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ARE YOUNG CHILDREN WITH ASTHMA MORE LIKELY TO BE LESS PHYSICALLY ACTIVE?

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ABSTRACT:

Background: Previous research suggests that children who experience asthma may be less physically active, however results have been inconclusive. This study aimed to investigate whether the presence of asthma or wheeze is associated with lower physical activity levels in children, and whether sex, body mass index or earlier asthma or wheeze status modifies the association.

Methods: This study was conducted in 391 HealthNuts participants in Melbourne, Australia. Asthma and wheeze data were collected via questionnaire at age 4 and 6 and physical activity was measured through accelerometry. Using adjusted linear regression models, the cross-sectional and longitudinal associations were investigated.

Results: There was no evidence of a difference in time spent in moderate-to-vigorous physical activity (MVPA) at age 6 years between children with and without asthma at age 4; children with asthma spent 8.3 minutes more time physically active per day (95%CI: -5.6, 22.1, p=0.24) than children without asthma. Similar results were seen for children with current wheeze (5.8 minutes per day more, 95%CI: -5.9, 17.5, p=0.33) or ever wheeze or asthma (7.7 min per day more, 95%CI: -4.8, 20.2, p=0.23) at age 4 years. Comparable null results were observed in the cross-sectional analyses. Interaction with BMI could not be assessed, however, previous asthma or wheeze status and sex were not found to modify these associations.

Conclusion: This analysis found no evidence of asthma hindering physical activity in these young children. These results are encouraging, as they indicate that the Australian asthma and physical activity public health campaigns are being effectively communicated and adopted by the public.

KEY MESSAGE: This prospective study investigates the association between asthma at 4 years and physical activity at 6 years. It provides evidence that asthma does not hinder subsequent moderate-to-vigorous physical activity in these young, Australian children. It provides evidence of a successful management model used in Australia that can and should be adopted by other settings wishing to address the issue of insufficient physical activity in children with asthma.

KEYWORDS: Asthma, Accelerometry, Children, Cohort, Physical activity, Wheeze

INTRODUCTION

Physical inactivity is a leading risk factor for the development of a variety of non-communicable diseases. Since physical activity tracks moderately through life, the promotion of a physically active lifestyle from a young age may be important and beneficial for future health (1). For this reason, the World Health Organization (WHO) and other national health guidelines currently recommend that children and adolescents between the ages of 5 and 17 years engage in a minimum of 60 minutes of

moderate-to-vigorous physical activity (MVPA) daily (2, 3). However, numerous international studies have demonstrated that large proportions of children and adolescents fail to meet the current physical activity recommendations (4, 5). It is believed that physical activity engagement decreases with age, and that subgroups of children are more likely to be insufficiently active than others.

Some studies have found that children who experience asthma may lead less physically active lives (6), however these results are inconsistent (7). Globally, asthma is the most common chronic condition in childhood, adversely affecting quality of life and constituting an important global health problem in childhood (8). Despite asthma guidelines encouraging physical activity as a non-pharmaceutical intervention for asthma, strenuous physical activity is a known trigger for asthma exacerbations (8). As such, some studies have found that children with asthma avoid physical activity for fear of triggering their asthma symptoms, or due to a fear of being mocked or stigmatised for these symptoms (9). Another study found that parents may impose physical activity restrictions on children with asthma (10).

Our recent systematic review concluded that children with asthma were equally as physically active as their unaffected peers (7). This finding was based mainly on cross-sectional studies as only one cohort study to date had been published (11). Therefore, the present study aimed to investigate the longitudinal relationship between asthma and wheeze at age 4 and objectively measured physical activity in children aged 6 years. The cross-sectional relationship at the age of 6 years was also examined, and whether a change in asthma status from age 4 to 6 is associated with physical activity. Finally, we explored whether BMI and sex modified the association between asthma and physical activity.

