelibrary.com]

different designs among the studies (retrospective, prospective, and cross-sectional).

9 | APPLICABILITY OF FINDINGS TO THE REVIEW QUESTION

Measuring the levels of PA in children and adolescents with CF provides information about one of the determining factors in the progression of morbidity and mortality in children with CF.[56] Strong evidence supports the importance of PA in CF patients: High levels of PA are associated with improved sputum clearance. PA influences the decrease in lung function decline and improves bone mineral density.[57] Children with CF with high levels of PA have better health-related quality of life.[32] Finally, PA is associated with decreased CF mortality.[15,16] These reasons justify a regular measure of PA in CF patients.

Regarding subjective measurements, this study found that questionnaires are an easy tool for quantifying levels of PA. However, these should be used with caution, since they may not adequately reflect the PA levels of children and adolescents, as most questionnaires lack adequate validity or reliability.[58]

This last point is very important when choosing this type of tool as a measurement of PA, since the performance of PA has a multifactorial origin (eg, gender, ethnicity, sexual orientation, level of education, physical abilities, geographic location, and social determinants).[59] Therefore, subjective tools should be chosen that address all the elements related to the context of CF patients and not only PA, since if it is not possible to analyze all these factors, it will be it difficult to stimulate the PA practice, remove barriers, and change habits.[60]

10 | LIMITATIONS

The most important limitation is the high heterogeneity in the selected studies, particularly that related to the different instruments of use. On the other hand, the studies do not classify the population between children and adolescents, which could give us specific information for each age group.

11 | CONCLUSION

Children and adolescents with CF have MVPA and sedentary time similar to that of controls. There are many options, subjective and objective, for assessing PA.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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