Review Article

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

Kelly A. Mackintosh1 | Melitta A. McNarry1 | Sveinung Berntsen2 | James Steele3,4 | Ellen Sejersted5 | Thomas Westergren2

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
accelerometry, chronic disease, pediatric, respiratory health, youth

1 INTRODUCTION

Asthma, an obstructive airway disease characterized by dyspnea, 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. In addition to the extensive benefits of leading an active lifestyle without sustained periods of sedentary behaviors in healthy populations, 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, as well as improved quality of life and lung function. However, paradoxically, symptoms may be triggered by physical exertion, particularly vigorous intensity, which, coupled with the fear of exercise-induced bronchoconstriction (EIB), may impact on the physical activity levels in those with asthma.

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

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. 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, 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. 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, others, particularly population-based cohorts (eg, the International Study of Asthma and Allergies in Childhood studies) have utilized self-reported asthma status, which is suggested to be associated with both under- and over-reporting of asthma. 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.

## METHODS

This review was performed in accordance with the Preferred Reporting items for Systematic Review and Meta-Analysis statement 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) browser and the Permutated 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 Plus 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 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. 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. 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.

| 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 |

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...
each study and outcome measure. The magnitude of Hedges' $g$ was interpreted with reference to Cohen's 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, 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. 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.

### 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 were evaluated as case-control studies (Supplementary Table 1, File 8), and seven as observational cross-sectional studies (Supplementary Table 2, File 9). Five case control studies were graded as “poor,” one case-control study was regarded as “fair,” whereas three studies were evaluated as “good.” Among cross-sectional studies, two studies were considered of “poor” quality, whereas four studies were considered “fair” and one 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 was the only intervention study that was included, in which they sought to increase children's physical activity levels. Nonetheless, Walders-Abramson and colleagues 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 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 and Smith et al presented results separately for boys and girls, and Willeboordse et al 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 to 1275 asthma and 3998 controls. 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, asthma was confirmed by objective criteria and/or a physician, while in eight studies, asthma was self-reported by participating children/parents.

In three studies, 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, the majority of participants did not achieve these recommendations or their equivalents (eg, 10 000 steps per day), whereas boys, but not girls, met
the recommended MVPA in Pike et al.\textsuperscript{20} Willeboordse et al.\textsuperscript{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.\textsuperscript{36} Due to a lack of sufficient reporting, we could not assess whether participants in the study by Fedele et al.\textsuperscript{44} met physical activity recommendations. Additionally, Jago et al.\textsuperscript{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...
| 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; 45) 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)
| 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)      | 79 asthma 42 controls | 9.8 ± 1.5 | GINA, mild-to-severe persistent | Power Walker-610 | No | Poor |
| Tsai et al (2012; 38)       | 27 asthma (19 males) 27 controls (16 males) | 9.9 ± 0.999 ± 0.7 | Wheezing or whistling last 12 months, parents reports of asthma diagnosis | ActiWatch 64 | Yes | Fair |
| Vahlkvist & Pedersen (2009; 24) | 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)   | 130 undiagnosed asthma (73 males) 81 diagnosed asthma (47 males) 202 controls (100 males) | 9.4 ± 0.794 ± 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) | 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) | 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) | 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) | 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 bronchoconstriction; BHR, bronchial hyper-responsiveness.
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

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
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 review17 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 accelerometry.
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. Specifically, season is suggested to have a significant effect on asthma control due to numerous factors including temperature, humidity and pollen, and pollution levels, 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. 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, poorer control or those recently hospitalized, whereas Matsunaga et al and Sousa et al 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. Despite the known overall health risk associated with sedentary time, only six studies included in the present review reported sedentary time, with one not separating sleep from sedentary awake/daytime minutes. In Cordova-Rivera and colleagues 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. In contrast, in both children and adolescents, 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. In accord with Pike et al, 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.\textsuperscript{60} This could be due to such messages not translating to higher intensities, fear of exacerbation,\textsuperscript{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\textsuperscript{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.\textsuperscript{62}

While age and sex differences are well established in children's physical activity levels and patterns,\textsuperscript{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.\textsuperscript{23} Indeed, in adolescents, Jago et al\textsuperscript{19} found a small association between those with asthma and fewer minutes of sedentary time in girls, whereas Pike et al\textsuperscript{20} reported no sex differences in sedentary time or physical activity. Nonetheless, robust comparisons to youth literature are not reported no sex differences in sedentary time or physical activity. These results are discordant with the adult literature, 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.\textsuperscript{62}

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,\textsuperscript{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.

