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REVIEW ARTICLE

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Physical activity and sedentary time in children and adolescents with asthma: A systematic review and meta-analysis

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The influence of asthma on physical activity (PA) in youth remains equivocal. This review synthesizes the evidence regarding the influence of asthma on PA and sedentary time and evaluates the role of key moderators for this relationship. In accordance with PRISMA guidelines, six electronic databases and gray literature were searched. Primary studies in English were included if they reported device-assessed PA in youth with and without asthma. Random effects meta-analyses examined the effect of asthma on PA and, separately, sedentary time. Mixed-effect meta-regression analyses were conducted using age and sex as moderators, with sub-group comparisons for study quality and asthma diagnosis criteria. Overall, of 3944 citations retrieved, 2850 were screened after the removal of supplication and 2743 citations excluded. Of the 107 full-text publications reviewed, 16 were included in data extraction and analysis, with 15 and five studies included in the PA and sedentary time meta-analyses, respectively. The robust effect size estimate for the influence of asthma on PA and sedentary time was −0.04 [95% CI = −0.11, 0.03] and −0.09 [95% CI = −0.12, −0.06], indicating a non-significant and significant trivial effect, respectively. The effect of asthma on PA levels or sedentary time was not associated with age or sex. Youth with controlled asthma are equally physically (in)active as their healthy peers, with asthma associated with less sedentary time. However, methodological limitations and a paucity of clear methodological reporting temper these conclusions. More rigorous device-based assessments, with a particular focus on sedentary time, and more robust diagnoses of asthma, especially with regard to severity, are needed.

KEYWORDS
accelerometery, chronic disease, pediatric, respiratory health, youth

1 | INTRODUCTION

Asthma, an obstructive airway disease characterized by dyspnoea, wheezing, coughing and chest tightness,[1] is one of the most common chronic childhood diseases.[2] Indeed, asthma is currently estimated to affect 1 in 11 children within the UK,[3] with similar levels reported in across Australasia, Europe, North America and parts of Latin America.[4] This prevalence continues to rise and is associated with considerable years lived with disability and early mortality.[4]

Regular physical activity is an important component in the management of asthma and is recommended in internationally recognized guidelines, irrespective of age.[1,5] In addition to the extensive benefits of leading an active lifestyle without sustained periods of sedentary behaviors in healthy populations,[6,7] being active elicits further health benefits for those with asthma. Specifically, those with higher levels of physical activity and lower sedentary time, in comparison to their peers, may lead to reduced, and improved management of, symptoms,[8-10] as well as improved quality of life[11,12] and lung function.[13] However, paradoxically, symptoms may be triggered by physical exertion, particularly vigorous intensity,[14] which, coupled with the fear of exercise-induced bronchoconstriction (EIB), may impact on the physical activity levels in those with asthma.[15]

Research regarding the influence of asthma on physical activity levels in youth remains equivocal.[16,17] Indeed, of the reviews conducted in youth with asthma to date, Williams et al[17] reported lower physical activity levels relative to their healthy peers, whereas Welsh et al[18] and Cassim et al[16] found no difference. However, recent research succeeding these reviews has encompassed much larger datasets and may, therefore, substantially advance our interpretation and their generalizability.[19,20] While sedentary time has received considerable less attention, the limited evidence available regarding the influence of asthma on time spent sedentary is equally contradictory.[19,20]

Inter-study discrepancies in physical activity levels and sedentary time according to asthma status could be due to methodological differences, such as the reliance on device-based or subjective measures of physical activity, or, at least in part, to age- and/or sex-related differences. Indeed, in healthy populations, research consistently reports lower physical activity levels in girls.[21,22] Although a recent systematic review in adults with asthma found that physical activity levels were lower in females with asthma compared to their male counterparts,[23] there was insufficient data to conduct a meta-regression to elucidate sex-related differences in the most recent systematic review conducted in children and adolescents in 2016.[16] Moreover, although physical activity declines with age, irrespective of sex, these declines are more pronounced in girls. It is also pertinent to note that while some studies have used a confirmed or objective measure to diagnose asthma,[24] others, particularly population-based cohorts (eg, the International Study of Asthma and Allegeries in Childhood studies)[25,26] have utilized self-reported asthma status, which is suggested to be associated with both under- and over-reporting of asthma.[27] Irrespective of the method of diagnosis, previous reviews have not been able to ascertain the mediatory or modulatory role of asthma severity or control, age or sex, on the relationship between asthma and physical activity or sedentary time due to insufficient data previously being reported. Such information could provide critical information for treatment strategies and ongoing care.

A consensus is urgently required regarding the influence, or lack thereof, of asthma on physical activity and sedentary time to ascertain whether there is a need to develop and implement population-specific physical activity intervention strategies. Therefore, the primary aim of this review was to synthesize the evidence regarding the influence of asthma on device-measured physical activity and, where available, sedentary time in children and adolescents. Furthermore, a meta-analysis was conducted to evaluate physical activity levels and sedentary time and the influence of age, sex, study quality and whether asthma was objectively or subjectively reported.

2 | METHODS

This review was performed in accordance with the Preferred Reporting items for Systematic Review and Meta-Analysis statement[28] and is registered on the International Prospective Register of Systematic Review (PROSPERO; registration ID: CRD42018114800).

2.1 | Search methods

A comprehensive strategic literature search was conducted. First, a pilot search was performed to ensure the suitability of the criteria and search terms. Key articles from different databases were reviewed to identify appropriate controlled terms and free text words, with the Medical Subject Headings (MeSH)[29] browser and the Permuted index (search tool in Ovid host) being used to check additional terms. Following this, a full search was conducted in October 2018 and updated in September 2019 using six reference databases (MEDLINE (Ovid), EMBASE (Ovid), SPORTDiscus (EBSCOhost), CINAHL Pluss with Full Text (EBSCOhost), Web of Science (the Core collection), and Cochrane Controlled Register of Trials (CENTRAL) in Cochrane Library). All searches were conducted with no limitations regarding study design, language, or publication date.

