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Associations of physical condition with lung function and asthma in adolescents from the general population

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Abstract

Background: The relation of physical condition with respiratory outcomes in adolescents is unclear. We examined the hypothesis that adolescents with a lower physical condition represented by a lower cardiorespiratory fitness and physical activity, and a higher screen time have a lower lung function and higher risk of asthma.

Methods: In a population-based prospective cohort study on 4854 children aged 13 years, we assessed cardiorespiratory fitness by using the peak work rate measured by the steep ramp test. Information on physical activity and screen time was obtained by self-reported questionnaires. Lung function was measured by spirometry and current asthma was assessed by a parental-reported questionnaire.

Results: Taking sociodemographic, lifestyle, and growth-related confounders and multiple hypothesis testing into account, a 1 SD lower cardiorespiratory fitness was associated with a lower FEV_1, FVC, and FEF_{75} (Z-score difference (95% CI): −0.31 (−0.35, −0.28), −0.30 (−0.33, −0.26), −0.13 (−0.17, −0.10), respectively), and a higher risk of asthma (Odds Ratio (95% CI) 1.25 (1.06, 1.46)). A 1 SD higher screen time was associated with a lower FVC (Z-score difference (95% CI): −0.06 (−0.10, −0.03)). Physical activity and screen time were not related to asthma. Results did not materially change after additional adjustment for respiratory outcomes at an earlier age.

Conclusion: Adolescents with a lower cardiorespiratory fitness had a lower lung function and a higher risk of asthma. Those with a higher screen time had a lower FVC. Further studies are needed to explore the effect of improvements in physical condition on long-term respiratory outcomes.

KEYWORDS
adolescent, asthma, epidemiology, physical fitness, respiratory function test, sedentary behavior

1 | INTRODUCTION

Asthma in adolescence is common, with a high risk of serious morbidity.[1] The physical condition, an important modifiable determinant of general health, is of particular interest since over 80% of the adolescents are insufficiently physically active.[2] In patients with asthma, more physical activity has been related to a better control of the disease.[3] However, inconclusive results have been observed on the associations of physical activity with lung function and asthma in adolescents from the general population.[4–7] This inconsistency might be due to individual differences in the effect of physical activity on cardiorespiratory fitness, as there is heterogeneity in the effect of the same dose of regular exercise on health outcomes.[8] A worse cardiorespiratory fitness has been related to a less favorable body fat distribution and cardiometabolic profile, which might subsequently lead to a lower lung function and increased risk of asthma.[9] Population-based cohorts studying the association of cardiorespiratory fitness with lung function and asthma in children and adolescents are scarce and show inconsistent results.[10–14] However, these studies had a small sample size or measured cardiorespiratory fitness with a prolonged or submaximal exercise test, which might not reflect the daily physical activity patterns of the children and adolescents as well as a short maximal exercise test.[15] The steep ramp test is a short maximal exercise test that measures the peak work rate (WRpeak), which is a valid and reliable estimation of the maximal aerobic exercise capacity and thus cardiorespiratory fitness.[9,16] Last, to have a more complete evaluation of the physical condition, adolescents spent a large part of the day in screen time, which has been suggested to higher the risk of asthma symptoms, probably independent of physical activity.[17]

We, therefore, aimed to examine 4854 adolescents at the age of 13 years; the associations of the physical condition include cardiorespiratory fitness, physical activity, and screen time with lung function and asthma.

Key Messages

Physical condition is known to affect the general health of children, but its relation with respiratory outcomes in adolescents is unclear. In this population-based prospective cohort study, we observed that a lower cardiorespiratory fitness was associated with a lower FEV_1, FVC, and FEF_{75}, and a higher risk of asthma in adolescence. These associations were stronger observed in boys than in girls, and only in boys, a lower cardiorespiratory fitness was related to a lower FEV_1/FVC ratio. A higher screen time was associated with a lower FVC, but both physical activity and screen time were not related to current asthma. These findings suggest that a lower cardiorespiratory fitness and a higher screen time are related to adverse respiratory outcomes in adolescence, and that improvement of physical condition may benefit respiratory health.