ACKNOWLEDGEMENTS

We would like to thank Andrey Wirgues, Márcio Donadio, Signe Vahlkvist, Katharine Pike, Mariana Reimberg, and Russ Jago for providing us with supplementary information and data for the current meta-analysis and -regression.
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.

ORCID
Kelly A. Mackintosh https://orcid.org/0000-0003-0355-6357
Melitta A. McNarry https://orcid.org/0000-0003-0813-7477
Sveinung Berntsen https://orcid.org/0000-0002-8250-4768
James Steele https://orcid.org/0000-0002-8003-0757
Ellen Sejersted https://orcid.org/0000-0003-1538-6121
Thomas Westergren https://orcid.org/0000-0003-4253-1996

REFERENCES
1. Global Strategy for Asthma Management and Prevention, 2020. www.ginasthma.org. 2020. https://ginasthma.org/wp-content/uploads/2020/04/GINA-2020-full-report-_final-_wms.pdf. [Accessed 28 Jun 2020].
2. Wanrooij VHM, Willeboordse M, Dompeling E, van de Kant KDG. Exercise training in children with asthma: a systematic review. Br J Sports Med. 2014;48(13):1024-1031.
3. Asthma UK. Asthma facts and statistics | Asthma UK. 2017.
4. Global Asthma Network. The Global Asthma Report. 2018. http://www.globalasthmareport.org/Global%20Asthma%20Report%202018.pdf.
5. Panagiotou M, Koulouris NG, Rovina N. Physical activity: a missing link in asthma care. J Clin Med. 2020;9(3):706.
6. Janssen I, Leblanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. Int J Behav Nutr Phys Act. 2010;7:40.
7. Wijndaele K, White T, Andersen LB, et al. Substituting prolonged sedentary time and cardiovascular risk in children and youth: a meta-analysis within the International Children's Accelerometry database (ICAD). Int J Behav Nutr Phys Act. 2019;16(1):96.
8. Walker TJ, Reznik M. In-school asthma management and physical activity: children's perspectives. J Asthma. 2014;51(8):808-813.
9. Andrade LBD, Emm-Collison L, Sebire SJ, Thompson JL, Lawlor DA. Association of BMI category with change in children’s physical activity between ages 6 and 11 years: a longitudinal study. Int J Obes (Lond). 2020;44(1):104-113.
10. Jago R, Salway RE, Ness AR, Shield JPH, Ridd MJ, Henderson AJ. Associations between physical activity and asthma, eczema and obesity in children aged 12–16: an observational cohort study. BMJ Open. 2019;9(1):e024858.
11. Pike KC, Griffiths LJ, Dezauteux C, Pearce A. Physical activity among children with asthma: cross-sectional analysis in the UK millennium cohort. Pediatr Pulmonol. 2019;54(7):962-969.
12. Cathcart KA, Evans AC, Wild DJ, et al. Exercise and the immune system in children with asthma: a systematic review. Allergy. 2015;70(9):1071-1081.
13. Mancuso CA, Choi TN, Westermann H, Wenderoth S, Wells MT, Charlson ME. Improvement in asthma quality of life in patients enrolled in a prospective study to increase lifestyle physical activity. J Asthma. 2013;50(1):103-107.
14. Tziczienecka-Green A, Bargiel-Matusiewicz K, Wilczynska-Kwiatek A. Quality of life and activity of children suffering from bronchial asthma. Eur J Med Res. 2009;14(Suppl 4):147-150.
15. Avallone KM, McLeish AC. Asthma and aerobic exercise: a review of the empirical literature. J Asthma. 2013;50(2):109-116.
16. Sidiropoulou MP, Fotiadou EG, Tsimaras VK, Zakas AP, Angelopoulou NA. The effect of interval training in children with exercise-induced asthma competing in soccer. J Strength Cond Res. 2007;21(2):446-450.
17. Winn CON, Mackintosh KA, Eddolls WTB, et al. Perceptions of asthma and exercise in adolescents with and without asthma. J Asthma. 2018;55(8):868-876.
18. Cassim R, Koplin JJ, Dharmage SC, et al. The difference in amount of physical activity performed by children with and without asthma: a systematic review and meta-analysis. J Asthma. 2016;53(9):882-892.