The database searches comprised of a combination of words from controlled vocabulary (index words such as MeSH[29] used in MEDLINE database, EMTREE in EMBASE, CINAHL Subject Headings in CINAHL database, and Sport Thesaurus used in SPORTDiscus), which were exploded where appropriate. Single, narrower terms were also applied with a wide range of text words for the concepts; children or adolescents with asthma; physical activity levels; objectively measured. Documentation of the full search strategy for all six databases executed in September 2019 is provided in online supplementary files. An additional search for gray literature was also conducted in appropriate databases and websites. Documentation of the database and gray literature search strategies are provided in Supplementary Files 1 and 2, respectively.

Finally, after screening and inclusion of full texts, forward and backward citation tracking was conducted. Specifically, the reference list in all the included studies, and articles citing the included studies, were searched through Scopus in November 2019. Google scholar was used for articles not indexed in Scopus. The citation tracking search strategy is also documented in Supplementary File 3.

2.2 | Eligibility criteria

Primary studies published in English were included if they reported device-assessed physical activity levels in children and/adolescents aged 5-18 years both with and without asthma. Conference abstracts and study protocols without a traceable full text were excluded. Studies including additional age range where results concerning 5- to 18-year-olds could not be isolated were also excluded. An EndNote X7 (Clarivate Analytics) database was created with potential studies. Two authors (MAM and TW) screened all the titles and abstracts independently and in a blinded manner using Rayyan software.[30] In the case of disagreement which could not be resolved through an initial discussion, the full texts were screened by two further co-authors (KAM and SB) according to the pre-established inclusion criteria. Supplementary information for each study was consulted where available. In the case of missing information or variables required for completion of the meta-analysis and/or meta-regression, study authors were contacted.

2.3 | Methodological quality assessment

The quality of studies was assessed independently by two authors (MAM and TW) using the National Institute of Health's quality assessment of case controls and quality of observational cohort and cross-sectional studies.[31] Disagreements were discussed by four authors (MAM, KAM, SB, TW) until a consensus was reached. Studies were classified as a case-control if they specifically sought to recruit those with asthma and a matched control group. Methodological quality was not evaluated for the purpose of including/excluding studies. Overall quality assessment criteria and risk of bias applied for case-control and cross-sectional studies, respectively, are shown in Table 1.

2.4 | Data extraction

A data extraction table (Supplementary File 4) was prepared to map: (a) author and year of publication; (b) study design; (c) sample age; (d) sample health status; (e) sample height, body mass, and body mass index (BMI); (f) sample ethnicity; (g) covariates of analysis; (h) accelerometer model; (i) number of axes; (j) placement; (k) sampling duration and wear-time criteria; (l) sampling frequency and low frequency extension; (m) epoch length; (n) cut-points; and (o) physical activity levels, in asthma and control groups, including standard deviation, 95% confidence intervals (CI), and p-values. Data extraction was conducted by four authors (KAM, MAM, SB, TW) and each data point was double-checked independently by at least two authors.

2.5 | Synthesis and analysis

The meta-analysis was performed independently by two members of the research team (TW and JS) using both Comprehensive Meta-Analysis (CMA) software (Biostat) and the “metafor” package in R (v 3.6.1; R Core Team, https://www.r-project.org/) and results were compared to ensure consistency. Results were broadly similar such that, although each software package differed in the specific values calculated for test statistics, point estimates and interval estimates, none of these differences impacted upon the conclusions drawn. Thus, for ease, only results conducted in R are presented in this paper, with analyses conducted in CMA presented in Supplementary File 5 for comparison.

Standardized between-group effect sizes using Hedges *g* and pooled pre- and post-test standard deviations were calculated for

TABLE 1 Overall quality assessment criteria and risk of bias applied for case-control and cross-sectional studies, respectively

Overall quality rating	Poor	Fair	Good
Case-control studies	Key potential confounding factors not measured/assessed	Neither use of concurrent controls, nor random or 100% selection of cases/controls Key potential confounding factors assessed	Key potential confounding factors assessed and use of concurrent controls and/or random/100% selection of cases/controls
Cross-sectional studies	Key potential confounding factors not measured/assessed	Key potential confounding factors assessed	Key potential confounding factors assessed, and exposure examined at different levels

each study and outcome measure.[32] The magnitude of Hedges *g* was interpreted with reference to Cohen's[33] thresholds: trivial (<0.2), small (0.2 to <0.5), moderate (0.5 to <0.8), and large (>0.8). Positive effect size values indicated higher scores of the outcome in favor of the group with asthma. Random effects meta-analyses were performed to examine the effect of asthma on physical activity levels and, separately, sedentary time, generating point estimates for pooled effect sizes and precision of those estimates using 95% confidence interval (CI) for between-group effect of reported physical activity levels and sedentary time in those with and without asthma. Where studies had two groups with asthma, multilevel models were used as their data were analyzed independently with the control group, thus yielding multiple effect sizes for that study and outcome. Both research study and intra-study groups were included as random effects in the model. Cluster robust estimates were produced, weighted by inverse sampling variance to account for the within- and between-study variance (tau-squared). Restricted maximal likelihood estimation was used in all models.