2 | METHODS

2.1 | Design

This cross-sectional analysis was embedded in the Generation R Study, an ongoing population-based prospective cohort study from early fetal life onward, as described previously.[18] A total of 4854 adolescents were included in the current analyses (Figure S1).

2.2 | Physical condition

We used cardiorespiratory fitness, physical activity, and screen time as measures for physical condition. Cardiorespiratory fitness was measured by the steep ramp test on an electronically braked cycle ergometer (Lode Corival; Lode BV, 117200) according to the pediatric modified Streep Ramp Test protocol (Appendix S1). The primary outcome of the steep ramp test was the absolute WRpeak, which was defined as the highest achieved work rate in Watt during the test. We divided the obtained absolute WRpeak by the predicted absolute WRpeak based on a sex- and age-specific population-based Dutch reference.[15] This resulted in the percent predicted absolute WRpeak, which was subsequently standardized into Z-scores [(observed value − mean)/standard deviation]. None of the children was hampered by observed asthma symptoms to perform the steep ramp test.

Detailed information on physical activity and screen time was obtained by a self-reported questionnaire (Appendix S1). Subsequently, physical activity and screen time score were calculated in hours per day. We constructed sex-specific Z-scores ([observed value−mean]/standard deviation) for physical activity and screen time to enable the comparison of effect estimates.

2.3 | Respiratory outcomes

Lung function parameters including Forced Expiratory Flow in 1 s (FEV_1), Forced Vital Capacity (FVC), FEV_1/FVC, and Forced Expiratory Flow after exhaling 75% of FVC (FEF_{75}) were measured by spirometry according to ATS and ERS recommendations at the age of 13 years.[19] All curves were verified for acceptability and reproducibility, and converted into sex-, height-, age-, and ethnicity-adjusted z-scores according to the Global Lung Initiative reference data.[20] We used questions adapted from the International Study on Asthma and Allergy in Childhood (ISAAC) core questionnaires to obtain information on physician-diagnosed asthma.[21] Current asthma was defined as ever physician-diagnosed asthma with either wheezing or any asthma medication use in the past 12 months. For additional analyses, we used data on lung function and current asthma measured at the age of 9 years according to the same methods as at the age of 13 years.

2.4 | Covariates

Information on potential covariates including sociodemographic, lifestyle, and growth factors was collected as described in the Appendix S1.

2.5 | Statistical analysis

We compared the characteristics of participants and non-participants by using Mann–Whitney U tests, *t*-tests, and chi-square tests. Linear and logistic regression models were used to examine the associations of physical condition with lung function and asthma at the age of 13 years. More information on the defined models, confounder selection, additional analyses, multiple imputations, and adjustment for multiple hypothesis testing is described in the Appendix S1. Statistical analyses were performed using SPSS version 25.0 for Windows (IBM Corp.). More information on the defined models, confounder selection (Figure S2), additional analyses, multiple imputations and adjustment for multiple hypothesis testing is described in the supplemental methods.

3 | RESULTS

3.1 | Subject characteristics

Table 1 shows the characteristics of the children and their mothers participating in our study, and the differences with non-participants are in Table S1. Physical activity correlated with cardiorespiratory fitness and with screen time; the correlation coefficients ranged from very low to low, but cardiorespiratory fitness and screen time were not correlated (Table S2).