METHODOLOGY

The HealthNuts study, is a population-based study of allergic disease burden in over 5,000 children (12). Between September 2007 and August 2011, children aged between 11 and 15 months who presented for routine 12-month vaccinations at immunization clinics within a 70 km radius of the Melbourne central business district were approached to participate (13). The cohort has been followed up twice, first between 2010 - 2014 and then between 2012 – 2016, when the children were aged 4 and 6, respectively. At each follow up, caregivers were invited to complete the study questionnaire, and at age 6, were invited for a clinical assessment (13). Ethical approval was obtained from the Human Research Ethics Committee (HREC) of the Office for Children, Government

of Victoria (ref. no. CDF/07/492), Department of Human Services, Government of Victoria (ref. no. 10/07) and The Royal Children's Hospital HREC (ref. no. 27047 and ref. no.32294).

Exposure variables were taken from the 4 and 6 year follow ups of the HealthNuts questionnaire. Standardized questions on asthma and wheeze from the validated International Study of Asthma and Allergies in Childhood (ISAAC) were used (13, 14). For this analysis, current asthma was defined as parental report of ever having doctor-diagnosed asthma and at least one of parent-reported wheeze or use of asthma medication in the past 12 months (14). Current wheeze was defined as parental report of any wheezing in the last 12 months (15). Ever wheeze or asthma was defined as a parental report of ever having had doctor-diagnosed asthma or wheeze at 4 and/or 6 years.

Participants who attended the 6 year follow up clinical appointment from March 2015 onward were asked to wear the waterproof GENEActiv (Gravity Estimator of Normal Everyday Activity, ActivInsights Ltd, Cambridgeshire, UK) triaxial accelerometer watch on the wrist of their non-dominant hand 24 hours per day for 8 consecutive days, including during sleep, while swimming and at bath time. Parents were given instructions for the use of these devices and were asked to note the child's waking and bedtime and to briefly describe the child's activities per day on the paper log provided. Furthermore, they were asked to note times when the watch was removed and replaced, and the reasons for device removal.

For this analysis, activity was sampled at 100 Hz then collapsed into 60-s epochs. Participant accelerometry files and paper log were combined, and activity cut points were applied using custom Matlab software. Data were then manually inspected, correcting for unreported periods of non-wear, and re-categorising documented non-wear as time spent in MVPA where the physical activity logs indicated that the device was removed for reasons pertaining to sport participation. Individual days containing less than 16 hours of wear within a 24-hour period, or less than 10 hours of wake wear time were excluded from analysis. Participants with less than 4 valid days, or with no weekend days of valid accelerometry, were excluded from analysis. Further detail of the accelerometry processing methodology is reported elsewhere (16).

The primary outcome of this analysis was daily minutes spent in MVPA, as measured by accelerometry at age 6 years, where MVPA was defined as >4350 g.min, as per the cut-offs presented by Phillips *et al* (17).

Potential confounders were identified from the existing scientific literature and selected for inclusion in these analyses based on a directed acyclic graph (DAG; Supplementary Figure). Sex, BMI, the presence of older siblings and familial history of allergy and asthma data were collected via

questionnaire at the HealthNuts follow ups (i.e. ages 1and 4 years). The Socio-Economic Indexes for Areas (SEIFA) was used as a proxy for socioeconomic status. Based on home postcode, each participant is allocated a SEIFA index of relative socioeconomic advantage or disadvantage, derived from the 2006 Australian census data (18). Participant BMI at age 4 was calculated from parent-reported height and weight and then categorised as "underweight", "normal weight" or "overweight" based on age appropriate cut-offs (19).

Statistical analysis

All statistical analyses were performed using Stata/MP 15.1 (StataCorp LLC, College Station, TX, USA). Descriptive statistics of the study sample are presented. Associations between individual exposures and MVPA were analysed in univariate linear regression models first, and then in multivariate linear regression models with adjustment for the confounders selected based on the DAG.

