Received: 19 November 2023 | Revised: 10 January 2024 | Accepted: 13 January 2024

DOI: 10.1111/pai.14079

ORIGINAL ARTICLE

WILEY

Abdominal fat and risk of impaired lung function and asthma in children: A population-based prospective cohort study

Tong Wu[1,2] | Tarik Karramass[1,3,4] | Vincent W. V. Jaddoe[1,3] | Stefan Klein[2] | Edwin H. G. Oei[2] | Liesbeth Duijts[4,5]

[1]The Generation R Study Group, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

[2]Department of Radiology and Nuclear Medicine, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

[3]Department of Pediatrics, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

[4]Division of Respiratory Medicine and Allergology, Department of Pediatrics, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

[5]Division of Neonatology, Department of Neonatal and Pediatric Intensive Care, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

Correspondence
Liesbeth Duijts, Erasmus MC - Sophia, University Medical Center Rotterdam, PO Box 2060, 3000 CB Rotterdam, The Netherlands.
Email: l.duijts@erasmusmc.nl

Funding information
China Scholarship Council (CSC); European Union's Horizon 2020 research and innovation program, Grant/Award Number: 874583, 824989 and 733206; ZonMW The Netherlands, Grant/Award Number: 10150062010006

Editor: Ömer KALAYCI

Abstract

Background: Obesity, specifically abdominal adiposity, is associated with increased risks of lung function impairment and asthma in children, but potential adverse effects among adolescents are unknown. We hypothesized that elevated amounts of specific abdominal fat depots during childhood and adolescence may lead to adverse respiratory outcomes in adolescents.

Methods: In a population-based prospective cohort study among 2877 children at 13 years, we measured specific abdominal fat depots including subcutaneous fat mass and visceral fat mass by magnetic resonance imaging. Lung function was measured by spirometry, and current asthma by a questionnaire. Conditional regression analyses were used to examine the associations of abdominal fat depots with respiratory outcomes in adolescence.

Results: After adjustment for confounders and child's body mass index, higher subcutaneous and visceral fat mass index at age 13 years, independent of these measures at earlier age, were associated with lower FEV_1, FEV_1/FVC, and FEF_{75} (range *Z*-score difference (95% CI): −0.10 (−0.15, −0.06) to −0.06 (−0.11, −0.01)). Also, an increase in subcutaneous and visceral fat between ages 10 and 13 years was associated with a decrease in FEV_1, FEV_1/FVC, and FEF_{75} during the same period. No associations of abdominal fat depots with asthma were observed.

Conclusion: Adolescents with higher amounts of subcutaneous and visceral fat, independent of that at an earlier age and body mass index, have an increased risk of lung function impairment.

KEYWORDS
asthma, abdominal fat mass, children, lung function, MRI, obesity

Edwin H. G. Oei and Liesbeth Duijts contributed equally.

1 | INTRODUCTION

Asthma and obesity are common health issues with increasing prevalences worldwide, with a suggested association between the two conditions.[1,2] The mechanisms behind the asthma-obesity link are not fully clear. In children, it has been suggested that obesity may result in dysanaptic growth of the lungs, resulting in decreased airway capacity and obstruction of airflow, and production of pro-inflammatory cytokines by fat tissue, which could induce airway inflammation.[3,4] Recent pediatric studies found that trunk body fat measured by waist-to-hip ratio served as an endotype in childhood obesity-related asthma.[5] Our previous cross-sectional studies showed that, unlike measures of general adiposity, a higher preperitoneal fat mass, a proxy of visceral fat, was associated with a higher fractional exhaled nitric oxide as a manifestation of pulmonary inflammation in children aged 6 years.[6] Most prominently in children aged 9 years, a higher visceral fat index measured by magnetic resonance imaging (MRI) techniques, was associated with a higher FVC, a lower forced expiratory volume in 1 s/forced vital capacity (FEV_1/FVC), and a higher risk of asthma, independent of fat mass index.[7] These results suggest that fat accumulated in specific body regions might be associated with children's lung health, but it is unclear whether these effects persist into adolescence. MRI is a safe and non-invasive imaging technique that is well-tolerated by most children, allowing advanced body composition and regional fat content assessments including subcutaneous fat and visceral fat in large-scale studies.[8]

Therefore, we examined the associations of abdominal subcutaneous fat and visceral fat assessed by MRI, independent of the child's body mass index (BMI), with lung function and asthma at age 13 years among 2877 children participating in a population-based cohort study. Additionally, we examined the change in abdominal fat depots between ages 10 and 13 years in relation to changes in lung function and asthma in the same period.