3.2 | Physical condition and respiratory outcomes

Results of the basic models on associations of physical condition with respiratory outcomes are presented in Table 2 and Figure 1. After adjustment for confounders and multiple hypothesis testing, a 1 SD lower cardiorespiratory fitness was associated with a lower FEV_1, FVC, and FEF_{75} (Z-score difference (95% CI): −0.31 (−0.35, −0.28), −0.30 (−0.33, −0.26), −0.13 (−0.17, −0.10), respectively), and with a higher risk of asthma (Odds Ratio (95% CI) 1.25 (1.06, 1.46); Table 2). After further adjustment for lung function or asthma at the age of 9 years to partly reduce the chance of reverse causation, the size and direction of the effect estimates remained similar for most of the associations, but the association of cardiorespiratory fitness with asthma became non-significant after multiple testing correction, and the association of cardiorespiratory fitness with the FEV_1/FVC ratio became statistically significant (Z-score difference (95% CI): −0.06 (−0.09, −0.04)). A lower physical activity was not consistently associated with lung function or asthma. A 1 SD higher screen time was, after adjustment for confounders and multiple testing, associated with a lower FVC (Z-score difference (95% CI): −0.06 (−0.10, −0.03) and persisted after additional adjustment for FVC at the age of 9 years.

We observed statistically significant interactions between cardiorespiratory fitness and sex in most of the associations with respiratory outcomes (*p*-values < .001 to .274). After stratification for sex, we observed similar directions of the associations of cardiorespiratory fitness with lung function and asthma in boys and girls. However, the magnitude of the effect estimates was higher in boys, and only in

TABLE 1 Characteristics of children and their mothers

	N = 4854
Maternal characteristics	
Pre-pregnancy BMI (kg/m^2)[a]	22.6 (17.9–34.3)
Age, years	31.2 (4.9)
Educational level, higher (%)	52.2 (2539)
History of asthma or atopy, yes (%)	37.8 (1833)
Parity, nullipara (%)	56.4 (2739)
Smoking during pregnancy, yes (%)	23.2 (1127)
Birth and infant characteristics	
Sex, female (%)	50.8 (2467)
Gestational age at birth (weeks)[a]	40.1 (35.6–42.3)
Birth weight (grams)	3443 (562)
Ethnic background, European (%)	69.8 (3389)
Ever breastfeeding, yes (%)	91.9 (4462)
Adolescent characteristics	
Age, years[a]	13.5 (13.1–14.6)
Pubertal status, early puberty	49.5 (2405)
Smoking, yes (%)	3.6 (175)
BMI (kg/m^2)[a]	19.1 (15.1–28.5)
Total fat mass (g)[a]	12,444 (6318-31,559)
Total lean body mass (g)[a]	36,626 (26,461-51,709)
Cardiorespiratory fitness (WRpeak, Watt)	274 (46)
Cardiorespiratory fitness (WRpeak, percent predicted)	96.3 (15.4)
Physical activity (h/day)[a]	0.74 (0.11–1.79)
Screen time (h/day)[a]	4.43 (1.46–10.79)
FEV_1 (z-score)	−0.14 (1.02)
FVC (z-score)	−0.04 (0.99)
FEV_1/FVC (z-score)	−0.19 (0.93)
FEF_{75} (z-score)	−0.21 (0.92)
Current asthma, yes (%)	5.8 (254)

Note: Values are means (SD), medians[a] (2.5–97.5th percentile), or valid percentages (absolute numbers) based on observed data. Peak Work Rate (WRpeak). Data on cardiorespiratory fitness (*n* = 478), physical activity (*n* = 1544), screen time (*n* = 1481), Forced Expiratory Volume in 1 s (FEV_1; *n* = 1158), Forced Vital Capacity (FVC; *n* = 1158), FEV_1/FVC ratio (*n* = 1158), Forced Expiratory Flow after exhaling 75% of FVC (FEF_{75}) (*n* = 1158), and current asthma (*n* = 479) was missing and not imputed.

