Effect of high-intensity interval training in adolescents with asthma: the eXercise for Asthma with Commando Joe's® (X4ACJ) trial

Running head: High-intensity training in asthma

Charles O.N. Winn[a,b], Kelly A. Mackintosh[b], William T.B. Eddolls[b], Gareth Stratton[b], Andrew M. Wilson[c], Melitta A. McNarry[b], Gwyneth A. Davies[a]

[a] Swansea University Medical School, Singleton Campus, Swansea University, Swansea, SA2 8PP, UK

[b] Applied Sports Technology, Exercise and Medicine (A-STEM) Research Centre, College of Engineering, Bay Campus, Swansea University, Swansea, SA1 8EN, UK

[c] Norwich Medical School, University of East Anglia, Norwich, England, UK

Please note: McNarry and Davies both contributed equally to the article

Corresponding Author: Melitta McNarry, m.mcnarry@swansea.ac.uk, +44 (0)1792 513069

<u>ORCHID ID's:</u>

Dr Charles Winn: 0000-0001-8769-2764

Dr Kelly Mackintosh: 0000-0003-0355-6357

Dr William Eddolls: 0000-0002-9590-8817

Prof Gareth Stratton: 0000-0001-5618-0803

Prof Andrew Wilson: 0000-0002-5514-4867

Prof Gwyneth Davies: 0000-0003-1218-1008

Dr Melitta McNarry: 0000-0003-0813-7477

Abstract

Background: Higher cardiorespiratory fitness is associated with reduced asthma severity and increased quality of life in those with asthma. Therefore, the purpose of this study was to evaluate the feasibility and effectiveness of a 6-month high-intensity interval training (HIIT) intervention in adolescents with and without asthma.

Methods: A total of 616 adolescents (334 boys; 13.0±1.1 years; 1.57±0.10m; 52.6±12.9kg), including 155 with asthma (78 boys), were recruited as part of a randomised control trial from 5 schools (4 control, 1 intervention). The 221 intervention participants (116 boys; 47 asthma) completed 6-months school-based HIIT (3x30min, 10-30s bouts at >90% age-predicted maximum heart rate with equal rest). At baseline, mid-intervention, post-intervention and 3-months follow-up, measurements of 20-metre shuttle run, body mass index (BMI), lung function, Pediatric Quality of Life Inventory, Paediatric Asthma Quality of Life Questionnaire and Asthma Control Questionnaire were collected. Additionally, 69 adolescents (36 asthma; 21 boys) also completed an incremental ramp test. For analysis, each group's data (intervention and control) was divided into those with and without asthma.

Results: Participants with asthma did not differ from their peers in any parameter of aerobic fitness, at any time-point, but were characterised by a higher BMI. The intervention was associated with a significant improvement in maximal aerobic fitness but no change in sub-maximal parameters of aerobic fitness, lung function or quality of life, irrespective of asthma status. Those in the intervention group maintained their BMI, whereas BMI significantly increased in the control group throughout the 6-month period.

Conclusions: HIIT represents an effective tool to improve aerobic fitness and maintain BMI in adolescents, irrespective of asthma status. HIIT was feasible and well-tolerated in those with asthma, who evidenced a similar aerobic fitness to their healthy peers and responded equally to a HIIT programme.

Keywords: High-intensity exercise, cardiorespiratory fitness, intervention, intermittent, quality of life, youth, body mass index.

1. Introduction

The prevalence of asthma and obesity have both risen dramatically over the past few decades, making them two of the most common chronic conditions in the UK.[1,2] This concomitant rise has led to suggestions that the two may be causatively linked,[3,4] with overweight and obesity more prevalent in those who suffer from asthma.[5]

Cardiorespiratory fitness has been suggested to be a key influential factor in the relationship between asthma and obesity,[6] although the nature and extent of this influence remains to be elucidated. Indeed, the influence of asthma on cardiorespiratory fitness requires clarification, with little consensus currently available in the literature.[5,7-10] These equivocal findings may be attributable, at least in part, to the exercise testing methodologies used to determine cardiorespiratory fitness. Specifically, some studies reporting a lower aerobic fitness in those with asthma have used indirect estimates obtained from tests such as the 20-metre shuttle run test.[11,12] Recent reports have highlighted the limitations associated with this measure,[13] issues which may be exacerbated in those with asthma given the commonly cited fear of exercise-induced bronchoconstriction,[14] leading to erroneous conclusions with regard to the pathophysiological influence of asthma. It is also pertinent to note the exclusive focus on peak oxygen uptake ($\dot{V}O_2$) within earlier studies concerning the influence of asthma on aerobic fitness. Whilst this is accepted to be a strong prognostic tool in many clinical conditions,[15] it lacks direct applicability to many, every day, functional abilities.