Key message

Adolescents with higher amounts of subcutaneous and visceral fat, independent of that at an earlier age and body mass index, have increased risks of lower lung function measures. Current findings highlight the importance of accurate assessment for specific abdominal fat depots beyond body mass index when studying the association of body weight with respiratory outcomes and reducing abdominal fat mass may improve respiratory health in children.

2 | METHODS

2.1 | Design

This study was embedded in the Generation R Study, a population-based prospective cohort from fetal life onward in Rotterdam, the Netherlands.[9] The Generation R Study has been approved by the Medical Ethical Committee of the Erasmus MC, University Medical Centre in Rotterdam (MEC-2012-165-NL40020.078.12). Written informed consent was obtained from all participants and their parents or legal representatives. Of 6842 participants at age 13 years, twins ($n=172$) and children with missing information on specific abdominal fat measurements (i.e., subcutaneous fat mass and visceral fat mass; $n=3765$), and lung function or current asthma ($n=28$) were excluded. This resulted in 2877 children for the current analyses (Figure 1).

2.2 | Specific abdominal fat measurements

Subcutaneous fat and visceral fat were measured at ages 10 and 13 years using a 3.0 Tesla MRI (GE Discovery MR750w, GE Healthcare, Milwaukee, WI, USA) at our research center. Children wore light clothing without metal objects while undergoing the total body scan in the supine position.[10] The scanner was operated by trained research technologists and all imaging data were collected according to standardized protocols. Detailed information on the measurements of subcutaneous fat and visceral fat at ages 10 and 13 years are described in the Data S1.

2.3 | Lung function and asthma

At ages 10 and 13 years, lung function parameters were measured by spirometry,[11] and converted into sex-, height- and age-, and ethnicity-adjusted *Z*-scores.[11,12] Information on physician-diagnosed asthma and wheezing was obtained by a parental questionnaire, based on the International Study on Asthma and Allergy in Childhood (ISAAC) Questionnaire.[13] Information on asthma medication use was obtained during the visit to our research center. Current asthma was defined as a diagnosis of asthma ever, with either wheezing or any asthma medication use in the past 12 months. We considered lung function measures and asthma at age 13 years as primary outcomes. Secondary outcomes were the change in lung function measures [(lung function at 13 years − lung function at 10 years)/time of follow up in years], and change in current asthma (no change, current asthma to no asthma, no asthma to current asthma, persistent current asthma) between age 10–13 years. Details on obtaining lung function parameters and information on asthma are described in the Data S1.