Mixed-effect meta-regression analyses were planned, using both age and sex (proportion of males) as a moderator of physical activity. Additionally, sub-group comparisons were performed for study quality (fair/good vs. poor) for both physical activity and sedentary time, and to compare studies with different asthma diagnosis methods (objective vs. subjective). Sub-group comparisons of sedentary time models by asthma diagnosis method were not conducted due to the number of studies available. Multilevel models were produced for each sub-group and a fixed effects with moderators model used to compare the models to ascertain whether there was a significant difference ($P < .05$). Sensitivity analyses were performed using the leave-one-out method to examine the impact of removal of individual effect sizes; the results are provided in the supplementary materials (Supplementary File 6). Heterogeneity was examined through the Q and I^2 statistic,[34] whereby a significant Q statistic was indicative of studies likely not being drawn from a common population. I^2 values indicate the degree of heterogeneity in the effects: 0%-40% were not important, 30%-60% moderate heterogeneity, 50%-90% substantial heterogeneity, and 75%-100% considerable heterogeneity.[35] Risk of small study bias was examined using Egger's linear regression test for funnel plot asymmetry and graphically presented by contour-enhanced funnel plots with Duval and Tweedie's trim and fill used. All coding utilized is presented in Supplementary File 7.

3 | RESULTS

3.1 | Search and screening results

Database, Google Scholar, gray literature, and forward and backward citation tracking searches resulted in 3944 citations. After removal of duplicates, 2850 citations were screened, and 2743 citations excluded. Of the 107 full-text publications that were retrieved, 91 were excluded with reasons (Supplementary File 6). Therefore, a total of 16 articles were included in data extraction and analysis, with 15 included in the physical activity meta-analysis, five of which were also included in the sedentary time meta-analysis. A detailed search and screening history is illustrated in Figure 1.

3.2 | Study quality and characteristics

During quality assessment, nine studies[24,36-43] were evaluated as case-control studies (Supplementary Table 1, File 8), and seven[20,44-48] as observational cross-sectional studies (Supplementary Table 2, File 9). Five case control studies[24,36,39-41] were graded as “poor,” one case-control study[38] was regarded as “fair," whereas three studies[37,42,43] were evaluated as “good.” Among cross-sectional studies, two studies[45,47] were considered of “poor” quality, whereas four studies[19,44,46,48] were considered “fair” and one [20] as “good.” All 16 studies failed to report a clear, valid, and reliable description of the data recording and/or management/analysis of the device-based physical activity measures. Moreover, none of the included studies could be reliably replicated based on the information provided.

Walders-Abramson et al[41] was the only intervention study that was included, in which they sought to increase children's physical activity levels. Nonetheless, Walders-Abramson and colleagues[41] study could not be included in the meta-analysis as neither the mean and SD, nor an independent t test p-value, was reported (Table 2). Yiallouros et al[43] was not included in the sedentary time meta-analysis due to the lack of differentiation between sleep and sedentary time. Given that Pike et al[20] and Smith et al[46] presented results separately for boys and girls, and Willeboordse et al[42] according to weight categorization (normal and overweight), each study group was included separately in the meta-analysis.

There were large differences in sample size in the included studies, ranging from 23 asthma and 23 controls[36] to 1275 asthma and 3998 controls.[19] The mean age in asthma groups ranged from 7.3-15.7 years, and the proportion of boys within studies ranged from 0% to 100%. In six studies,[24,36,39,40,42,47] asthma was confirmed by objective criteria and/or a physician, while in eight studies,[19,37,38,43-46,48] asthma was self-reported by participating children/parents.

In three studies,[37,38,40] participants were reported to exceed the World Health Organization recommendations of a minimum of 60 minutes of moderate-to-vigorous physical activity (MVPA) per day. In contrast, in eight studies,[19,24,39,41,43,45-47] the majority of participants did not achieve these recommendations or their equivalents (eg, 10 000 steps per day), whereas boys, but not girls, met