Further to improvements in fitness,[16-18] exercise is suggested to elicit additional health benefits in those with asthma, such as reduced symptoms and severity and an improved quality of life.[19-21] Specifically, a higher aerobic fitness in children is associated with a higher quality of life[22] while a higher BMI is related to a poorer quality of life.[23,24] Therefore, these measures should be targeted in future exercise interventions aimed at improving a population's quality of life. However, whilst adolescents with asthma have highlighted exercise as one of their favourite activities,[14] few adolescents actively engage in exercise on a regular basis.[5] This may be attributable to the use of conventional, moderate-intensity, continuous exercise in previous exercise interventions in children with asthma;[20,25] Winn et al.[14] recently reported that adolescents with asthma prefer varied exercises, such as circuits or team games, with apprehension expressed towards long-distance running. Indeed, such variation would avoid monotony during sessions which is associated with increased dropout rates.[26]

High-intensity interval training (HIIT) has received considerable attention in recent years as it is suggested to be a time-efficient method of exercise that can elicit significant improvements in both cardiorespiratory fitness and body composition in youth.[27,28] Given the potential relationship between asthma, obesity and fitness, and the decreased likelihood of exercise-induced bronchoconstriction due to the intermittent nature,[29] HIIT represents a promising management strategy for those with asthma. However, it is important to acknowledge that some have raised concerns regarding the safety of HIIT, with suggestions that it may be an inappropriate exercise modality for non-athlete populations.[30] In contrast to these concerns, children with asthma have previously been reported to tolerate HIIT similarly to their healthy peers.[16,31] Furthermore, whilst comparable data is not available in youth with asthma, healthy children and adolescents perceive HIIT as being more enjoyable to participate in compared to constant-intensity exercise,[32] with enjoyment a key component in eliciting the effort required for reaching high intensities.[33] Indeed, in adults with asthma, interval exercise is associated with lower ratings of perceived exertion and dyspnoea, likely due to the rest periods.[34] Whether HIIT is similarly well perceived in adolescents with asthma remains to be elucidated, with continued debate regarding whether HIIT is associated with feelings of considerable discomfort that would prevent long-term adherence.[35]

The aim of the present study was therefore to ascertain the feasibility and effectiveness of 6-month, field-based HIIT intervention in adolescents with asthma compared to their healthy peers. Furthermore, a secondary aim of this study was to determine the sustainability of any adaptations elicited by the intervention using a 3-month follow-up. It was hypothesised that HIIT would lead to improvements in cardiorespiratory fitness and quality of life and a reduction in BMI in adolescents, irrespective of asthma, but that these beneficial adaptations would be lost within three months following the intervention cessation.

2. Materials and methods

2.1. Experimental design

The eXercise for Asthma with Commando Joe's® (X4ACJ) was a randomised control trial. Cluster randomisation was used to select one intervention and four control schools in South Wales, matched for free school-meal status. The exercise intervention began at the start of the school year in September and ended in March, with data collection continuing to July. Ethical approval was granted by the institutional research ethics committee (ref: 140515 and PG/2014/29). Parent/guardian and head teacher consent in addition to child assent were obtained prior to participation.

2.2. Participants

In total, 616 adolescents (334 boys; Table 1), of which 155 had asthma (78 boys), agreed to participate in the study. Two-hundred and twenty-one participants (116 boys) were recruited in the intervention school of the study, of which 47 suffered from asthma (24 boys). Asthma severity was assessed using the Global Initiative for Asthma guidelines[36] and classified as mild, moderate or severe according to the medication step required to achieve asthma control. For the purpose of analysis, moderate and severe asthma were grouped to power the statistics. Participants were excluded if they did not have stable asthma (n = 4).