2.4 | Covariates

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

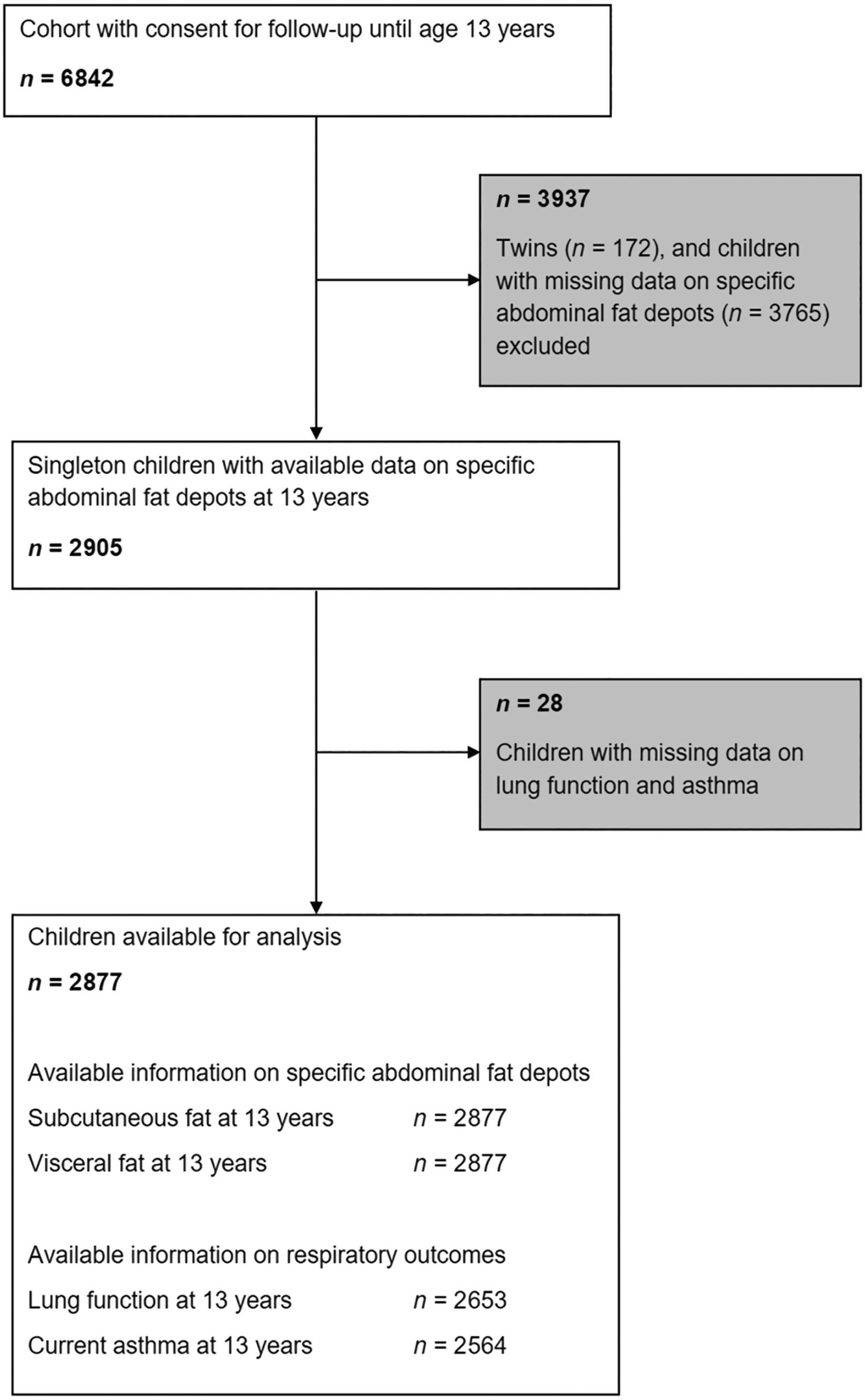

FIGURE 1 Flowchart of participants included for analysis.

2.5 | Statistical analysis

We assessed the characteristics of children included and not included in the study using Student's *t*-tests, Mann–Whitney *U* tests, and Chi-square tests. We performed conditional regression analyses to assess the independent associations of specific abdominal fat depots with respiratory outcomes at age 13 years.[14,15] More information on the multistage models, confounder selection (Figure S1), additional analyses, and multiple imputations is described in the Data S1. Statistical analyses were performed using SPSS, version 28.0 for Windows (IBM Crop., Armonk, NY, USA) and R version 4.2.0 (R Foundation, Vienna, Austria).

3 | RESULTS

3.1 | Participants characteristics

Table 1 shows the characteristics of mothers and children. Current asthma was present in 6.0% ($n = 154$) of children. Non-response analyses showed that children included in the analyses had mothers who were highly educated, more likely to be non-smokers during pregnancy and nulliparous, had a higher gestational age at birth, a higher birth weight, and were often from a European ethnic background (p value $< .05$; Table S1). The correlation coefficients of

TABLE 1 Characteristics of children and their mothers.

	Total	Missing
Maternal characteristics		
Pre-pregnancy age (years)	31.2 (4.9)	0
Pre-pregnancy body mass index (kg/m^2)†	22.5 (18.3–34.6)	25.2% (725)
Educational level (%)		
Low	6.8 (180)	7.7% (222)
Mid	40.3 (1069)	
High	53.0 (1406)	
History of asthma or atopy (%)		
No	62.3 (1538)	14.3% (410)
Yes	37.7 (929)	
Parity (%)		
Multiparous	41.2 (1151)	2.9% (83)
Nulliparous	58.8 (1643)	
Psychiatric symptoms (%)		
No	92.3 (2037)	2.3% (671)
Yes	7.7 (169)	
Smoking during pregnancy (%)		
No	77.6 (1946)	12.9 (370)
Yes	22.4 (561)	
Birth and infant characteristics		
Sex (%)		
Girl	48.1 (1384)	0
Boy	51.9 (1493)	
Gestational age at birth (weeks)†	40.1 (35.6–42.3)	0.6% (16)
Birth weight (g)	3437 (566)	0.1% (3)
Ethnic background, European (%)		
No	29.9 (844)	1.9% (56)
Yes	70.1 (1977)	
Ever breastfeeding (%)		
No	6.4 (156)	15.9% (457)
Yes	93.6 (2264)	
Childhood characteristics		
Age at visit (years)	9.8 (0.3)	5.7% (164)
Diet (kcal/day)	1493 (387)	26.5% (761)
Physical activity (hours/day)†	1.3 (0.3–3.6)	21.5% (618)
Inhalant allergic sensitization (%)		
No	68.1 (1442)	26.4% (759)
Yes	31.9 (676)	
Body mass index (kg/m^2)	17.4 (2.6)	6.1% (176)
Subcutaneous fat mass (g)†	1267 (602–4870)	42.3% (1216)
Visceral fat mass (g)†	352 (161–979)	42.3% (1216)
Adolescent characteristics		
Age at visit (years)	13.6 (0.4)	0
Pubertal status, Tanner (%)		
Stages 1–3	48.6 (988)	29.4% (845)
Stages 4–5	51.4 (1044)	

