Infant lung function and maternal physical activity in the first half of pregnancy

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Shareable abstract (@ERSpublications)
There is an association between self-reported maternal physical activity in the first half of pregnancy and lung function in healthy 3-month-old infants, with higher odds of low lung function among infants of inactive compared to active mothers https://bit.ly/3BVVv39


Abstract

**Background and aim** Physical activity (PA) in pregnancy is important for maternal and possibly offspring health. To study the early origins of lung function we aimed to determine whether PA in the first half of pregnancy is associated with lung function in healthy 3-month-old infants.

**Methods** From the general population-based Preventing Atopic Dermatitis and Allergies in Children birth cohort recruiting infants antenatally in Norway and Sweden, all 812 infants (48.8% girls) with available tidal flow–volume measures in the awake state at 3 months of age and mid-pregnancy data on PA were included. PA was self-reported by the mothers and, based on intensity, we categorised them as active or inactive during pregnancy. Furthermore, we defined active mothers as fairly or highly active. The main outcome was a ratio of time to peak tidal expiratory flow to expiratory time ($t_{PTEF}/t_{E}$) <0.25. Associations were analysed by logistic regression, adjusting for maternal age, education, parity, pre-pregnancy body mass index, in utero nicotine exposure and parental atopy.

**Results** The mean±SD $t_{PTEF}/t_{E}$ was 0.391±0.08 and did not differ significantly according to maternal PA level in pregnancy. The 290 infants of inactive mothers had higher odds of having $t_{PTEF}/t_{E}$ <0.25 compared to infants of all active mothers (OR 2.07, 95% CI 1.13–3.82; p=0.019) and compared to infants (n=224) of fairly active (OR 2.83, 95% CI 1.26–7.24; p=0.018) but not highly active mothers (n=298).

**Conclusion** Based on self-reported maternal PA in the first half of pregnancy, 3-month-old infants of inactive compared to active mothers had higher odds of a low $t_{PTEF}/t_{E}$.

Introduction

Impaired infant lung function precedes wheezing and asthma both in childhood [1–3] and adulthood [4] as well as persistently lower lung function values [5, 6], suggesting that asthma likely originates in early life. Development of the respiratory system starts in the first weeks of fetal life [6, 7], and both genetics and the intrauterine environment impact lung function at birth [8].

Regular physical activity (PA) is an important contributor to a healthy lifestyle and is recommended during pregnancy in many countries [9, 10]. Staying physically active during pregnancy is safe for the fetus [11, 12], beneficial for maternal wellbeing, and reduces the risk of pregnancy complications [13–17] and
the risk of caesarean deliveries in nonobese women [13, 14, 18]. For healthy women, PA in pregnancy is not associated with preterm delivery [10, 12–14] or abnormal birth weight [12, 13]. Accordingly, Norwegian guidelines recommend $\geq 150$ min moderate or high intensity PA per week [19] although many women do not meet these recommendations [20]. However, the potential impact of maternal PA on early fetal airways and lung development is not clear.

Tidal flow-volume (TFV) loops in awake or naturally sleeping infants is a feasible method to measure lung function from the first day of life. The TFV ratio of time to peak tidal expiratory flow to expiratory time ($t_{\text{PTEF}/t_E}$) is a measure of expiratory airflow that correlates with maximal flow at functional residual capacity, using the rapid thoracoabdominal compression technique in sedated infants [5, 21]. Maternal asthma [22, 23], maternal hypertension in pregnancy [22] and smoking in pregnancy [22, 24] are among risk factors that have been associated with impaired lung function observed as lower $t_{\text{PTEF}/t_E}$ values in offspring. A $t_{\text{PTEF}/t_E} \leq 0.25$ is associated with obstructive lung disease, while values $\geq 0.30$ are usually considered normal [1, 3, 7, 21, 25, 26] and higher ratios are unlikely to represent improved health. Previous studies have shown lung function differences between girls and boys, with infant $t_{\text{PTEF}/t_E}$ values tending to be higher in girls [6, 23, 27].

Tidal volume ($V_T$) increases after birth [28, 29], with lower volumes in early infancy observed with prematurity [30] and lung hypoplasia [31]. While most studies exploring lung function in infancy have been performed in sleeping or sedated infants, both $t_{\text{PTEF}/t_E}$ and $V_T$ seem to be higher in the awake compared to the sleeping state [32].

In the quest to identify modifiable factors during pregnancy that may impact infant lung health, here, we hypothesise that PA positively influences infant lung function and that lack of PA may be associated with lower lung function. The aim of the present study was therefore to determine, in a large cohort of infants from a general population, whether self-reported maternal PA in the first half of pregnancy is associated with infant lung function at 3 months of age primarily as lower lung function by $t_{\text{PTEF}/t_E} < 0.25$ and, secondarily, by $V_T$ corrected for body weight (in kilograms).

Subjects and methods

Study design and setting

3-month-old infants with available lung function measurements and information on maternal PA in the first half of pregnancy from the Preventing Atopic Dermatitis and Allergies in Children (PreventADALL) cohort were included in this prospective observational study (figure 1). The PreventADALL study, described in detail elsewhere [33], is a Scandinavian general population-based mother–child birth cohort study including 2394 antenatally recruited mother–child pairs. Pregnant women planning to give birth at Oslo University Hospital or Østfold Hospital Trust, Norway, or in the region of Stockholm, Sweden, were eligible for participation. From December 2014 to October 2016, 2697 women at approximately 18 weeks of pregnancy (range 15.7–22.7 weeks) were recruited. Their healthy singletons or twins, born at $\geq 35.0$ gestational weeks, were included at birth.