2.3. Intervention

The intervention design was devised based on formative work.[14] The intervention consisted of a 6-month HIIT programme, delivered by a Commando Joe's® personal trainer, involving 3 x 30-minute sessions per week (Monday, Wednesday and Friday). Participants were able to attend sessions before or after school but were asked to only attend one session per day. The sessions consisted of a combination of circuits and games-based activities (Table 2) lasting between 10 – 30 seconds, followed by an equal period of rest (1:1 work-to-rest ratio). Throughout each exercise bout, participants were asked to exercise maximally with exercise activities designed to elicit a heart rate (HR) of >90% of heart rate maximum (HRmax).[37] Maximal HR was predicted according to Tanaka, Monaham and Seals,[38] which has been validated for use in children and adolescents.[39] During each session participants' HR was continuously monitored (Activio AB, Stockholm, SWE) and used to individually encourage those who were not achieving the target heart rates. Attendance and effort were further incentivised by a reward-based system whereby those who regularly engaged were entered in to a prize draw at the mid- and end-intervention point. Those in the control group engaged in their usual day-to-day activities.

2.4. Procedures

Measurements were taken from both intervention and control groups at four time-points (baseline, mid-intervention, post-intervention and at 3-month follow-up), irrespective of condition.

2.4.1. Anthropometrics

Stature and body mass were measured according to the techniques outlined by International Society for the Advancement of Kinanthropometry.[40] Stature, sitting stature and waist circumference were measured to the nearest 0.1 cm (Seca213, Hamburg, Germany) and body mass to the nearest 0.1 kg (Seca876, Hamburg, Germany). Body mass index was subsequently calculated and grouped using age and sex specific child percentiles.[41] Maturity offset was calculated according to Mirwald et al.,[42] lower limb length was calculated as the difference between stature and sitting stature

2.4.2. Lung Function

Forced Expiratory Volume in 1 second (FEV_1), Forced Vital Capacity (FVC), FEV_1/FVC ratio, Peak Expiratory Flow (PEF), and Forced Expiratory Flow between 25-75% of vital capacity (FEF_{25-75}) was measured using a portable dry spirometer (Vitalograph, Buckingham, UK). Participants were asked to sit up straight, breathe in as deeply as possible, place their lips around the mouthpiece tube and, when they were instructed, “blow out” into the mouthpiece as hard and as fast as possible until no further air could be exhaled; this was explained and demonstrated before the test. Each participant was asked to complete three “acceptable” tests, requiring each exhalation to be performed within 5% of each other. The best of three measurements were taken according to American Thoracic Society guidelines[43] and to the standardised protocol[44] and expressed as a percentage of the age-sex-stature predicted value.[45]

2.4.3. Fractional Exhaled Nitric Oxide (FeNO)

Fractional exhaled nitric oxide (FeNO) was measured prior to spirometric testing. The FeNO test was performed in accordance with the American Thoracic Society guidelines.[46] Participants were asked to completely exhale and then inhale to total lung capacity through the device (NIOX MINO, Aerocrine AB, Solna, Sweden), before immediately exhaling for 10 seconds at 50 ± 5 ml·sec^{-1}. Visual and audio cues were provided by the computer software throughout. One test was completed at all time-points except 3-month follow-up. The final three seconds of exhalation were evaluated.

2.4.4. Asthma control

Asthma control was assessed using the Asthma Control Questionnaire ACQ,[47] which consists of 7-items focusing on reliever inhaler use and symptoms over the previous week and their FEV_1 score. Items of the ACQ are scored from 0 to 6, with ACQ scores of $\leq$0.75 or $\geq$1.5 indicating well-controlled and poorly-controlled asthma, respectively. The ACQ has been validated in children between the ages of 6 and 16 years,[47] and was found to be responsive to change in asthma control with a minimal important difference of 0.52±0.45. Internal consistency, measured using Cronbach's alpha coefficients,[48] for the ACQ were deemed acceptable (α = 0.73-0.82).