TABLE 1 (Continued)

	Total	Missing
Subcutaneous fat mass (g)[†]	841 (246–4046)	0
Visceral fat mass (g)[†]	232 (90–867)	0
FEV_1 (L)	3.1 (0.5)	7.8% (224)
FVC (L)	3.6 (0.6)	7.8% (224)
FEV_1/FVC	0.9 (0.1)	7.8% (224)
FEF_{75} (L/s)	1.8 (0.6)	7.8% (224)
Current asthma at age 13 years (%)		
No	94.7 (2217)	10.9% (313)
Yes	6.0 (154)	

Note: Values are means (SD), medians[†] (2.5–97.5th percentile) or valid percentages (absolute numbers) based on observed data. Data on subcutaneous fat mass at 13 years ($n=2877$), visceral fat mass at 13 years ($n=2877$), and forced expiratory volume in 1 s (FEV_1; $n=2653$), forced vital capacity (FVC; $n=2653$), FEV_1/FVC ratio ($n=2653$), forced expiratory flow after exhaling 75% of FVC (FEF_{75}; $n=2653$) and current asthma ($n=2564$) was missing and not imputed.

BMI with abdominal fat depot measures were moderate to strong (Table S2).

3.2 | Specific abdominal fat depots and respiratory health

We studied the associations of specific abdominal fat depots with respiratory outcomes at age 13 years. In our confounder model, a higher subcutaneous fat mass index was associated with lower FEV_1, FEV_1/FVC, and FEF_{75}. Higher visceral fat mass index was associated with lower FEV_1/FVC and FEF_{75}. After additional adjustment for child's BMI, both subcutaneous and visceral fat mass index were consistently associated with lower FEV_1 (*Z*-score difference (95% CI): −0.06 (−0.11, −0.01), −0.09 (−0.14, −0.04), respectively), FEV_1/FVC (*Z*-score difference (95% CI): −0.10 (−0.15, −0.05), −0.08 (−0.13, −0.04), respectively) and FEF_{75} (*Z*-score difference (95% CI): −0.10 (−0.15, −0.05), −0.10 (−0.15, −0.06), respectively; Table 2). After further adjustment for lung function or asthma at age 10 years, the size and direction of the effect estimates remained similar for most of the associations (Table S3).

Secondary outcome analyses showed that each unit increase in the change of subcutaneous fat mass index and visceral fat mass index between ages 10 and 13 years were associated with decreasing FEV_1, FEV_1/FVC, and FEF_{75} between similar ages (range *Z*-score difference (95% CI): −0.13 (−0.18, −0.08) to −0.06 (−0.11, −0.01)), based on our main model and after taking lung functions at age 10 years into account (Table 3). No associations of change in abdominal fat depots with change in asthma were observed (Table 4). For the main models, we observed no consistent interaction between specific abdominal fat depot measures and the child's sex, allergic sensitization, or puberty status for the associations with lung function and asthma ($p > .05$), except for subcutaneous fat mass index at age 13 years with child's sex on the associations with FEV_1 ($p = .012$) and FVC ($p = .010$). Results of analyses stratified for sex showed that the size of effect estimates for associations of subcutaneous and visceral fat mass index at age 13 years with lower FEV_1 and FVC at age 13 years were larger in boys than in girls (Table S4). No non-linearity was observed for the associations of abdominal fat measurements with respiratory outcomes in adolescents. When we performed sensitivity analyses and excluded underweight children, non-European ancestry, or non-reproducible spirometry curves, no changes in directions and magnitudes of the effect estimates were found (Tables S5–S7). When exploratively examining the extremes, we observed large effect sizes, although some were non-significant, for the associations of a very high subcutaneous fat mass index with a higher risk of FEV_1, FEV_1/FVC ratio, and FEF_{75} below the lower limit of normal (range *Z*-score change (95% CI): 1.62 (0.86, 3.07)–2.77 (1.37, 5.60)), and of a high visceral fat mass index with a higher risk of FEV_1 FVC, FEV_1/FVC ratio, and FEF_{75} below the lower limit of normal (1.40 (0.74, 2.65)–2.33 (1.18, 4.59); Table S8).

4 | DISCUSSION

In this population-based prospective cohort study, we found that higher subcutaneous and visceral fat mass index, as assessed by MRI, were associated with lower FEV_1, FEV_1/FVC, and FEF_{75} at age 13 years, independent of adiposity measures and BMI at age 10 years. Furthermore, we observed that an increase in these fat mass indices between ages 10 and 13 years was associated with a decrease of FEV_1, FEV_1/FVC, and FEF_{75} during similar ages. We observed no associations of abdominal fat indices with asthma.