TABLE 2 Associations of cardiorespiratory fitness, physical activity, and screen time with lung function and asthma at the age of 13 years

Physical condition (Z-score)	FEV_1 Z-score change (95% CI) *n* = 3696	FVC Z-score change (95% CI) *n* = 3696	FEV_1/FVC Z-score change (95% CI) *n* = 3696	FEF_{75} Z-score change (95% CI) *n* = 3696	Current asthma OR (95% CI) *n* = 4375
Cardiorespiratory fitness					
Basic model	*n* = 3561	*n* = 3561	*n* = 3561	*n* = 3561	*n* = 3905
	−0.28 (−0.32, −0.25)**	−0.29 (−0.32, −0.26)**	0.01 (−0.03, 0.04)	−0.08 (−0.11, −0.05)**	1.20 (1.05, 1.37)**
Main model	*n* = 3561	*n* = 3561	*n* = 3561	*n* = 3561	*n* = 3905
	−0.31 (−0.35, −0.28)**	−0.30 (−0.33, −0.26)**	−0.03 (−0.07, 0.01)	−0.13 (−0.17, −0.10)**	1.25 (1.06, 1.46)**
Reverse causation model	*n* = 2802	*n* = 2802	*n* = 2802	*n* = 2802	*n* = 3255
	−0.19 (−0.22, −0.17)**	−0.17 (−0.19, −0.14)**	−0.06 (−0.09, −0.04)**	−0.13 (−0.15, −0.10)**	1.26 (1.02, 1.57)*
Physical activity					
Basic model	*n* = 2421	*n* = 2421	*n* = 2421	*n* = 2421	*n* = 3225
	0.05 (0.01, 0.08)*	0.02 (−0.02, 0.06)	0.04 (0.00, 0.08)*	0.06 (0.02, 0.09)**	0.95 (0.81, 1.10)
Main model	*n* = 2421	*n* = 2421	*n* = 2421	*n* = 2421	*n* = 3225
	−0.01 (−0.05, 0.03)	−0.03 (−0.07, 0.00)	0.03 (−0.01, 0.07)	0.02 (−0.02, 0.05)	0.90 (0.77, 1.06)
Reverse causation model	*n* = 1973	*n* = 1973	*n* = 1973	*n* = 1973	*n* = 2786
	−0.01 (−0.03, 0.02)	−0.02 (−0.04, 0.01)	0.01 (−0.02, 0.04)	−0.00 (−0.03, 0.02)	0.90 (0.74, 1.10)
Screen time					
Basic model	*n* = 2475	*n* = 2475	*n* = 2475	*n* = 2475	*n* = 3287
	0.02 (−0.02, 0.06)	−0.00 (−0.04, 0.04)	0.04 (0.01, 0.08)*	0.05 (0.01, 0.08)**	1.16 (1.00, 1.34)*
Main model	*n* = 2475	*n* = 2475	*n* = 2475	*n* = 2475	*n* = 3287
	−0.04 (−0.08, −0.00)*	−0.06 (−0.10, −0.03)**	0.04 (0.00, 0.08)*	0.01 (−0.02, 0.05)	1.15 (0.99, 1.34)
Reverse causation model	*n* = 2023	*n* = 2023	*n* = 2023	*n* = 2023	*n* = 2840
	−0.02 (−0.04, 0.01)	−0.03 (−0.06, −0.01)**	0.03 (0.00, 0.06)*	0.02 (−0.01, 0.05)	1.07 (0.88, 1.30)

Values are derived from linear or logistic regression models and reflect changes in Z-scores or odds ratios (OR) (respectively) with a 95% confidence interval (95% CI) per SD decrease in cardiorespiratory fitness and physical activity, and increase in screen time. Forced Expiratory Flow in 1 s (FEV_1), Forced Vital Capacity (FVC), Forced Expiratory Flow after exhaling 75% of FVC (FEF_{75}). '*N*' represents the number of the total group. The basic model is adjusted for the child's sex and age. The main model is additionally adjusted for maternal pre-pregnancy BMI, age, education level, history of asthma and atopy, parity and smoking during pregnancy, and child's gestational age at birth, birth weight, ethnic background, ever breastfeeding, and child's current pubertal stage and BMI. The reverse causation model comprises the main model and is additionally adjusted for the child's lung function at the age of 9 years (only models with lung function as outcome) or child's asthma at the age of 9 years (only models with asthma as outcome).