19. Williams B, Powell A, Hoskins G, Neville R. Exploring and explaining low participation in physical activity among children and young people with asthma: a review. BMC Fam Pract. 2008;9:40.
20. Welsh L, Roberts RG, Kemp JG. Fitness and physical activity in children with asthma. Sports Med. 2004;34(13):861-870.
21. Jago R, Salway R, Emm-Collison L, Sebire SJ, Thompson JL, Lawlor DA. Association of BMI category with change in children’s physical activity between ages 6 and 11 years: a longitudinal study. Int J Obes (Lond). 2020;44(1):104-113.
22. Cordova-Rivera L, Gibson PG, Gardner PA, McDonald VM. A Systematic review of associations of physical activity and sedentary time with asthma outcomes. J Allergy Clin Immunol Pract. 2018;6(6):1968-81 e2.
23. Vahlkivist S, Pedersen S. Fitness, daily activity and body composition in children with newly diagnosed, untreated asthma. Allergy. 2009;64(11):1649-1655.
24. Hansen TE, Evjenth B, Holt J. Increasing prevalence of asthma, allergic rhinoconjunctivitis and eczema among schoolchildren: three surveys during the period 1985–2008. Acta Paediatr. 2013;102(1):47-52.
25. Lai CK, Beasley R, Crane J, et al. Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax. 2009;64(6):476-483.
26. Aaron SD, Boulet LP, Reddel HK, Gershaw AS. Underdiagnosis and overdiagnosis of asthma. Am J Respir Crit Care Med. 2018;198(8):1012-1020.
27. Moher D, Shamseer L, Cook DJ, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4:1.
28. Medical Subject Headings 2020. National Institutes of Health. 2020. https://meshb.nlm.nih.gov/search. [Accessed 01 Feb 2020].
29. Medical Subject Headings 2020. National Institutes of Health. 2020. https://meshb.nlm.nih.gov/search. [Accessed 01 Feb 2020].
30. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Syst Rev. 2020;9(1):6.
31. Study Quality Assessment Tools. National Institutes of Health. 2020. [Accessed 01 Mar 2020] https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools.
32. Morris SB. Estimating effect sizes from pretest-posttest-control group designs. Organizational Res Methods. 2008;11(2):364-386.
33. Cohen J. Statistical Power Analysis for the Behavioural Sciences. Hillsdale, NJ: Erlbaum; 1988.
34. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-560.
35. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. London, UK: The Cochrane Collaboration; 2011.
36. Alshammari BSN. The Movement Continuum in Children with Asthma Attacks in Kuwait. University of Glasgow; 2017.
37. Berntsen S, Carlsen KC, Anderssen SA, et al. Norwegian adolescents with asthma are physical active and fit. Allergy. 2009;64(3):421-426.
38. Tsai SY, Ward T, Lentz MJ, Kieckhefer GM. Daytime physical activity levels in school-age children with and without asthma. Nurs Res. 2012;61(4):252-259.
39. Reimberg MM, Pachi JRS, Scalco RS, et al. Patients with asthma have reduced functional capacity and sedentary behavior. J Pediatr (Rio J). 2020;96(1):53-59.
40. van Gent R, van der Ent CK, van Essen-Zandvliet LE, et al. No difference in physical activity in (undiagnosed asthma and healthy controls. Pediatr Pulmonol. 2007;42(11):1018-1023.
41. Walders-Abramson N, Wamboldt FS, Curran-Everett D, Zhang L. Encouraging physical activity in pediatric asthma: a case-control study of the wonders of walking (WOW) program. Pediatr Pulmonol. 2009;44(9):909-916.
42. Willeboordse M, van der Kant KD, van der Velden CA, van Schayck CP, Dompeling E. Associations between asthma, overweight and physical activity in children: a cross-sectional study. BMC Public Health. 2016;16:919.
43. Viallouros PK, Economou M, Kolokotroni O, et al. Gender differences in objectively assessed physical activity in asthmatic and non-asthmatic children. Pediatr Pulmonol. 2015;50(4):317-326.