Prior to an investigation of effect modification by sex, BMI, or asthma or wheeze at age 4, the number of individuals within each stratum was considered. Where small numbers were found within strata, the investigation was not further pursued, however, where numbers permitted, potential effect modification was assessed by fitting individual interaction terms in the multivariate regression models and comparing models using Likelihood Ratio Tests. Stratified results were presented if the p value for interaction was less than or equal to 0.05.

RESULTS

Of those children who attended the 6 -year clinical follow up, 1709 children had a full assessment after March 2015 and were invited to participate in the accelerometry testing. Accelerometers were sent to 682 (40%) of these children, and data were returned for 495 participants. Of these, 104 files were excluded because they did not contain sufficient valid data or were corrupted. Hence, this study analysed valid data from a sample of 391 children (Figure 1).

In this study sample, 50.6% of children were male and 48.3% were female (Table 1). The proportion of children who experienced wheeze was 12.8% at age 4 years and 17.4% at age 6 years. The proportion of children with current asthma was 8.7% at age 4 and 12.5% at 6 years. At age 6, the mean [standard deviation] time spent in MVPA for all HealthNuts children was 98 [35] min per day, and on average boys spent more time in MVPA than girls (111 [35] vs. 85 [30] min per day, respectively). Overall, 88.5% (82% girls and 95% of boys) of the study children met the WHO recommendation of 60 min of MVPA per day.

Association between exposures at age 4 and physical activity at age 6

Children with current asthma at age 4 participated in an average of 8.3 (95% Confidence Interval (CI):: -5.6, 22.1, p = 0.24) min more MVPA per day at age 6 than children without asthma (Table 2). Similarly, there were no associations seen for current wheeze (5.8 min 95%CI: -5.9, 17.5, p = 0.33) or ever wheeze or asthma at age 4 years (7.7 min 95%CI: -4.8, 20.2, p = 0.23) for time spent in MVPA at 6 years.

Association between exposures at age 6 and physical activity at age 6

Children who experienced current asthma at age 6 years participated in an average of 2.9 min more MVPA per day (95%CI: -12.8, 18.6) than those who did not experience current asthma (Table 2). Similarly, children who experienced current wheeze at 6 years spent an average of 1.3 (95% CI: -13.2, 10.6) min less in MVPA than those without current wheeze and children with a history of asthma or wheeze spent an average of 5.3 (95% CI: -7.4, 17.9) more minutes in MVPA than their peers, with no evidence of a difference between these groups (p = 0.72, p = 0.83 and p = 0.41, respectively).

Investigation of effect modification

The small number of observations within some strata prohibited the investigation of effect modification by BMI at both ages (Supplementary Table 1-3). However, likelihood ratio testing for interaction found no evidence of effect modification by sex for any of the asthma/wheeze variables at 4 or 6 years, on time spent in MVPA (all p-values for interaction >0.3) (Table 2). Similarly, there was no evidence of effect modification between exposure status at age 4 and either current asthma (p = 0.17), current wheeze (p = 0.59), or ever asthma or wheeze (p = 0.70).

DISCUSSION

This study is among the first to look at the longitudinal relationship between asthma and wheeze and objectively measured MVPA in a population of young children. We found no evidence of associations between current asthma, current wheeze, or a history of ever having asthma and wheeze at 4 or 6 years and MVPA as measured by accelerometer at 6 years of age. Statistical tests for interaction also found no evidence for effect modification by either sex, or asthma or wheeze status at 4 years. We were unable to explore effect modification by BMI due to insufficient power. Within this sample, the majority (88.5%) of children met the WHO recommendation of 60 mins of MVPA per day. A greater proportion of boys (95%) than girls (82%) achieved this recommended amount. The mean time spent in MVPA in this study was 98 [35] minutes per day. This suggests that

the cohort was highly active, contrary to reports of inadequate physical activity on other studies of this age group (20, 21).