2.4.5. Asthma-related quality of life

The Paediatric Asthma Quality of Life Questionnaire (PAQLQ) was used to compare the asthma-specific quality of life between those in the intervention and the control groups, as well as assessing the changes over the course of the intervention. Specifically, the participants were asked to recall the previous week in response to 23 questions (scored on a Likert scale from 1 to 7), with a higher score indicative of a better asthma status. The questions are divided into three domains of activity limitations (5 questions), symptoms (10 questions) and emotional function (8 questions), with a mean score for each and a total overall score. The PAQLQ has been validated in children between the ages of 6 and 16 years[49] and was found to be responsive to change in quality of life with a minimal important difference of 0.5. Internal reliability for the PAQLQ was deemed excellent (α = 0.96-0.97).

2.4.6. Quality of life

The Pediatric Quality of Life Inventory (PedsQL) Teenager Report (Version 4.0)[50] was used to compare the perceived quality of life between those participants with and without asthma and to assess any changes throughout the intervention. The participants were asked to recall their previous week and answer questions accordingly. A widely validated measure in adolescents aged 12-18 years,[51-53] the 23-item PedsQL consists of domains on the participants' physical, emotional, social and school functioning quality, with higher scores indicating a better quality of life. Internal reliability for the PedsQL was deemed excellent ($\alpha = 0.89$-0.90).

2.4.7. Cardiorespiratory fitness

20-metre shuttle run

Cardiorespiratory fitness was estimated using the 20-metre progressive shuttle run test, a previously validated field measure in children.[11] The test involved participants walking or running between two lines, 20-metres apart in time with pre-recorded beeps that progressively increased in speed throughout the test. The number of shuttles completed before voluntary exhaustion was recorded.

Peak $\dot{V}O_2$

Sixty-nine adolescents (39 boys) inclusive of 36 with asthma (21 boys) were selected using stratified randomisation to complete incremental ramp tests. The groups were stratified for age, sex and condition to provide a representative sample of the wider population. Participants performed an incremental ramp exercise test to volitional exhaustion on an electromagnetically-braked cycle ergometer (Ergoselect 200, Ergoline GmbH, Lindenstrasse, Germany), with individually-adjusted seat and handlebar height. The ramp protocol consisted of 3 minutes of "unloaded" pedalling (0 W) followed by an increase in work rate of 12 - 24 $W \cdot min^{-1}$ dependant on the age and height of the participant. Participants were asked to maintain a constant cadence (75 ± 5 revolutions per minute) until voluntary exhaustion. Breath-by-breath pulmonary ventilation (VE) and gas exchange ($\dot{V}O_2$ and $\dot{V}CO_2$) were recorded throughout (Jaeger Oxycon Mobile, Jaeger, Hoechberg, Germany).

2.5. Data analysis

Peak $\dot{V}O_2$ was taken as the highest 10-second mean attained prior to the end of the test. The gas exchange threshold (GET) was determined using the V-slope method.[54] The GET was also expressed relative to peak $\dot{V}O_2$ (GET%$\dot{V}O_2$). Analysis of covariance (ANCOVA) was used to determine the allometric relationship between peak $\dot{V}O_2$ and body mass to account for body size using log-transformed data. Common allometric exponents were confirmed for the data and power function ratios (Y/X^b) were computed. Breath-by-breath data were then averaged into 10-second time bins and the Mean Response Time (MRT) and gain ($\Delta\dot{V}O_2/\Delta W$) calculated according to the methods reported by Barstow et al.[55] Specifically, the gain was determined by linear regression over three segments: S_1, from 1-minute into the ramp to GET; S_2, from GET to peak $\dot{V}O_2$; and S_T, over the total range of $S_1 + S_2$. Baseline $\dot{V}O_2$ was taken as the mean of the first 45 seconds of the last minute prior to the increase in work rate. The MRT was calculated as the point of intersection between the baseline $\dot{V}O_2$ and a backwards linear extrapolation of the $\dot{V}O_2$ by time slope from the onset of the ramp protocol. The MRT was also determined using two segments, S_1 (MRT_1) and S_T (MRT_T).