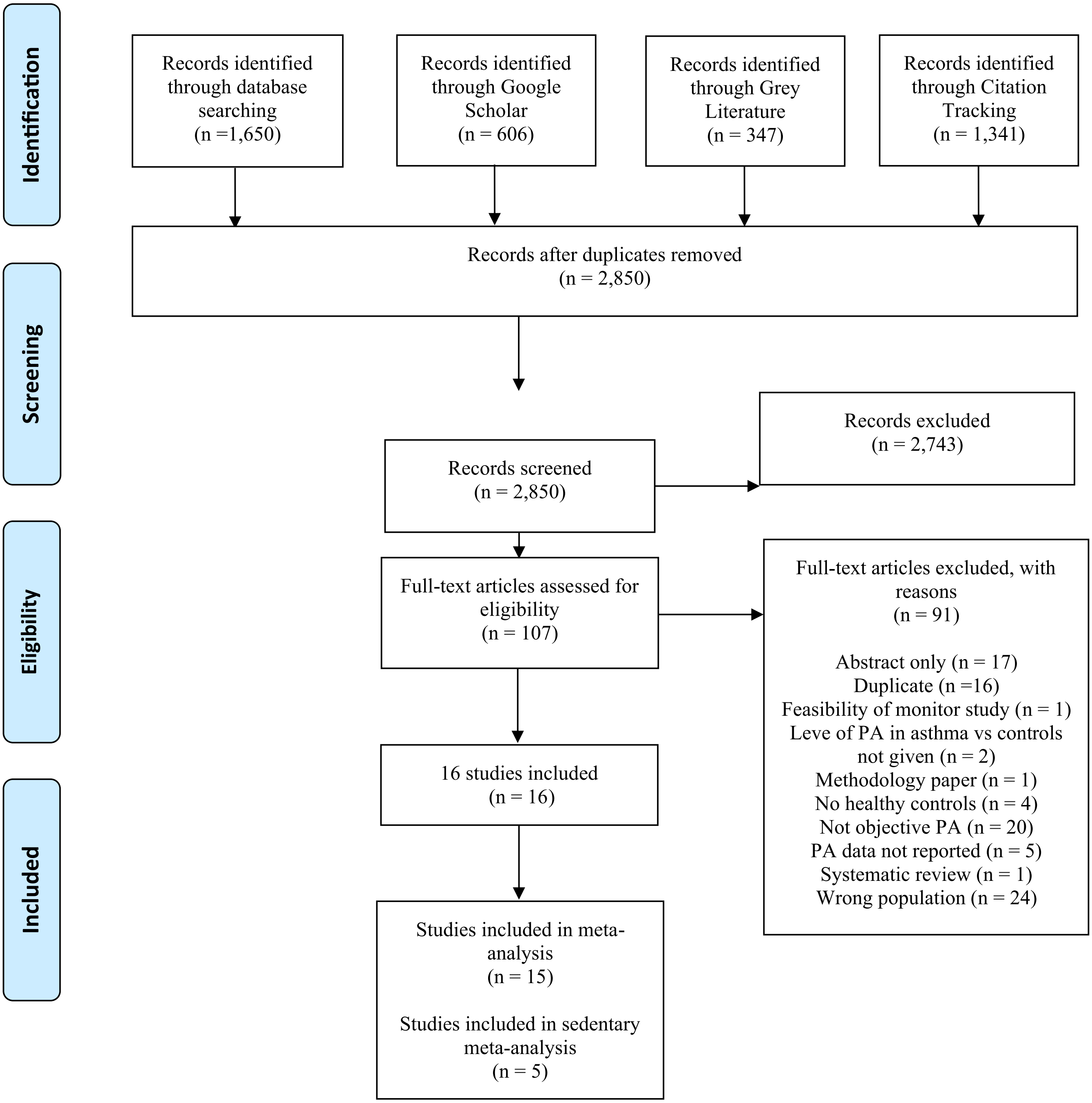

FIGURE 1 PRISMA Flow Diagram documenting identification, screening, eligibility, and inclusion of studies in the current review

the recommended MVPA in Pike et al.[20] Willeboordse et al[42] reported that only one of four study groups (those with asthma who were normal weight) averaged above 10 000 steps per day, which was similar to the findings of Alshammari.[36] Due to a lack of sufficient reporting, we could not assess whether participants in the study by Fedele et al[44] met physical activity recommendations. Additionally, Jago et al[19] reported a reduction in physical activity levels with increasing age.

3.3 | Overall difference in physical activity levels and sedentary time – meta-analysis

The robust effect size estimate for the influence of asthma on physical activity levels and sedentary time was −0.04 [95% CI = −0.11, 0.03] (Figure 2) and −0.09 [95% CI = −0.12, −0.06] (Figure 3), indicating a non-significant and significant trivial effect, respectively, with high precision indicated by the CIs which ranged from a trivial negative to a trivial

TABLE 2 Study characteristics of included studies

Author, year, study design	Sample Size	Sample age (years)	Asthma diagnosis	Device to record PA	Sedentary time reported	Overall study quality
Alshammari (2017; 36) case-control	23 asthma (17 males) 23 healthy control (17 males)	8.1 ± 2.0 9.0 ± 1.7	Prior to admission and had a history of previous asthma-related admissions. CACT	ActivPAL	Yes, sitting time	Poor
Berntsen et al (2009, 37) case-control	95 (66 boys) asthma 79 (41 boys) healthy control	13.6 (12.8-14.3) 13.6 (12.6-14.3)	ISAAC	SenseWear Pro2 Armband	No	Good
Fedele et al (2014; 454 cross-sectional	175 (75 males) obese 73 (37 males) obese + asthma	9.8 ± 1.4 10.1 ± 1.5	Asthma = self-reported health personnel diagnosis	SenseWear Armband	No	Fair
Heinzmann-Filho et al (2016; 45) cross-sectional	133 asthma (63 males) 181 controls (91 males) (30 + 30 with device-based PA)	11.0 ± 2.2 11.4 ± 2.5	ISAAC	ActiGraph wGT3X	Yes	Poor
Jago et al (2019; 19) cross-sectional	6473 cases with accelerometer data at one timepoint and 1619 (25%) at all three timepoints. 12 y; 5735 (24% asthma) 14 y; 4078 (23% asthma) 16 y; 2198 (27% asthma)	12, 14 and 16	Self-reported doctor´s diagnosis of asthma (ever) at ages 8, 11 and 14 y	ActiGraph AM7164	Yes	Fair
Pike et al (2019; 20) cross-sectional	6497 participants (979 asthma ever and 512 current asthma) 3176 (51%) females (409 (13%) asthma ever, 208 (7%) current asthma 3321 (49%) males (570 (19%) asthma ever, 304 (10%) current asthma	7	ISAAC	ActiGraph GT1 M	Yes	Good
Reimberg et al (2018; 39) case-control	43 with asthma 24 controls	6-18 (asthma 10 ± 3 and control 11 ± 3)	GINA step median 3 (25%-75%; 2-4)/C-ACT 20 (25%-75%; 17-22), all sedentary defined as <11 500 steps/d	ActiGraph, GT3X	No	Poor
Smith et al (2016; 46) cross-sectional	1137 (538 males) 590 lung healthy (238 males) 94 asthma (53 males)	Boys Healthy – 15.6 ± 0.5 Asthma – 15.6 ± 0.5 Girls Healthy – 15.6 ± 0.5 Asthma 15.7 ± 0.6	Diagnosis, wheezing and medication for asthma	ActiGraph GT3X	No	Fair

(Continues)

TABLE 2 (Continued)