44. Fedele DA, Janicke DM, Lim CS, Abu-Hasan M. An examination of comorbid asthma and obesity: assessing differences in physical activity, sleep duration, health-related quality of life and parental distress. J Asthma. 2014;51(3):275-281.
45. Heinzmann-Filho JP, Vendrusculo FM, Woszezenki CT, et al. Inspiratory muscle function in asthmatic and healthy subjects: influence of age, nutrition and physical activity. J Asthma. 2016;63(9):893-899.
46. Smith MP, Berdel D, Bauer CP, et al. Asthma and rhinitis are associated with less objectively-measured moderate and vigorous physical activity, but similar sport participation, in adolescent German boys: GINIplus and LISAplus cohorts. PLoS One. 2016;11(8):e0161461.
47. Sousa AW, Cabral AL, Martins MA, Carvalho CR. Daily physical activity in asthmatic children with distinct severities. J Asthma. 2014;51(5):493-497.
48. Vangeepuram N, McGovern KJ, Teitelbaum S, et al. Asthma and physical activity in multicultural girls from three US sites. J Asthma. 2014;51(2):193-199.
49. Lucas SR, Platts-Mills TA. Physical activity and exercise in asthma: relevance to etiology and treatment. J Allergy Clin Immunol. 2005;115(5):928-934.
50. Winn CON, Mackintosh KA, Eddolls WTB, et al. Asthma, body mass and aerobic fitness, the relationship in adolescents: The exercise for asthma with commando Joe’s(R) (X4ACJ) trial. J Sports Sci. 2020;38(3):288-295.
51. McNarry MA, Winn CON, Davies GA, Eddolls WTB, Mackintosh KA. Effect of High-Intensity Training and Asthma on the V'O2 Kinetics of Adolescents. Med Sci Sports Exerc. 2020;52(6):1322-1329.
52. Beauchamp MK, Nonoyama M, Goldstein RS, et al. Interval versus continuous training in individuals with chronic obstructive pulmonary disease- a systematic review. Thorax. 2010;65(2):157-164.
53. Atkin AJ, Sharp SJ, Harrison F, Brage S, Van Sluijs EM. Seasonal variation in children's physical activity and sedentary time. Med Sci Sports Exerc. 2016;48(3):449-456.
54. Samoli E, Nastos PT, Palatsos AG, Katsouyanni K, Pritfis KN. Acute effects of air pollution on pediatric asthma exacerbation: evidence of association and effect modification. Environ Res. 2011;111(3):418-424.
55. Johansson H, Norlander K, Berglund L, et al. Prevalence of exercise-induced bronchoconstriction and exercise-induced laryngeal obstruction in a general adolescent population. Thorax. 2015;70(1):57-63.
56. Lam KM, Yang YH, Wang LC, Chen SY, Gau BS, Chiang BL. Physical activity in school-aged children with asthma in an Urban City of Taiwan. Pediatr Neonatol. 2016;57(4):333-337.
57. Holderness H, Chin N, Ossip DJ, Fagnano M, Reznik M, Haltermann JS. Physical activity, restrictions in activity, and body mass index among urban children with persistent asthma. Ann Allergy Asthma Immunol. 2017;118(4):433-438.
58. Matsunaga NY, Oliveira MS, Morcillo AM, Ribeiro JD, Ribeiro M, Toro A. Physical activity and asthma control level in children and adolescents. Respirology. 2017;22(8):1643-1648.
59. Kuzik N, Carson V, Andersen LB, et al. Physical activity and sedentary time associations with metabolic health across weight statuses in children and adolescents. Obesity(Silver Spring). 2017;25(10):1762-1769.
60. British Thoracic Society. BTS/SIGN British Guideline on the Management of Asthma. https://birt-thoracic.org.uk/quality-improvement/guidelines/asthma/: BTS/SIGN 2019.
61. Tremblay MS, Carson V, Chaput JP. Introduction to the Canadian 24-hour movement guidelines for children and youth: an integration of physical activity, sedentary behaviour, and sleep. Appl Physiol Nutr Metab. 2016;41(6 Suppl 3):iii-iv.
62. Gabel L, Macdonald HM, Nettlefold L, McKay HA. Physical activity, sedentary time, and bone strength from childhood to early adulthood: a mixed longitudinal HR-pQCT study. J Bone Miner Res. 2017;32(7):1525-1536.

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