*p-value < .05. **p-value < .019 (after multiple testing correction).

boys, a statistically significant association of a lower cardiorespiratory fitness with a lower FEV_1/FVC ratio and a higher risk of asthma was observed (Figure 1). No interaction was observed between physical condition and pubertal stage (p-values > .10). Statistically significant interactions were observed between cardiorespiratory fitness or physical activity and BMI for the associations with respiratory outcomes (p-values < .001 to .734). After stratification for BMI, higher magnitudes of the effect estimates were mainly observed for the associations of a lower cardiorespiratory fitness with a lower FEV_1, FVC, and FEF_{75} in overweight or obese children as compared to underweight or normal weight children, whereas the association with asthma was stronger in the underweight or normal weight group (Table S3). No other statistical interactions of sex, pubertal stage, or BMI in the associations of physical condition with respiratory outcomes were observed. When we restricted our population to children with a Dutch ethnic background, non-smokers, or to children with a heart rate peak ≥85% of their predicted peak, we observed similar size and directions of the effect estimates for the associations of physical condition with respiratory outcomes as in the whole population (Tables S4-S6). Last, when we adjusted for fat mass index and lean body mass index instead of BMI, we mainly observed that the magnitude of the association of cardiorespiratory fitness with FEV1, FVC, and FEF_{75} attenuated, and the association of lower physical activity with a higher FEV_1 and FEF_{75} became stronger (Table S7).

4 | DISCUSSION

Results from this population-based study showed that a lower cardiorespiratory fitness was associated with a lower FEV_1, FVC, and FEF_{75}, and a higher risk of asthma in adolescents. Effect estimates were stronger in boys than in girls, and only in boys, a lower