Author, year, study design	Sample Size	Sample age (years)	Asthma diagnosis	Device to record PA	Sedentary time reported	Overall study quality
Sousa et al (2014; 47) cross-sectional	79 asthma 42 controls	9.8 ± 1.59.7 ± 1.7	GINA, mild-to-severe persistent	Power Walker-610	No	Poor
Tsai et al (2012; 38) case-control	27 asthma (19 males) 27 controls (16 males)	9.9 ± 0.99.9 ± 0.7	Wheezing or whistling last 12 months, parents reports of asthma diagnosis	ActiWatch 64	Yes	Fair
Vahlkvist & Pedersen (2009; 24) case-control	57 asthma (32 males) 155 controls (84 males)	9.6 (9.1,10.1) 9.7 (9.4,10.0) mean & 95% CI	Respiratory symptoms, airway reversibility, EIB	RT3 accelerometer	No	Poor
van Gent et al (2007; 40) case-control	130 undiagnosed asthma (73 males) 81 diagnosed asthma (47 males) 202 controls (100 males)	9.4 ± 0.79.4 ± 0.8 9.4 ± 0.7	Respiratory symptoms, medications, airway reversibility, BHR, parents reports of physician diagnosed asthma	PAM accelerometer	No	Poor
Vangeepuram et al (2013; 48) cross-sectional	262 girls with asthma symptoms out of 1182	7.3 ± 0.7 in the total sample	Questionnaire with respect to asthma-related symptoms + parents reports of asthma diagnosis	Yamax SW-200 digi-Walker	No	Fair
Walders-Abramson et al (2009; 41) case-control/intervention	59 asthma (50.8% males) 59 controls (50.8% males)	13.3 ± 1.8 13.2 ± 1.8	Physician diagnosis, prescriptions for asthma medications	Omron Pedometer model HJ-112	No	Poor
Willeboordse et al (2016; 42) case-control	29 asthma (69% males) 33 controls (36% males) 30 overweight (40% males) 30 asthma & overweight (63% males)	10.1 ± 2.5 10.3 ± 2.1 11.2 ± 1.9 11.9 ± 2.1	Physician diagnosis, current asthma symptoms, use of asthma medication, reversibility of airway obstruction	Yamax EX510 Power walker	No	Good
Yiallouros et al (2015; 43) case-control	68 active asthma, 36 inactive asthma (67 males) 99 controls (59 males)	8.5 ± 0.4 in the total sample	Physician diagnosis of asthma, wheeze	ActiGraph, model not reported	Yes, but sleep not excluded	Good

Mean ± SD or Mean (Range). Abbreviations: PA, physical activity; CACT, Childhood Asthma Control Test; ISAAC, The International Study of Asthma and Allergies in Childhood; EIB, exercise-induced bronchioconstriction; BHR, bronchial hyper-responsiveness.

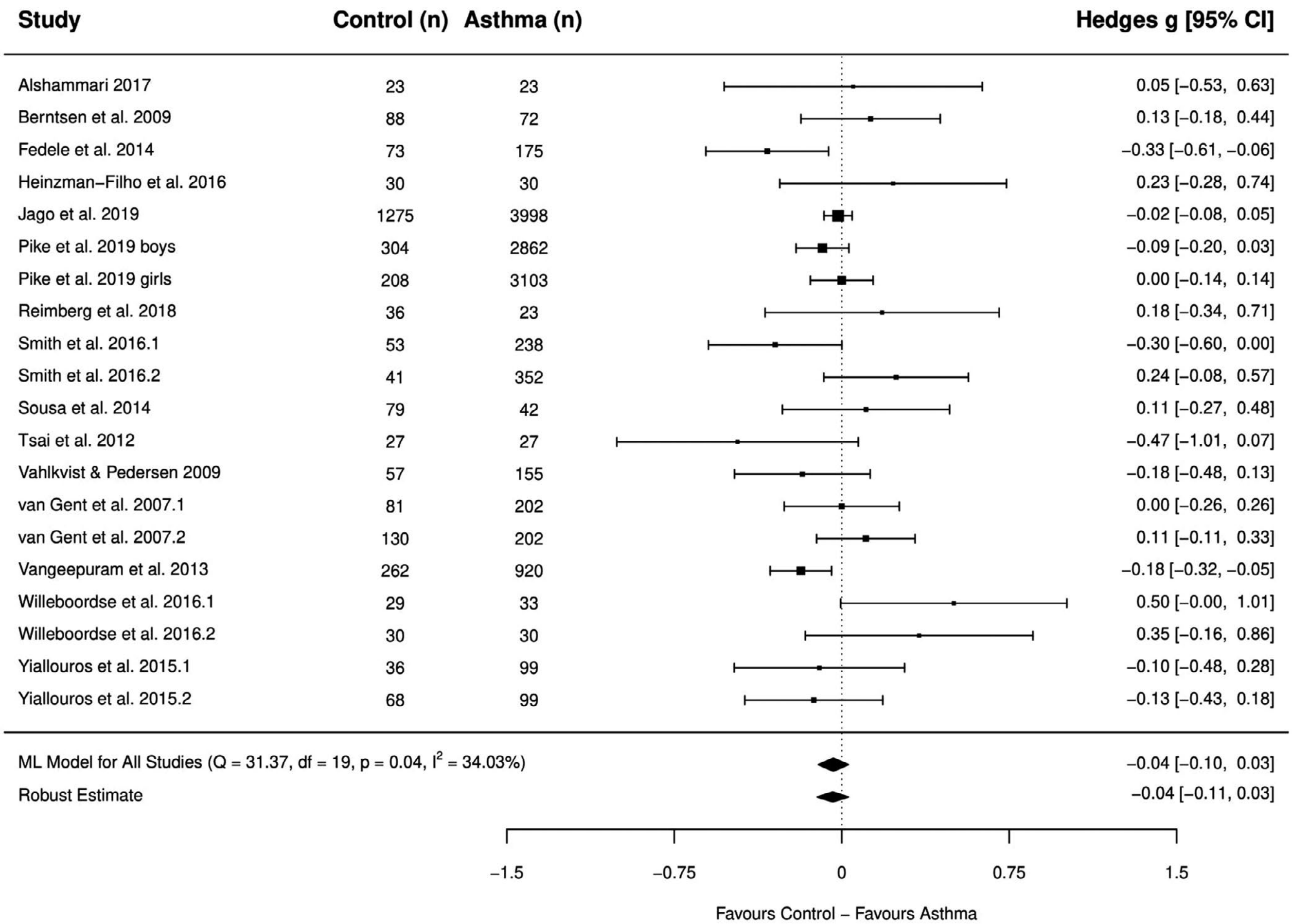

FIGURE 2 Forest plot of studies reporting physical activity levels in children and adolescents with and without asthma. Numbers in groups may diverge from numbers given in papers for author-shared data. ML, Multilevel