4.1 | Comparison with previous studies

Previous meta-analyses have shown that children with overweight or obesity had a more pronounced FEV_1/FVC deficit with unchanged or higher FEV_1 or FVC, and an increased risk of asthma.[3,16] In terms of specific abdominal fat depots, a systematic review of studies found inconsistent evidence regarding the link between

TABLE 2 Associations of specific abdominal fat depots with lung function and asthma at the age of 13 years.

	FEV_1 *Z*-score difference (95% CI) *n* = 2653	FVC *Z*-score difference (95% CI) *n* = 2653	FEV_1/FVC *Z*-score difference (95% CI) *n* = 2653	FEF_{75} *Z*-score difference (95% CI) *n* = 2653	Current asthma OR (95% CI) *n* = 2564
Subcutaneous fat mass index *Z*-score (*n* = 2877)					
Basic model	−0.04 (−0.10, 0.01)	0.01 (−0.04, 0.06)	−0.10 (−0.15, −0.05)	−0.09 (−0.14, −0.04)	1.12 (0.91, 1.37)
p value	.092	.706	<.001	<.001	.302
Confounder model	−0.07 (−0.12, −0.02)	−0.01 (−0.06, 0.04)	−0.11 (−0.16, −0.06)	−0.11 (−0.16, −0.06)	1.10 (0.88, 1.37)
p value	.009	.743	<.001	<.001	.399
BMI model	−0.06 (−0.11, −0.01)	−0.00 (−0.05, 0.04)	−0.10 (−0.15, −0.05)	−0.10 (−0.15, −0.05)	1.08 (0.87, 1.34)
p value	.023	.868	<.001	<.001	.504
Visceral fat mass index *Z*-score (*n* = 2877)					
Basic model	−0.01 (−0.06, 0.04)	0.03 (−0.02, 0.08)	−0.07 (−0.12, −0.03)	−0.06 (−0.10, −0.01)	0.97 (0.78, 1.20)
p value	.743	.231	.003	.018	.757
Confounder model	−0.05 (−0.10, 0.00)	0.00 (−0.05, 0.05)	−0.09 (−0.14, −0.04)	−0.09 (−0.14, −0.05)	0.95 (0.75, 1.19)
p value	.074	.965	<.001	<.001	.654
BMI model	−0.09 (−0.14, −0.04)	−0.04 (−0.09, 0.01)	−0.08 (−0.13, −0.04)	−0.10 (−0.15, −0.06)	0.94 (0.74, 1.19)
p value	<.001	.085	<.001	<.001	.620

Note: 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 increase in specific fat depot measures, independent from abdominal fat depot measures at earlier age. The basic models were for child's age and sex. The confounder models were adjusted for maternal age, pre-pregnancy BMI, educational level, history of asthma or atopy, parity, psychiatric symptoms and smoking during pregnancy, and child's age, sex, gestational age at birth, birth weight, ethnic background, breastfeeding, diet, and physical activity. The BMI (main) models were additionally adjusted for child's body mass index. FEV_1, Forced Expiratory Flow in 1 s; FEF_{75}, Forced Expiratory Flow after exhaling 75% of FVC; FVC, forced vital capacity.

TABLE 3 Associations of the changes in specific abdominal fat depots between 10 and 13 years with changes in lung function measures in the same period.

	Change in FEV_1 Z-score difference (95% CI) n = 2234	Change in FVC Z-score difference (95% CI) n = 2234	Change in FEV_1/FVC Z-score difference (95% CI) n = 2234	Change in FEF_{75} Z-score difference (95% CI) n = 2234
Change in subcutaneous fat mass index Z-score (n = 1661)				
BMI model	−0.06 (−0.11, −0.01)	0.01 (−0.04, 0.06)	−0.11 (−0.16, −0.06)	−0.11 (−0.16, −0.06)
p value	.025	.727	<.001	<.001
Change in visceral fat mass index Z-score (n = 1661)				
BMI model	−0.08 (−0.13, −0.03)	−0.02 (−0.07, 0.03)	−0.11 (−0.16, −0.06)	−0.13 (−0.18, −0.08)
p value	.002	.482	<.001	<.001

Note: Values are derived from linear regression models and reflect changes in Z-scores, with a 95% confidence interval (95% CI) per SD increase in changes of specific fat depot measures. The BMI (main) models were adjusted for maternal age, pre-pregnancy BMI, educational level, history of asthma or atopy, parity, psychiatric symptoms and smoking during pregnancy, and child's age, sex, gestational age at birth, birth weight, ethnic background, breastfeeding, diet, physical activity, and body mass index, and additionally adjusted for respiratory outcomes at age 10 years. FEV_1, Forced Expiratory Flow in 1 second; FEF_{75}, Forced Expiratory Flow after exhaling 75% of FVC; FVC, forced vital capacity.