2.6. Statistical analysis

Shapiro-Wilk tests were used to assess normality. Following identification of normal distribution, the influence of asthma and the intervention, and their interaction, was assessed using a mixed-model ANOVA (groups – asthma intervention, non-asthma intervention, asthma control, non-asthma control). Tukey's post-hoc analyses were conducted to ascertain where differences in time were found. If significant differences were found, mixed-design ANCOVA tests were run to adjust for baseline maturity. Asthma-specific measures were analysed using repeated measures ANOVAs. Data presented within the tables include the participant numbers providing data at every time-point and therefore participant numbers differ between measurements. All analyses were conducted using an intention-to-treat approach, thereby including all participants with measures at any time-point; data were subsequently analysed using sensitivity analysis on participants who participated in the majority of the intervention sessions (>70%). Eta-squared (η_p^2) effect sizes were determined from baseline to 3-month follow-up. All statistical analyses were conducted using SPSS v22 (IBM Corp, Armonk, NY). All data are presented as mean ± standard deviation (SD) with statistical significance accepted as $P < 0.05$.

3. Results

The participants with asthma in the intervention group consisted of 87% with mild persistent and 13% with moderate or severe asthma, whilst the participants with asthma in the control group consisted of 77% and 23%, respectively. This prevalence was similar in both the intention-to-treat and sensitivity analyses. Where no differences between intention-to-treat and sensitivity analysis were found, results refer to the former. Furthermore, no differences were observed when co-varying for maturity offset or Tanner stages and are therefore not reported below.

3.1. Lung function

A lower FEV_1% and FEF_{25-75} were found in participants with asthma indicating more airway obstruction and more marked small airways obstruction, respectively (Table 3). Those with asthma did not have an obstructed FEV_1/FVC ratio. Mixed methods ANOVAs revealed no differences between intervention and control, asthma and non-asthma for lung function ($P > 0.05$) according to group or time or a time by group interaction. There was, however, a trend for FeNO to reduce in the intervention asthma group.

3.2. Asthma control and quality of life

The intervention had no effect on asthma control or asthma-related quality of life. The Minimal Important Difference (MID) for both the ACQ and PAQLQ was a change in score of 0.5. Both intervention and control asthma participants demonstrated similar results, with 33 and 35 % and 19 and 16 % for ACQ and PAQLQ, respectively, scoring above the MID. The results of the PedsQL revealed no significant differences between those with and without asthma in either the intervention or control group. The intervention was associated with no significant change at any time-point, in any of the groups (Table 5.4).

3.3. Body Mass Index

Body Mass Index was found to be significantly higher in participants with asthma at baseline in comparison to their peers (22.2 ± 4.8 vs. 20.4 ± 3.7 kg·m^{-2}). There was a significant effect of time on BMI ($F(2.23, 782) = 15.4$, $P < 0.05$ $\eta_p^2 = 0.04$) and a significant difference between groups ($F(3, 351) = 5.29$, $P < 0.05$ $\eta_p^2 = 0.04$), but no interaction between time and group ($F(6.68, 782) = 1.16$, $P = 0.33$ $\eta_p^2 = 0.01$). Specifically, whilst the intervention participants maintained their baseline BMI to post-intervention, BMI in control participants, both with and without asthma, increased throughout the intervention (asthma: 21.4 ± 4.4 to 21.8 ± 4.4; non-asthma: 19.8 ± 3.3 to 20.3 ± 3.4; kg·m^{-2}, $P < 0.05$). At 3-months follow-up, all groups (intervention and control, asthma and non-asthma) had significantly higher BMI than their baseline scores.

3.4. 20-metre shuttle run

No significant effects were found for group or time, and no interaction was reported between group and time, for the 20-metre shuttle run. However, when applying sensitivity analyses, there was a significant effect of time ($F(3, 386) = 5.44$, $P < 0.05$ $\eta_p^2 = 0.04$) and a significant interaction of group by time ($F(9, 386) = 3.23$, $P < 0.05$ $\eta_p^2 = 0.06$). Post-hoc analyses revealed a significant increase in the number of shuttles completed in both asthma and non-asthma intervention participants with time, which returned to baseline at the 3-month follow-up.