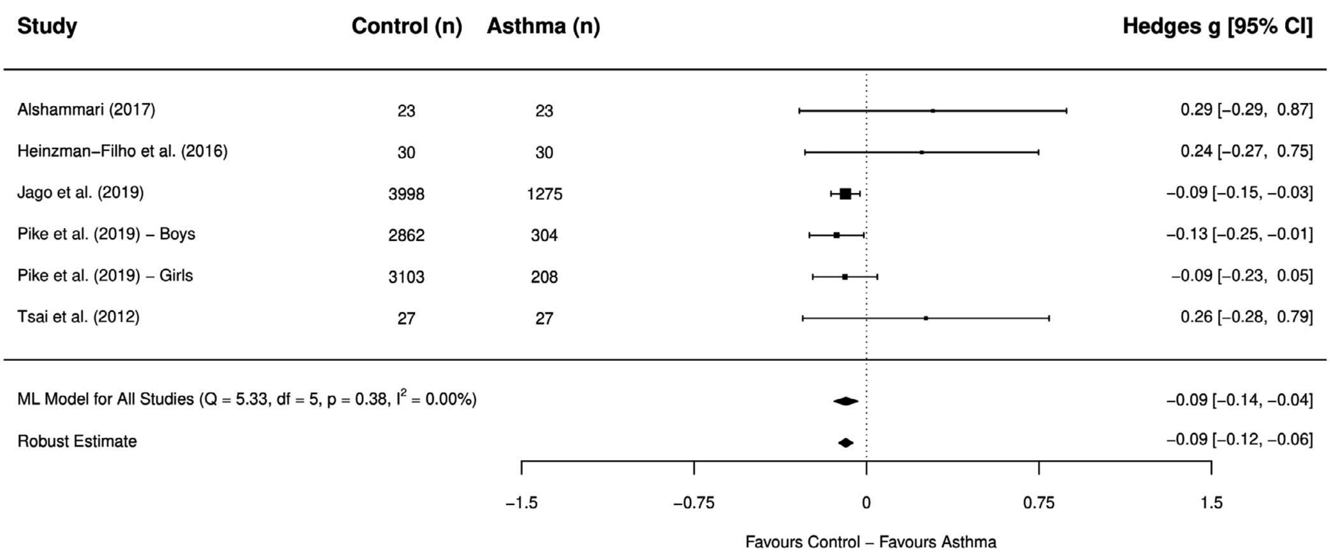

FIGURE 3 Forest plot of studies reporting sedentary time in children and adolescents with and without asthma. ML, Multilevel

positive effect. Cochrane's Q showed a significant heterogeneity ($Q = 31.38$, $df = 19$, $P = .04$) and I^2 showed moderate inconsistency ($I^2 = 34.03\%$) for physical activity level analyses.

For sedentary time, Cochrane's Q did not suggest evidence of significant heterogeneity (Q = 5.33, $df = 5$, $P = .38$) and I^2 showed negligible inconsistency ($I^2 < 0.001\%$). Sensitivity analysis did not reveal any influential effect sizes, irrespective of outcome.

3.4 | Moderating factors

The robust mixed-effect meta-regression models showed that the effect of asthma on physical activity levels was not associated with age (0.02 [95% CI = −0.01, 0.04]) or with the proportion of males (−0.0005 [95% CI = −0.004, 0.003]). The effect of the method of diagnosis was trivial for both objective (0.08 [95% CI = −0.04, 0.20]) and subjective (−0.05 [95% CI = −0.10, −0.01]), though was significantly different between the two models (z = 1.975, P = .048). The effect of study quality was trivial for both fair/good (−0.05 [95% CI = −0.09, 0.004]) and poor (0.05 [95% CI = −0.08, 0.17]) and was not significantly different between the two models (z = −1.365, P = .17). For sedentary time, the robust mixed-effect meta-regression models showed that the effect of asthma was not associated with age (0.01 [95% CI = −0.13, 0.15]) or with the proportion of males (−0.0003 [95% CI = −0.001, 0.0006]). The effect of study quality was trivial for fair/good (−0.10 [95% CI = −0.15, −0.04]) and small for poor (0.26 [95% CI = −0.12, 0.64]), and was not significantly different between the two models (z = −1.81, P = .07).

3.5 | Assessment of small study bias

Eggers linear regression test for bias effects was non-significant for physical activity (z = 1.2353, P = .2167) and sedentary time (z = 1.9406, P = .052). There was no obvious indication of bias upon inspection of the funnel plot for physical activity (Figure 4A), but the small number of studies reporting sedentary time meant the funnel plot was difficult to interpret (Figure 4B). Imputation of missing studies in the funnel plot using trim and fill would slightly accentuate the effect (−0.10 [95% CI = −0.15, −0.05]), suggesting more sedentary time in healthy controls than in children with asthma, though it was still trivial in magnitude.

4 | DISCUSSION

This study sought to synthesize the current evidence regarding whether children and adolescents' physical activity levels and sedentary time differ according to asthma status, as well as evaluating the moderating influence of age and sex. Overall, 16 studies were included which reported device-measured physical activity levels in children and adolescents with and without asthma. Children and adolescents, irrespective of asthma status, engage in similar levels of physical (in)activity. This finding was not moderated by age, sex, or study quality, but rather whether asthma was objectively confirmed or self-reported within studies. Of interest, youth with asthma spend less time sedentary than their healthy counterparts, though the effect was trivial.