The null results obtained in the present study are concordant with the other longitudinal study of the association between wheeze and physical activity in young children (11), and with the few additional studies that have found no longitudinal association between asthma and physical activity in youth (22, 23). Further, this result supports the finding of our previously published systematic review (7), and multiple studies that have found no cross-sectional associations (24, 25). These null results are a positive indication that, at least within Australia, these young children with asthma are not restricting their physical activity engagement on account of their asthma. Of course, these results are likely to be age dependent, with older children and adolescents partaking in less physical activity. However, these results suggest that the current asthma guidelines and public health messaging on the importance of physical activity in childhood are being effectively disseminated to, and well adopted by parents. Additionally, it signifies that general practitioners are providing children with asthma and their parents or caregivers with appropriate and effective management plans and knowledge, thus adequately controlling asthma symptoms and allowing these children to participate in physical activity without fear. These results and their implications may not be generalisable to other settings around the world, where a variety of different social, health care and economic factors may influence the relationship between asthma and physical activity.

A major strength of this analysis is the use of robust tools for the outcome measurement of MVPA. The present study is one of few that have used accelerometers to measure physical activity in children as young as six years. The use of the validated ISAAC questionnaire (26), together with objective accelerometry measurements, inspire confidence in the data. The use of an objective measurement technique is particularly important for the collection of physical activity data in children of this age, since subjective measurements of physical activity in young children may be over- or underestimated (27). Measurements by proxies such as parents or caregivers may be inaccurate; since young children tend to have brief bursts of activity that can be difficult to quantify through observation (28). An additional strength is the data drawn from a prospective, population-based cohort of young children which enables the assessment of data in a longitudinal manner to account for the temporality of the association, unlike previous studies which have been cross-sectional in nature (25, 29).

This study also had several shortcomings. First, the high proportion of HealthNuts children that met the WHO's physical activity recommendations may be due to potential selective participation for children who were more active. Children from higher socioeconomic status have higher levels of

physical activity (30), this may be reflected in the current results, where families with a higher SEIFA index were found to be more likely to participate in the HealthNuts study (12). This limits the external generalisability of these results. Further, major limitations with accelerometry persist through the lack of an agreed and standardized processing, analysing and reporting method (31). For example, the threshold used to define moderate-to-vigorous physical activity can vary widely, resulting in substantially different results and conclusions (31). However, as our study focused on comparative differences in MVPA, the choice of cut point should have no effect on the findings. Secondly, when the accelerometer was removed for sport, we replaced the entire non-wear period with MVPA. This likely results in an overestimation of MVPA for these periods, since the removal period may also include time to get changed, shower etc. As a result, this could create misclassification if some participants reported significantly more sport non-wear than others. This issue is discussed in greater detail elsewhere (16), however, any misclassification is likely to be non-differential across categories of children with and without asthma as their reporting of physical activity was independent of their knowledge of this study's research questions and exposures of interest. Finally, a substantial amount of missing data at the 4 year follow up meant there was insufficient power to present reliable results for interaction between BMI and asthma. Future longitudinal studies with greater statistical power should explore the signal for asthma and BMI in more depth.

CONCLUSION

We found no evidence of either longitudinal or cross-sectional associations between current asthma, current wheeze or a history of ever having had asthma or wheeze and the amount of time spent in objectively measured moderate-to vigorous physical activity at 6 years of age. These results suggest that in this Australian setting, asthma guidelines and management strategies seem to be working effectively, so that physical activity is not restricted in young children with asthma.

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Table 1: Comparison of descriptive characteristics of children with accelerometry data at age 6.

CHARACTERISTIC	N (%) OR MEAN [SD]
MEASURED AT 1 YEAR	
SEX,	
MALE	198 (50.7)

FEMALE	189 (48.3)
MISSING	4 (1.0)
MATERNAL ASTHMA,	
YES	65 (16.6)
NO	326 (83.4)
MISSING	0
PATERNAL ASTHMA,	
YES	55 (14.1)
NO	336 (85.9)
MISSING	0
OLDER SIBLINGS,	
N (%)	
YES	185 (47.3)
NO	204 (52.2)
MISSING	2 (0.5)
SEIFA INDEX,	
1 (MOST DISADVANTAGED)	74 (18.9)
2	71 (18.2)
3	95 (24.3)
4	76 (19.4)
5 (LEAST DISADVANTAGED)	75 (19.2)
MEASURED AT 4 YEARS	
BMI,	