3.5. Incremental ramp test

A significant effect of time and interaction between time and the group was observed, with no significant effect of group on peak $\dot{V}O_2$. When scaled for body size, these differences were maintained with time ($F(3, 138) = 8.47$, $P < 0.05$ $\eta_p^2 = 0.16$), group by time ($F(9, 138) = 2.70$, $P < 0.05$ $\eta_p^2 = 0.15$), and group ($F(3, 46) = 1.55$, $P = 0.22$ $\eta_p^2 = 0.09$). Post-hoc analyses revealed significant increases in peak $\dot{V}O_2$ in both asthma and non-asthma intervention groups, with 3-month follow-up results showing a return to baseline levels. No differences were observed in either of the asthma or non-asthma control groups across the intervention for peak or scaled peak $\dot{V}O_2$ (Table 5.5).

There were no differences in GET between groups, however, there was a significant increase over time in all groups ($F(2.23, 138) = 41.56$, $P < 0.05$ $\eta_p^2 = 0.48$). There was no significant between group differences for GET as a percentage of peak $\dot{V}O_2$. Post-hoc analyses showed significant increases at post-intervention for the non-asthma intervention and both asthma and non-asthma control groups, however, inclusive of the asthma intervention group, all groups significantly increased GET from baseline to 3-month follow-up. Sensitivity analysis also showed that there were no significant increases throughout the intervention in GET% $\dot{V}O_2$ for participants in the non-asthma intervention group. There were no significant differences to either section of the MRT according to time, group or time by group interaction across all time-points. The gain, however, was found to significantly increase in the intervention asthma group for both S_2 and S_T, with no significant differences observed in any of the other groups.

3.6. Intervention intensity

Throughout the intervention sessions, exclusive of warm-up and cool-down, participants' mean HR (155 ± 18 beats per minute (bpm), 78 ± 9 $\%HR_{max}$) and mean HR_{max} (188 ± 18 bpm, 95 ± 6 $\%HR_{max}$) were calculated for each session. During the main body of the session, inclusive of both the exercise and rest intervals, HR exceeded the threshold of >90$\%HR_{max}$ 24% of the total time.

3.7. Correlations

All measures were positively correlated with themselves between baseline and post-intervention, with the exception of the MRT and gain. A weak negative correlation was observed between BMI and fitness ($r = -0.34$, $P < 0.05$), quality of life ($r = -0.11$, $P < 0.05$) and lung function ($r = -0.21$, $P < 0.05$) at baseline, but only fitness ($r = -0.33$, $P < 0.05$) at post-intervention. Fitness was also weakly correlated with quality of life ($r = 0.26$, $P < 0.05$) and lung function ($r = 0.34$, $P < 0.05$) at all time-points. However, scaled peak $\dot{V}O_2$ was not associated with quality of life or lung function ($P > 0.05$).

4. Discussion

This was the first study to evaluate the feasibility and effectiveness of a 6-month field-based HIIT intervention in adolescents with asthma compared to their healthy peers. The main findings of this study were that adolescents with asthma did not differ to their healthy counterparts in cardiorespiratory fitness at baseline, despite a higher BMI, and demonstrated a similar response to the HIIT intervention. Specifically, HIIT elicited significant improvements in cardiorespiratory fitness and maintained BMI in adolescents, irrespective of asthma. However, HIIT did not elicit significant improvements in lung function, asthma control or quality of life. These findings have important implications for the design of future interventions for those with asthma, highlighting that they are able to tolerate, and benefit from, similar exercise stimuli recommended for their healthy counterparts. This study demonstrates the fallacy of the perception that adolescents with asthma should be excluded as they are unable to participate and "keep-up" during similar activities to their peers.[56,57]