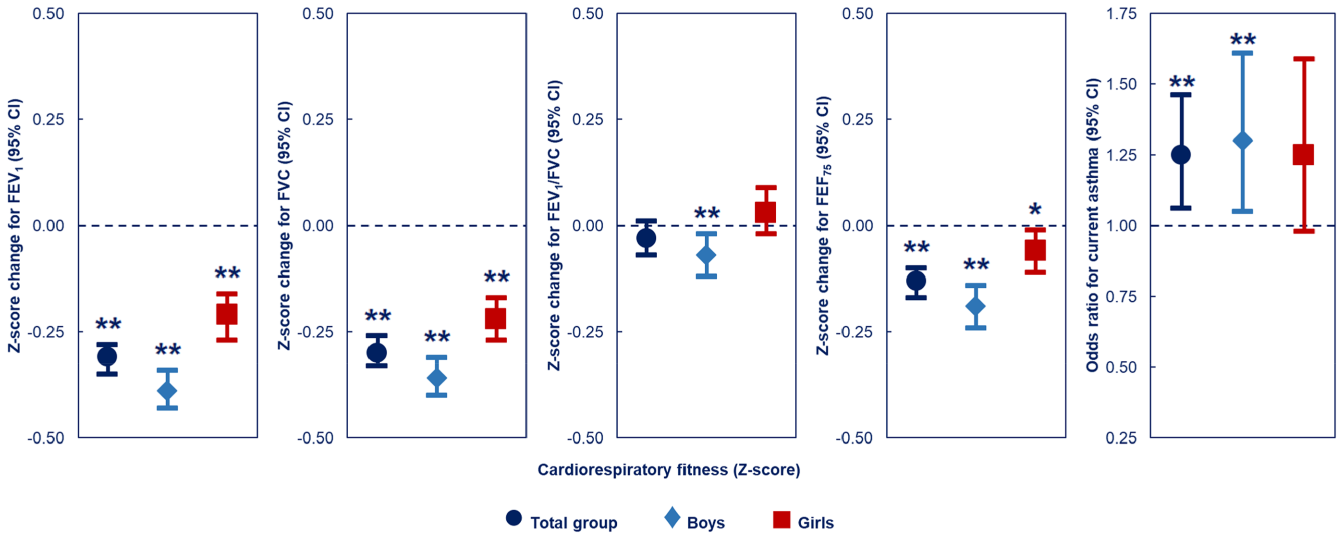

FIGURE 1 Associations of cardiorespiratory fitness with lung function and asthma at the age of 13 years. Values are derived from linear or logistic regression models and reflect changes in Z-scores or odds ratios (OR) (respectively) with a 95% confidence interval (95% CI) per SD decrease in cardiorespiratory fitness in the total group, and in boys and girls separately. Forced Expiratory Flow in 1 s (FEV_1), Forced Vital Capacity (FVC), and Forced Expiratory Flow after exhaling 75% of FVC (FEF_{75}). The models are adjusted for maternal pre-pregnancy BMI, age, education level, history of asthma and atopy, parity and smoking during pregnancy and child's sex (only for the models in the total group), gestational age at birth, birth weight, ethnic background, ever breastfeeding, and child's current pubertal stage, BMI and age. *p-value < .05. **p-value < .019 (after multiple testing correction)

cardiorespiratory fitness was related to a lower FEV_1/FVC ratio. A higher screen time was associated with a lower FVC, but both physical activity and screen time were not related to current asthma.

4.1 | Comparison with previous studies

Our findings that a lower cardiorespiratory fitness was associated with a lower FEV_1, FVC, and FEF_{75} are in line with the results of a previous study that used data of two population-based cohorts. These observed that a lower physical fitness was associated with a lower percentage of predicted FEV_1 and FVC in children and adolescents, but not with the FEV_1/FVC ratio.[10] Our results additionally suggest that these associations are also present in the smaller airways as shown by the association of cardiorespiratory fitness with FEF_{75}. Although FEF_{75} has been suggested as a marker of early peripheral airway patency on a group level, the use of this measure remains the subject of much debate in individuals.[22] In contrast, two other studies that examined cardiorespiratory fitness in late childhood or repeatedly from adolescence until early adulthood did not find an association of cardiorespiratory fitness with lung function outcomes.[12,14] The present and previous studies show inconsistent results on the associations of cardiorespiratory fitness with asthma in childhood and adolescence.[11,13] Differences in findings might be due to the low sample sizes in previous studies and thereby a lack of power, or the use of different tests to assess cardiorespiratory fitness.[9] We did not find consistent associations of physical activity with respiratory outcomes. Comparison with other cross-sectional or longitudinal studies is problematic due to heterogeneity in physical activity assessment.[4–6] We observed an association of a higher screen time with a lower FVC, and not with asthma. Other studies did not find a consistent longitudinal association of screen time with lung function outcomes and observed inconsistent results on the association of screen time with asthma.[7,23,24] More studies with robust and objective measurements of different types of physical activity and inactivity in relation to respiratory outcomes are needed.

4.2 | Interpretation of the results

Several mechanisms are suggested to play a role in the observed relation of a lower cardiorespiratory fitness with a lower lung function and higher risk of asthma. During regular exercise training, a determinant of cardiorespiratory fitness, forceful inspiration, and expiration might strengthen the respiratory muscles, increase the pulmonary perfusion and surfactant release, and subsequently lead to higher lung volumes and potentially protect against asthma symptoms.[25,26] In contrast, during screen time, there might be a decreased frequency of spontaneous sighs, which might affect lung function by reducing airway elasticity and thereby explain the association of higher screen time with a lower FVC.[27] Although a lower cardiorespiratory fitness was related to a higher risk of asthma, the association with airway obstruction defined by a lower FEV_1/FVC was less pronounced in our study. These differences in results may presumably be because not all children with well-treated asthma have an abnormal lung function. However, other potential underlying mechanisms also require further investigation, such as the role of systemic inflammation and body composition, as the associations of cardiorespiratory fitness and physical activity with lung function outcomes slightly changed after additional adjustment for fat mass and lean body mass indices.[9,14] Cardiorespiratory fitness and physical activity are interrelated but are different entities, as cardiorespiratory fitness reflects the capacity to be physically active, whereas physical activity is an actual behavior.[9] The absence of an association of physical activity with respiratory outcomes might be due to our inability to distinguish between the intensity of physical activity, as especially vigorous activity might affect cardiorespiratory fitness, and differences in the effect of the same dose of physical activity on cardiorespiratory fitness between individuals.[8,9]