abdominal subcutaneous fat and respiratory outcomes in adults.[17] However, there is strong evidence linking abdominal visceral fat to asthma in adults.[17] The evidence about the relationship between abdominal fat depots and respiratory outcomes in children is scarce.[17] In children, most previous studies used computed tomography to measure areas of abdominal subcutaneous or visceral fat at the umbilical level, instead of volumes.[17] Our study is the first to examine the longitudinal associations between quantitative measures for abdominal fat depots, using MRI during childhood and adolescence, and lung function and asthma in adolescence. We found that higher levels of visceral fat at age 13 years were associated with obstructive lung pattern at age 13 years, which is consistent with our previous cross-sectional study conducted when the children were 10 years old.[7] Our current longitudinal findings indicate that visceral fat at age 10 years is not associated with lung function measures at age 13 years, but that change in fat indices between age 10 and 13 years are associated with lung function changes in the same period indicating that changes in body composition around puberty are important for lung health. The associations of specific abdominal fat depot measures at age 13 years with FEV_1 and FVC at age 13 years were stronger in boys than girls, which may be due to the differences in the way that fat is distributed in the body between males and females during pubertal years.[18] We did not observe associations of abdominal fat indices with asthma, which could imply that during puberty an increase of abdominal fat depots may more prominently affect dysanaptic growth of the lungs, resulting in decreased airway capacity and obstruction of airflow, rather than affecting the production of pro-inflammatory cytokines by fat tissue resulting in airway inflammation and asthma symptoms.

4.2 | Interpretation of the results

It is well known that obesity leads to an inflammatory response involving the release of inflammation-related adipokines within adipose tissue, which might contribute to airway inflammation and remodeling occurring in asthma.[4] Meta-analyses including pediatric studies have revealed a dose–response relationship between abdominal weight status and asthma, with a stronger correlation found in adolescents compared to younger school-age children.[19] To date, several types of adipose tissue have been identified in various specific anatomical locations throughout the abdomen. As a result, the impact of adipose tissue dysfunction becomes varying due to adipose tissue depot-specific adipokines, inflammatory profiles, and metabolism specific to each depot.[20,21] This makes it challenging to compare the effects of subcutaneous and visceral fat between childhood and adolescence on respiratory morbidity. Our finding of a significant association between fat depot measures at age 13 years and impaired lung function at age 13 years, independent of fat depot measures taken at age 10 years, suggests that the accumulation of subcutaneous and visceral fat may have a greater impact on lung function during adolescence

TABLE 4 Associations of the changes in specific abdominal fat depots between 10 and 13 years with the change in current asthma in the same periods.

	No change OR (95% CI) *n* = 2206	Current asthma to no asthma OR (95% CI) *n* = 2206	No asthma to current asthma OR (95% CI) *n* = 2206	Persistent current asthma OR (95% CI) *n* = 2206
Change in subcutaneous fat mass index *Z*-score (*n* = 1661)				
BMI model	0.99 (0.69, 1.42)	0.70 (0.37, 1.31)	1.01 (0.71, 1.45)	1.43 (0.76, 2.69)
p value	.941	.264	.941	.264
Change in Visceral fat mass index *Z*-score (*n* = 1661)				
BMI model	1.17 (0.81, 1.70)	0.96 (0.55, 1.65)	0.85 (0.59, 1.24)	1.05 (0.61, 1.81)
p value	.410	.871	.410	.871

Note: Values are derived from logistic regression models and reflect changes in odds ratios (OR), with a 95% confidence interval (95% CI) per SD increase in changes of specific fat depot measures. The BMI (main) models were adjusted for maternal age, pre-pregnancy BMI, educational level, history of asthma or atopy, parity, psychiatric symptoms and smoking during pregnancy, and child's age, sex, gestational age at birth, birth weight, ethnic background, breastfeeding, diet, physical activity, and body mass index, and additionally adjusted for respiratory outcomes at age 10 years.

compared to earlier school-age years. Adolescence is a period of rapid growth and change, which may also involve shifts in body composition.[18] Consequently, changes in body fat distribution, such as an increase in abdominal subcutaneous and visceral fat, during this stage could have a more considerable impact on lung function than adiposity level measured at age 10 years. Other factors such as genetics, diet, and environment may also contribute to this difference.[22]