In accord with previous research and recent systematic reviews,[27,58] the present study found that HIIT was associated with increased cardiorespiratory fitness in adolescents. Specifically, in the overall population, 20-metre shuttle run scores significantly improved, irrespective of condition, with no significant changes noted for the controls. Furthermore, both absolute and body size scaled peak $\dot{V}O_2$ increased throughout the intervention, providing evidence of true physiological improvements in cardiorespiratory fitness. Interestingly, the asthma intervention group increased their scaled $\dot{V}O_2$ to a greater extent than their non-asthma peers (19 vs. 10%) and considerably more than previously reported to be elicited through conventional training programmes in healthy adolescents.[59] This greater increase may be related to the (non-significantly) lower baseline fitness in those with asthma; baseline fitness has been reported to influence the magnitude of change elicited by an intervention in youth.[60-62] Although improvements in peak $\dot{V}O_2$ following moderate-intensity exercise have been noted in those with asthma over a shorter time-frame,[16,17,63,64] the suitability of continuous exercise in those with asthma is questionable. Indeed, research has suggested that prolonged continuous exercise is not enjoyable[26] and may trigger the onset of asthma symptoms,[29] both of which are key barriers to exercise in those with asthma.[14] Furthermore, traditional endurance training, which typically involves a greater time commitment than HIIT, may also be less appealing than the suggested HIIT format to "time poor" adolescents.[27] Importantly, the beneficial adaptations in the peak $\dot{V}O_2$ of those with asthma were sustained to 3-months following intervention cessation. Whilst it is beyond the scope of the present study to ascertain whether this was because these participants maintained a higher exercise level post-intervention, this finding is encouraging for the long-term efficacy of HIIT in adolescents with asthma.

In contrast to suggestions that submaximal parameters of aerobic fitness may demonstrate greater sensitivity to exercise stimuli than peak $\dot{V}O_2$, but in agreement with previous studies, [65] the absolute GET was unaffected by the intervention in the present study, irrespective of asthma status. This may indicate that training above the GET for short intermittent periods is not an effective strategy to increase the GET in youth. Elucidating the influence of training *per se* is confounded, however, by the concomitant changes in the relative GET (GET%$\dot{V}O_2$) that were observed in all groups throughout the study which may have masked training-related adaptations. These apparent age- and/or maturation-related changes in the relative GET are in contrast to previous reports,[26] therefore requiring further research to ascertain the influence of growth and maturation on the GET.

In addition to the GET, irrespective of condition, HIIT did not significantly improve the MRT. These findings are perhaps surprising considering the nature of HIIT training, involving repeated transitions from rest to vigorous-intensity exercise. The MRT in the present study was longer than previously reported in healthy children,[66,67] but did not differ between those with and without asthma. The longer MRT may reflect a lower aerobic fitness, although, given that this increased throughout the intervention with no concomitant speeding of the MRT, this seems unlikely. The lack of effect of asthma in the present study is in contrast to the slower MRT reported in those with Cystic Fibrosis. [68] This may be attributable to the different disease aetiologies and therefore influences on exercise tolerance but may also be related to the relatively mild asthma of the majority of the participants in the present study. Further inter-study comparisons are precluded as the ramp rate of the incremental test, which differs significantly between studies, profoundly affects the MRT.[69] Interestingly, there were no differences in MRT between those with and without asthma, suggesting asthma does not impede the response to exercise.

The increase in gain observed over the intervention in participants with asthma is suggestive of a positive adaptation in the delivery and utilisation of oxygen by the muscles during exercise.[70] Of note, although no differences in gain were observed at baseline, S_2 and S_T gain increased post-intervention for participants with asthma to similar levels to those reported elsewhere in healthy adolescents.[68] This increase in gain may indicate that HIIT elicits different adaptations in those with and without asthma, although this may also be a function of the lower baseline levels in those with asthma allowing greater capacity for improvement. The lower levels of aerobic efficiency in participants with asthma may be related to a decreased lung function and may be a contributory mechanism to the onset of early fatigue and the perception that people with asthma are not as fit as their peers, although it is worth noting they were not correlated in the current study. Indeed, Fielding et al.,[68] found a reduced gain in Cystic Fibrosis patients and suggested that this this, at least in part, explained the reduced exercise intolerance in Cystic Fibrosis compared to their healthy peers. Importantly, the current study demonstrates that the gain of participants with asthma, but not adolescents without asthma, can be improved with a HIIT programme.