The meta-analysis of 15 primary studies including 15 645 children and adolescents found that there was no significant difference between physical activity levels in those with and without asthma. Moreover, Walders-Abramson et al,[41] which was not included due to lack of sufficient information (ie, no mean, SD, or t test values reported), further supported this conclusion. Although the lack of association between physical activity and asthma is discordant with suggestions by some that children with asthma are less active than their healthy peers,[17,18] these results are congruent with the meta-analysis conducted by Cassim et al,[16] which included 3375 children across nine studies. The discrepancy with an earlier systematic review[17] is likely due to the device-based assessment inclusion criteria of physical activity employed in the present review. Indeed, the inclusion of Jago et al[19] and Pike et al[20] substantially increased the sample size of the current meta-analyses and may explain, at least in part, such findings. However, Eggers linear regression test for bias effects was not significant, nor was this obvious from inspection of the funnel plots.

Although our results suggest there is no difference in physical activity levels for youth with asthma relative to their apparently healthy counterparts, physical activity levels remain low in most studies, with few achieving the physical activity guidelines. Indeed, low physical activity levels and fitness have been suggested as risk factors for asthma onset, with exercise shown to improve markers of asthma control.[49] Our results do not, however, allow us to draw conclusions regarding the need for condition-specific behavior change programs as, while the baseline levels may be similar, the basis for, and thus the most effective method to promote increases in these levels, may differ according to condition and, indeed, asthma severity. Nonetheless, it is important to note the findings of a recent high-intensity interval training intervention in adolescents with and without asthma which reported similar changes in exercise capacity, irrespective of asthma status,[50,51] although the translation of such changes in exercise capacity to physical activity levels remains to be elucidated.

It is pertinent to note that while the physical activity levels do not differ by condition, the pattern in which different intensities of physical activity are accumulated (bout frequency, duration and intensity distribution) may vary. Indeed, given reports that intermittent activity may be associated with a reduced risk of exacerbation for those with asthma,[52] it could be speculated that different activity patterns will be evident and, further, that the association between these activity patterns and pertinent health outcomes may be stronger than previously reported in healthy children. Further conclusions are largely limited by the lack of consistency in accelerometery

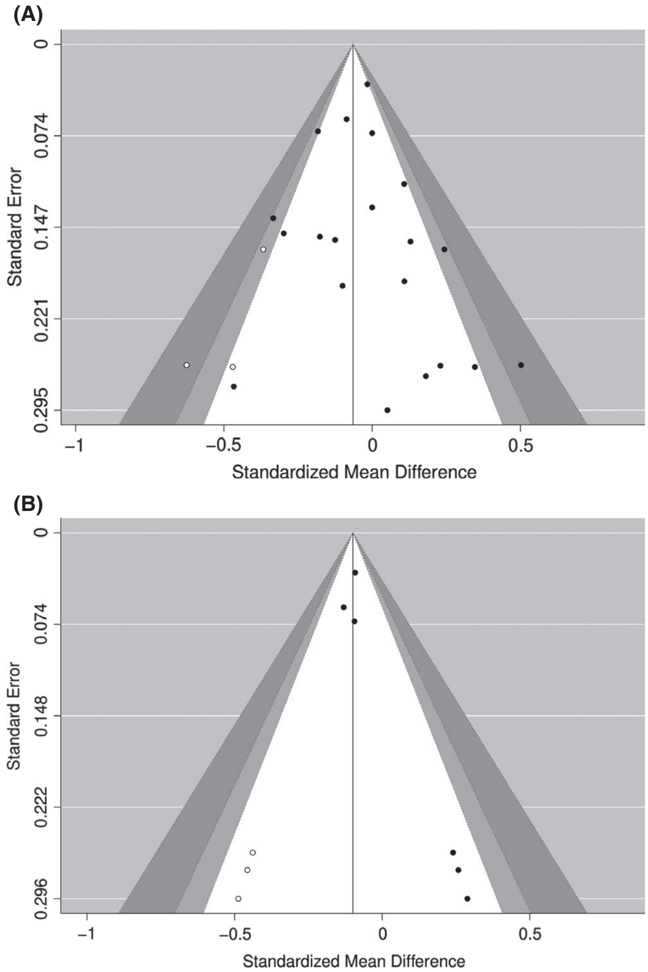

FIGURE 4 Contour enhanced funnel plot with Duval and Tweedie's trim and fill (white dots) for (A) physical activity levels and (B) sedentary time

processing across studies, with many studies failing to report key details. Future studies should consider the pattern of accumulation and composition of physical activity and sedentary time in youth with asthma and the use of raw acceleration metrics that do not rely on largely arbitrary processing decisions.

While it was not possible to ascertain the influence of season within the present meta-analysis due to the majority of studies not reporting the season in which the measures were taken, this is a key consideration for future studies. Indeed, while it is likely that the physical activity data were collected simultaneously, and thus within the same season, in healthy children and those with asthma within each study, the potentially significant effect of season on physical activity levels in those with asthma largely precludes comparisons between studies conducted in different seasons.[53] Specifically, season is suggested to have a significant effect on asthma control due to numerous factors including temperature, humidity and pollen, and pollution levels,[54] which are likely to impact physical activity levels, although this largely remains to be investigated.

Of interest, asthma diagnosis criteria appeared to influence the difference in physical activity levels in children with asthma compared to their healthy counterparts. Specifically, there was a positive effect direction (ie, higher physical activity levels) in those whose asthma was objectively reported (clinical populations), with the opposite effect direction for those with self-reported asthma (population-based studies), in comparison to their healthy peers. It is worth noting, however, that both effect sizes were trivial. Nonetheless, it could be postulated that such findings are due the type of diagnosis, rather than the severity of asthma per se, which can have an impact on how individual's lead their lives. Indeed, those whose asthma is objectively reported are more likely to have the associated clinical support and guidance on the benefits on physical activity. However, most studies utilize population-based cohorts, rather than clinical, whereby asthma is largely self-reported and are therefore likely to encompass more mild-to-moderate asthma and/or hide differential diagnosis such as exercise laryngeal obstruction.[55] Future research investigating such hypotheses is therefore required.