A few studies in adults have found no association between subcutaneous fat and lung function, and they have identified a negative association between visceral fat and lung function.[23,24] This has led to the argument that visceral fat may be more important than subcutaneous fat for adverse respiratory health. However, our study found the same direction of effect estimates of both subcutaneous and visceral fat on potential obstructive lung function pattern and lower small airway function. Conversely, studies have more consistently identified a negative association between abdominal visceral fat and lung function and asthma risk in both adults and children.[6,7,17] This was mostly explained by the fact that visceral fat produces hormones and other substances such as CRP, IL-6, and TNF-α that can cause airway inflammation and limit lung function.[5,20] Additionally, both subcutaneous and visceral fat depots can hinder breathing by compressing the diaphragm, resulting in reduced lung capacity and function. In our explorative analysis, we observed large effect estimates for the associations of a very high subcutaneous or visceral fat mass index with lung function outcomes, although some associations were not statistically significant when compared to our associations in the conditional regression analyses. This could suggest that a portion of our observed effect estimates might not be clinically relevant, particularly at an individual level, or that we lacked power. Further research is needed to explore the causality and potential underlying mechanisms between specific abdominal fat depots and respiratory health measures, especially longitudinally from childhood into adolescence, and further into adulthood.

4.3 | Strengths and limitations

The major strength of this study was that it is embedded in a population-based prospective cohort study with a large sample size. To detect the amount of specific abdominal fat depots, and the use of MRI techniques that enabled high-precision estimation for adipose tissue. Several potential covariates were considered, such as physical activity, diet, BMI and previous lung function, and asthma. However, some limitations apply to our study. First, non-response might have given a selection toward a more healthy and affluent population, which could have led to biased effect estimates. Second, non-differential misclassification due to parental-report asthma might have been present although asthma was defined based on validated questionnaires which are widely used in epidemiological studies.[13] Post-bronchodilation spirometry tests may have supported the diagnosis of asthma more objectively. However, we considered it not ethically feasible to give medication or substances with potential side effects or trigger of an asthma attack to a large, general, and relatively healthy pediatric population. Third, despite adjusting for multiple confounders, residual confounding such as imperfect measures, and unmeasured or unknown factors may still have occurred as in all observational studies. Last, the observed sizes of effect estimates were relatively small to moderate and may not hold clinical significance at an individual level for adolescents, but they might be of importance from a population-based perspective.

5 | CONCLUSION

We observed that higher amounts of specific abdominal fat depots were associated with lower lung function in adolescents, independent of previous adiposity measures and BMI. An increase in these abdominal fat depots between age 10 and 13 years was associated with a decrease in lung function measures during similar ages. These findings suggest that reducing abdominal fat mass in specific compartments in adolescents may be an effective strategy for improving respiratory health.

AUTHOR CONTRIBUTIONS

Tong Wu: Conceptualization; data curation; formal analysis; writing – original draft; writing – review and editing; software; methodology; visualization; investigation. **Tarik Karramass:** Conceptualization; methodology; data curation; formal analysis; writing – original draft; writing – review and editing; investigation. **Vincent W. V. Jaddoe:** Conceptualization; data curation; methodology; writing – review and editing; supervision; project administration; investigation. **Stefan Klein:** Conceptualization; methodology; data curation; formal analysis; writing – original draft; writing – review and editing; supervision; investigation. **Edwin H. G. Oei:** Conceptualization; methodology; data curation; formal analysis; writing – original draft; writing – review and editing; supervision; investigation. **Liesbeth Duijts:** Conceptualization; methodology; data curation; formal analysis; writing – original draft; writing – review and editing; supervision; investigation.

ACKNOWLEDGMENTS

The Generation R study is managed by the Erasmus Medical Centre in close collaboration with the School of Law and the Faculty of Social Sciences at the Erasmus University, Rotterdam, the Municipal Health Service, Rotterdam area, and the Stichting Trombosedienst and Artsenlaboratorium Rijnmond (Star-MDC), Rotterdam. We gratefully acknowledge the contribution of children and their parents, general practitioners, hospitals, midwives, and pharmacies in Rotterdam.

FUNDING INFORMATION

The Generation R Study is made possible by financial support from the Erasmus Medical Centre, Rotterdam, the Erasmus University Rotterdam, and the Netherlands Organization for Health Research and Development. TW is supported by the China Scholarship Council (CSC) PhD Fellowship for his PhD study at Erasmus Medical Center, Rotterdam, the Netherlands. The scholarship file number is 201906260304, CSC URL: http://www.csc.edu.cn/. LD is supported by funding for projects from the European Union's Horizon 2020 research and innovation program (LIFECYCLE, grant agreement No. 733206, 2016; EUCAN-Connect grant agreement No. 824989; ATHLETE, grant agreement No. 874583), ZonMW The Netherlands (CoKIDS study No. 10150062010006). The researchers are independent of the funders. The study sponsors had no role in the study design, data analysis, interpretation of data, or writing of this report.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/pai.14079.