In accord with previous findings in non-asthma populations,[71] Cardiorespiratory fitness was found to have a weak but significant correlation with quality of life in those with asthma at baseline, highlighting the importance of exercise as a management strategy for those with asthma. However, despite this correlation and the increase in cardiorespiratory fitness observed in the current study, quality of life did not change over time, irrespective of treatment group or asthma status, contrary to previous exercise interventions.[20,21] Furthermore, there was no change over time for perceived asthma-related quality of life, symptoms or asthma control. It could be postulated that the lack of improvement in asthma-related quality of life may be due to the mild severity of asthma or participants having high baseline values,[1,21,72] thereby decreasing the likelihood of an effect, or indeed need for an effect. Finally, the lack of improvement in quality of life may be due to HIIT reducing participants' time in total physical activity due to the compensation effect,[73] suggesting increased physical activity in general may be associated with a higher quality of life in comparison to specifically HIIT or increased cardiorespiratory fitness.

Whilst the present study is consistent with the majority of the literature which similarly found that exercise did not affect lung function,[1] it is pertinent to note that two studies reported a significant increase in FEV_1% (8 - 20%), both of which implemented intermittent training.[29,31] This discrepancy may be related to the severity of asthma, or to the intervention duration; although longer than many previous studies,[72,74] 6-months may have been insufficient to elicit significant adaptations in lung function. It is perhaps interesting to note that both studies that previously reported beneficial adaptations in lung function involved younger, largely pre-pubertal, children.[29,31] Furthermore, the actual exercise time, despite being based on intermittent bouts, was significantly longer in Latorre-Roman et al.,[31] whilst the participants in Sidiropoulou et al.[29] had exercise-induced bronchoconstriction rather than asthma *per se*. These factors therefore limit further conclusions being drawn as to the discrepancy in these findings with regards to lung function.

In accord with previous findings, the current findings suggest BMI increases linearly with age in youth.[75] Of importance, the intervention was able to maintain the baseline BMI and prevent this progressive rise in both those with and without asthma. Given that childhood obesity is known to track strongly into adolescence and adulthood, with evidence suggesting that 80% of obese adolescents will become obese adults,[76] the current findings may have important implications in terms of effective exercise interventions which may help to ameliorate this rise. Furthermore, exercise and physical activity have previously been suggested to be influential in the self-management of asthma.[77] This is the first study to address whether HIIT may aid in a non-pharmacological management of asthma. Whilst the maintenance of BMI is a promising finding in addition to increased fitness, HIIT did not improve lung function, asthma control and quality of life. Therefore, taking all findings together, 6-months of HIIT may not be effective at improving mild asthma in adolescents, however, due to the maintenance of BMI and increased fitness, HIIT may be an important non-pharmacological strategy in the management of the condition.

A key strength of the present study was the more sensitive measures of aerobic fitness (GET, MRT and gain) which have not previously been assessed across multiple time-points in adolescents with asthma. Nonetheless, several limitations should be acknowledged. As with any exercise intervention, there may have been a self-selection bias with voluntary participant recruitment. Furthermore, although the HIIT intervention was designed using formative research,[14] participants who signed up to the intervention either committed fully, attending a large proportion of the sessions throughout the 6-months, or had minimal attendance over the intervention. This may be indicative that this type of intervention is effective for those who will engage in it but that it is not acceptable to all. Whilst this may be considered to question the utility of the intervention, it may be that the timing of the exercise sessions reduced participation and that if more optimal timings were possible, a stronger adherence could be achieved.

In conclusion, HIIT, a previously underutilised method of managing asthma in adolescents with asthma, may be an effective tool to increase peak aerobic fitness and prevent increases in BMI in adolescents, irrespective of asthma. Of importance, this adds to literature by demonstrating that adolescents with asthma elicited similar physiological adaptations in comparison to their healthy peers, thereby demonstrating that asthma does not influence aerobic fitness or trainability in adolescents. Furthermore, the lack of exercise-induced asthma attacks suggests that HIIT is safe for, and well-tolerated by, adolescents with asthma.

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Authors’ contributions

CONW conceptualised and designed the study, collected data, conducted the statistical analysis, interpreted the data, and drafted the manuscript. MAM, KAM and GAD conceptualised and designed the study, supervised, interpreted the data and critically revised the manuscript. GS and AMW interpreted the data and critically revised the manuscript. WTBE collected data, interpreted the data and critically revised the manuscript. All authors read and approved the final manuscript and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

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