To date, research comparing physical activity levels in children with severe or poorly controlled asthma, in comparison to those classified as mild-to-moderate or well-controlled, remains equivocal. For example, research has found lower physical activity levels in children with more severe asthma,[56] poorer control[57] or those recently hospitalized,[20] whereas Matsunaga et al[58] and Sousa et al[47] found no differences. This lack of consensus may be attributable to discrepancies in the quality and reliability of asthma diagnosis between studies and the confounding effect of greater support and facilitation of those with more severe asthma to be physically active serving to mask the impact of disease severity itself.

A recent meta-analysis has shown that substituting sedentary time for MVPA is important for waist circumference, systolic blood pressure, and clustered cardiometabolic risk in healthy children.[7] Despite the known overall health risk associated with sedentary time,[59] only six studies included in the present review reported sedentary time, with one not separating sleep from sedentary awake/daytime minutes.[43] In Cordova-Rivera and colleagues[23] meta-analysis in adults with asthma, measures of sedentary time were scarce, but indicated a similar time spent sedentary between those with and without asthma. Moreover, higher sedentary time was associated with higher healthcare use and poorer lung function, asthma control, and exercise capacity.[23] In contrast, in both children[20] and adolescents,[19] asthma has been suggested to be associated with less time spent sedentary, in accord with the findings of the current meta-analysis. Nonetheless, it is pertinent to note that such differences were small relative to the overall time spent sedentary and, while statistically different, the clinical significance remains unknown.[20] In accord with Pike et al,[20] the lack of differences in physical activity, coupled with less time sedentary in those with asthma, found in the current meta-analysis, may support the hypothesis that light physical activity is encouraged over sedentary time for children in response to the asthma management guidelines.[60] This could be due to such messages not translating to higher intensities, fear of exacerbation,[15] or a reflection of the lack of population-specific cut-points. However, it could also be a result of increased sleep time in children and adolescents with asthma compared to healthy controls. Future research should consider 24-hour movement guidelines[61] and ensure the measurement and analyses of sleep and light physical activity. Furthermore, the scant literature resulted in data being pulled across all studies, and consequently the youth age range, thereby precluding the analysis of the concomitant, but likely distinct, influence of maturation, which plays an instrumental role in time spent being physically active and sedentary.[62]

While age and sex differences are well established in children's physical activity levels and patterns,[21,22] little is known about the presence of such differences in those with asthma, with the majority of studies relying on pooled samples. However, it is pertinent to note that when age and the proportion of boys were accounted for in the moderation analyses, there appeared to be no effect. Although such analyses do not directly provide age and sex comparisons, our results suggest that the statistically similar physical activity levels, irrespective of disease status, cannot be attributed to age or the larger proportion of boys included in the studies, the latter of which, based on previous literature in healthy populations, would likely increase the samples overall total physical activity. These results are discordant with the adult literature, whereby a recent systematic review concluded that physical activity levels were lower in females with asthma compared to their male counterparts.[23] Indeed, in adolescents, Jago et al[19] found a small association between those with asthma and fewer minutes of sedentary time in girls, whereas Pike et al[20] reported no sex differences in sedentary time or physical activity. Nonetheless, robust comparisons to youth literature are not possible due to insufficient data to conduct a meta-regression for age or sex in the most recent systematic review.[16]

The comprehensive search strategy and exclusion criteria employed are a major strength of this systematic review. Moreover, the meta-analysis and -regression extend the review of Cassim and colleagues,[16] while maintaining the incorporation of only studies which used device-measured physical activity. However, no studies clearly reported their methods and analyses of device-measured physical activity levels, and within those who did, there was a broad range of devices utilized, along with varying processing techniques, which make inter-study comparisons and pooling of data more questionable and preclude firm conclusions being drawn. Nonetheless, it is important to acknowledge that study quality did not significantly influence the models. Further, the lack of data reporting within the included studies meant the meta-analysis to summarize sedentary time was more limited, and it was not possible to account for weight status within the meta-regression. Although there were large differences in sample size, age range, the percentage of each sex included, how asthma was diagnosed, and the quality of studies, a key strength, and indeed novelty, is that our analyses controlled for all of these aspects. Future research should seek to ascertain the effect of weight status and asthma severity, control, and differential respiratory diagnosis, on youth physical activity levels.

5 | CONCLUSIONS

Overall, this review, including 16 studies, refutes ongoing concerns that children and adolescents with controlled asthma are less physically active than healthy peers. Nonetheless, children and adolescents largely remain insufficiently active and interventions to enhance physical activity across the intensity and health spectrum are still urgently required. It is, however, noteworthy that the quality of the studies incorporated tempers these conclusions. Future research should therefore incorporate, and report, more rigorous device-based physical activity assessment, with a particular focus on sedentary time, as well considering the influence of the identification, reporting, and severity of asthma.

6 | PERSPECTIVES

The current review suggests that those with asthma do not demonstrate different physical activity levels to their peers but, interestingly, do spend less time sedentary. While the depth and quality of the data on which these conclusions are drawn must be considered, especially with regard to sedentary time, these findings highlight the need for future studies to consider the pattern of physical activity and sedentary time accrual according to asthma status. Indeed, given recent research suggesting that the intensity distribution of physical activity may be more important for health in youth than the volume of physical activity, further studies are urgently required which provide a more detailed insight in physical activity and sedentary time in those with asthma. Furthermore, the current review highlights that there is a paucity of data that has considered the potentially divergent relationship between physical activity and asthma depending on the severity, or phenotype, of asthma. As we become increasingly aware of the different etiologies of asthma according to phenotype, if we are to develop appropriate, palatable, and sustainable interventions for those with asthma, further research is required that explores the impact of such factors on physical activity and sedentary time.

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CONFLICT OF INTEREST

The authors of this review have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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SUPPORTING INFORMATION

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

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