UNDERWEIGHT	36 (9.2)
NORMAL WEIGHT	179 (45.8)
OVERWEIGHT	34 (8.7)
MISSING	142 (36.3)
CURRENT ASTHMA,	
YES	34 (8.7)
NO	258 (66)
MISSING	99 (25.3)
CURRENT WHEEZE,	
YES	50 (12.8)
NO	238 (60.9)
MISSING	103 (26.3)
EVER ASTHMA OR EVER WHEEZE,	
YES	57 (14.6)
NO	304 (77.8)
MISSING	30 (7.7)
MEASURED AT 6 YEARS	
BMI, N (%)	
UNDERWEIGHT	80 (20.5)
NORMAL WEIGHT	265 (67.8)
OVERWEIGHT	41 (10.5)
MISSING	5 (1.3)
MATERNAL EDUCATION, N (%)	

HIGH SCHOOL	49 (12.5)
TECHNICAL OR TRADE QUALIFICATION	86 (22)
UNIVERSITY QUALIFICATION	237 (60.6)
MISSING	19 (4.9)
PATERNAL EDUCATION, N (%)	
HIGH SCHOOL	45 (11.5)
TECHNICAL OR TRADE QUALIFICATION	116 (29.7)
UNIVERSITY QUALIFICATION	200 (51.1)
MISSING	30 (7.7)
CURRENT ASTHMA, N (%)	
YES	49 (12.5)
NO	337 (86.2)
MISSING	5 (1.3)
CURRENT WHEEZE, N (%)	
YES	68 (17.4)
NO	305 (78.0)
MISSING	18 (4.6)
EVER ASTHMA OR EVER WHEEZE, N (%)	
YES	57 (14.6)
NO	332 (84.9)
MISSING	2 (0.5)
MINUTES SPENT IN MVPA,	
TOTAL	97.9 [35.1]

BOYS	110.7 [35]
GIRLS	84.8 [30.3]
MET WHO RECOMMENDATION FOR MVPA,	
TOTAL	346 (88.5)
BOYS	188 (94.9)
GIRLS	154 (81.5)

SD – standard deviation; BMI – body mass index; SEIFA – Socioeconomic Indexes for Areas; MVPA – moderate to vigorous physical activity

Table 2: Table of adjusted regression coefficients, 95% confidence intervals for cross-sectional and longitudinal models and p values for the likelihood ratio tests for interaction.

	CURRENT ASTHMA COEFFICIENT (95% CI)	**P VALUE**	**CURRENT WHEEZE COEFFICIENT (95% CI)**	**P VALUE**	**EVER WHEEZE OR ASTHMA COEFFICIENT (95% CI)**	**P VALUE**
LONGITUDINAL (EXPOSURE AT 4 YEARS)	8.3 (-5.6, 22.1)	0.24	5.8 (-5.9, 17.5)	0.33	7.7 (-4.8, 20.2)	0.23
INTERACTION WITH **SEX**		0.41		0.51		0.89
CROSS-SECTIONAL (EXPOSURE AT 6 YEARS)	2.9 (-12.8, 18.6)	0.72	-1.3 (-13.2, 10.6)	0.83	5.3 (-7.4, 17.9)	0.41
INTERACTION WITH **SEX**		0.44		0.39		0.31
INTERACTION WITH **EXPOSURE**		0.17		0.59		0.70

STATUS AT AGE 4			

Longitudinal models adjusted for sex, SEIFA, older siblings, maternal and paternal asthma and BMI at 4 years. Cross-sectional models adjusted for sex, SEIFA, older siblings, maternal and paternal asthma, BMI at 6 years and the respective exposure status at 4 years.

Figure legend: **Figure 1: Flow of participants through the HealthNuts study.**

HealthNuts Paper Figure