ORCID

Tong Wu https://orcid.org/0000-0001-9822-3103

Liesbeth Duijts https://orcid.org/0000-0001-6731-9452

REFERENCES

1. Asher MI, Rutter CE, Bissell K, et al. Worldwide trends in the burden of asthma symptoms in school-aged children: global asthma network phase I cross-sectional study. *Lancet*. 2021;398(10311):1569-1580.
2. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the global burden of disease study 2013. *Lancet*. 2014;384(9945):766-781.
3. Forno E, Han Y-Y, Mullen J, Celedón JC. Overweight, obesity, and lung function in children and adults—a meta-analysis. *J Allergy Clin Immunol Pract*. 2018;6(2):570-581.e10.
4. Peters U, Suratt BT, Bates JH, Dixon AE. Beyond BMI: obesity and lung disease. *Chest*. 2018;153(3):702-709.
5. Thompson D, Wood LG, Williams EJ, McLoughlin RF, Rastogi D. Endotyping pediatric obesity-related asthma: contribution of anthropometrics, metabolism, nutrients, and CD4+ lymphocytes to pulmonary function. *J Allergy Clin Immunol*. 2022;150(4):861-871.
6. den Dekker HT, Ros KP, de Jongste JC, Reiss IK, Jaddoe VW, Duijts L. Body fat mass distribution and interrupter resistance, fractional exhaled nitric oxide, and asthma at school-age. *J Allergy Clin Immunol*. 2017;139(3):810-818.e6.
7. Mensink-Bout SM, Santos S, van Meel ER, et al. General and organ fat assessed by magnetic resonance imaging and respiratory outcomes in childhood. *Am J Respir Crit Care Med*. 2020;201(3):348-355.
8. Borga M, West J, Bell JD, et al. Advanced body composition assessment: from body mass index to body composition profiling. *J Invest Med*. 2018;66(5):1-9.
9. Kooijman MN, Kruithof CJ, van Duijn CM, et al. The generation R study: design and cohort update 2017. *Eur J Epidemiol*. 2016;31:1243-1264.
10. Langeslag SJ, Schmidt M, Ghassabian A, et al. Functional connectivity between parietal and frontal brain regions and intelligence in young children: the generation R study. *Hum Brain Mapp*. 2013;34(12):3299-3307.
11. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *Eur Respir J*. 2005;26(2):319-338.
12. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. *Eur Respir Soc*. 2012;40:1324-1343.
13. Me A, Keil U, Anderson H, et al. International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J*. 1995;8(3):483-491.
14. Toemen L, de Jonge LL, Gishti O, et al. Longitudinal growth during fetal life and infancy and cardiovascular outcomes at school-age. *J Hypertens*. 2016;34(7):1396-1406.
15. Keijzer-Veen MG, Euser AM, van Montfoort N, Dekker FW, Vandenbroucke JP, Van Houwelingen HC. A regression model with unexplained residuals was preferred in the analysis of the fetal origins of adult diseases hypothesis. *J Clin Epidemiol*. 2005;58(12):1320-1324.
16. Egan KB, Ettinger AS, Bracken MB. Childhood body mass index and subsequent physician-diagnosed asthma: a systematic review and meta-analysis of prospective cohort studies. *BMC Pediatr*. 2013;13:1-13.
17. Wu T, Jahangir MR, Mensink-Bout SM, Klein S, Duijts L, Oei EH. Visceral adiposity and respiratory outcomes in children and adults: a systematic review. *Int J Obes (Lond)*. 2022;46(6):1083-1100.
18. Loomba-Albrecht LA, Styne DM. Effect of puberty on body composition. *Curr Opin Endocrinol Diabetes Obes*. 2009;16(1):10-15.

19. Jiang D, Wang L, Bai C, Chen O. Association between abdominal obesity and asthma: a meta-analysis. *Allergy Asthma Clin Immunol*. 2019;15(1):16.
20. Chait A, Den Hartigh LJ. Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease. *Front Cardiovasc Med*. 2020;7:22.
21. Tchkonia T, Thomou T, Zhu Y, et al. Mechanisms and metabolic implications of regional differences among fat depots. *Cell Metab*. 2013;17(5):644-656.
22. Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. *Front Pediatr*. 2019;7:246.
23. Choe EK, Kang HY, Lee Y, Choi SH, Kim HJ, Kim JS. The longitudinal association between changes in lung function and changes in abdominal visceral obesity in Korean non-smokers. *PloS One*. 2018;13(2):e0193516.
24. Thijs W, Dehnavi RA, Hiemstra PS, et al. Association of lung function measurements and visceral fat in men with metabolic syndrome. *Respir Med*. 2014;108(2):351-357.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Wu T, Karramass T, Jaddoe VWV, Klein S, Oei EHG, Duijts L. Abdominal fat and risk of impaired lung function and asthma in children: A population-based prospective cohort study. *Pediatr Allergy Immunol*. 2024;35:e14079. doi:10.1111/pai.14079