We observed stronger associations of cardiorespiratory fitness with respiratory outcomes in boys than in girls. This might partly be explained by a higher amount of oxygen that is extracted from the blood in boys than in girls.[28] Also, boys have a faster airway growth during puberty.[29] These mechanisms could make the lungs more susceptible to the beneficial effects of a better cardiorespiratory fitness. The associations of cardiorespiratory fitness with BMI are complex and possibly bidirectional.[9] It has been suggested that high levels of cardiorespiratory fitness can attenuate the adverse health effects of obesity and vice versa, which might explain the differences in the associations of cardiorespiratory fitness with respiratory outcomes in overweight or obese children and underweight or normal weight children in our study.

Our findings can be of special importance since both cardiorespiratory fitness and lung outcomes track into adulthood. Determinants of cardiorespiratory fitness include genetics, sex, age, ethnic background, and sociodemographic and lifestyle-related factors such as BMI and body composition, and these factors are partly modifiable potentially leading to a lower lung function decline.[9,15]

4.3 | Strengths and limitations

The major strengths of this study are the population-based design with a large sample size and the use of objective and validated measures as cardiorespiratory fitness and lung function. However, some methodological limitations of this study need to be addressed. First, due to the cross-sectional and observational design of this study, we cannot draw any conclusions about causality. However, the associations did not materially change after additional adjustment for lung function or asthma at the age of 9 years, which reduces the possibility that respiratory outcomes earlier in life have affected physical condition at the age of 13 years, thereby partially reducing the possibility of reverse causation in the observed association of physical condition and respiratory outcomes at the age of 13 years. Second, the steep ramp test was performed on all participants after the lung function test to limit the chance of bias through an exercise-induced bronchospasm. Although none of the participants had asthma symptoms during the test, the performance of the steep ramp test might be somewhat limited by muscle fatigue.[16] The study population is a multiethnic population, but the steep ramp test has only been validated in children with a Dutch ethnic background. However, a sensitivity analysis restricted to children with a Dutch ethnic background showed similar results as in the whole population, indicating that our results were not affected by ethnic background. Third, obtaining data on physical activity or screen time from questionnaires might not be as accurate as objective data from accelerometers. Nevertheless, questionnaires might be easier to apply in a large study population and better reflect daily habits as accelerometers are insensitive to many forms of physical activity including bicycling.[30] Last, we cannot rule out residual confounding due to the child's muscle strength, which was not measured.

5 | CONCLUSION

In adolescents, a lower cardiorespiratory fitness is associated with a lower lung function and a higher risk of asthma. Higher screen time is related to a lower FVC. Future intervention studies should examine whether improving cardiorespiratory fitness or reducing screen time in adolescence has a beneficial effect on respiratory outcomes in the long term.

AUTHOR CONTRIBUTIONS

Sara M Mensink-Bout: Conceptualization (equal); formal analysis (lead); investigation (supporting); methodology (equal); writing – original draft (lead); writing – review and editing (lead). **Marc Jahangir:** Formal analysis (supporting); writing – original draft (supporting); writing – review and editing (supporting). **Johan C de Jongste:** Conceptualization (supporting); supervision (supporting); writing – review and editing (supporting). **Hein Raat:** Conceptualization (equal); methodology (supporting); writing – review and editing (supporting). **Vincent WV Jaddoe:** Conceptualization (equal); funding acquisition (lead); supervision (supporting); writing – review and editing (supporting). **Liesbeth Duijts:** Conceptualization (equal); formal analysis (supporting); funding acquisition (lead); investigation (lead); methodology (equal); supervision (lead); writing – original draft (lead); writing – review and editing (lead).

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CONFLICT OF INTEREST

The authors declare that they have no relevant conflicts of interest.

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