Informed consent was signed by the mothers at recruitment and by both parents at birth. The study was approved by the regional committees for medical and health research ethics in Norway (2014/518) and Sweden (2014/2242–31/4), and registered at www.clinicaltrials.gov (identifier number NCT02449850).

Participants

In this substudy, we included all 812 3-month-old infants with a successful TFV measure of lung function in the awake state and available information on self-reported maternal PA in the first half of pregnancy. Lung function was measured at the Oslo and Stockholm study sites. Except for somewhat higher gestational age (GA) at birth, a higher rate of breastfeeding and less exposure to maternal use of nicotine after the first few weeks of pregnancy, the included infants were similar to the remaining infants ($n=1582$) from the PreventADALL cohort (table 1). The mothers of the included, compared to the remaining, infants were slightly older, had lower pre-pregnancy body mass index (BMI) and weight gain in the first half of pregnancy, and more were nullipara and highly educated, in line with previously described differences between the PreventADALL study sites [33]. Lung function measurements missing, unsuccessful or performed in the sleeping state were the main reasons for exclusion from the present study.

Methods

Maternal PA in the first half of pregnancy was self-reported using electronic questionnaires sent to the mothers in relation to study recruitment. They answered how frequently they had performed different types of activities (strolling, brisk walking, jogging, bicycling, strength training, aerobics, skiing, ballgames,
swimming, horse riding, yoga/Pilates and other types of PA) so far in their pregnancy. The usual intensity (low, moderate or high) and duration (<30 min, 30–60 min, 1–2 h or >2 h) of exercise was also reported. Low intensity was defined as “no sweating or shortness of breath”, moderate as “sweaty and some shortness of breath” and high as “very sweaty and very heavy breathing”. Based on all available answers, the general activity level for 2349 women in the PreventADALL cohort was estimated [20]. We defined women reporting PA of moderate or high intensity as “active” and calculated their minimum number of active minutes per week by multiplying the minimum number of sessions per week with their usual duration of exercise. Women with active minutes per week at or above the median of 120 min were further defined as “highly active” and those below the median as “fairly active”. Women reporting only low intensity or no exercise at all were defined as “inactive”. For further information, see the supplementary material.

Additionally, the questionnaire included questions on socioeconomic factors, health and lifestyle as well as family history of atopic diseases.

TFV loops were measured in calm infants by trained study personnel at the 3-month follow-up visit, using the Exhalyzer D (Eco Medics, Duernten, Switzerland) equipment [35]. An appropriately sized face mask was connected to the ultrasonic flow head with a dead space reducer, a filtering spirette and a carbon dioxide adapter with a Capnostat carbon dioxide sensor in between. The face mask was held tight over the infant’s nose and mouth while as many TFV loops as possible were recorded (supplementary table S1). All infants included in the present study were awake, with measurements performed with head and neck on the midline in the supine position on a firm pillow on their caregiver’s lap or in a stroller/bed. A procedure for selection of TFV loops in awake infants was tested and validated prior to analyses, with details on visual inspection and loop selection reported elsewhere [35]. Mean values for $f_{PTEF/FE}$, $V_T$ and respiratory rate were registered for each infant.

Information about the delivery and the newborn was taken from electronic hospital records. At 3 months post partum, the mothers answered questions about their infants’ health and nutrition. Infant weight and length were measured at the follow-up visit by trained study personnel.

**FIGURE 1** Study population. The present study population includes all 812 infants from the Preventing Atopic Dermatitis and Allergies in Children (PreventADALL) cohort with a successful tidal flow-volume (TFV) measurement in the awake state at 3 months of age and available information on maternal physical activity in the first half of pregnancy. To ensure independency of all participants, the second-born twin was consecutively excluded.
### TABLE 1
Baseline characteristics of the 812 infants included in the present study and the 1582 remaining infants from the Preventing Atopic Dermatitis and Allergies in Children (PreventADALL) mother–child birth cohort

<table>
<thead>
<tr>
<th>Included infants</th>
<th>Remaining cohort</th>
<th>p-value*</th>
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<tbody>
<tr>
<td><strong>Infants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>812</td>
<td>1582</td>
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**Infant characteristics**

- Females: 396/812 (48.8%) vs. 743/1582 (47.0%) (0.403)
- Age at examination¶, days: 93±7.2 vs. 93±7.3 (n=549) (0.686)
- Weight at 3 months, kg: 6.3±0.78 (n=808) vs. 6.3±0.78 (n=1318) (0.914)
- Length at 3 months, cm: 61.9±2.40 (n=802) vs. 61.9±2.39 (n=1299) (0.892)
- Weight gain until 3 months, kg: 2.7±0.65 (n=804) vs. 2.7±0.65 (n=1313) (0.493)
- GA at birth+, weeks: 40.1±1.32 (n=810) vs. 40.0±1.36 (n=1578) (0.022)
- Birth weight, kg: 3.6±0.46 (n=808) vs. 3.6±0.49 (n=1576) (0.398)
- Placenta weight, g: 668±133.2 (n=754) vs. 654±136.0 (n=1051) (0.002)
- BW/PW ratio: 5.46±0.98 (n=753) vs. 5.61±0.97 (n=1051) (0.002)
- Caesarean birth: 129/811 (15.9%) vs. 268/1579 (17.0%) (0.507)
- Breastfeeding at 3 months§: 691/721 (95.8%) vs. 1037/1131 (91.7%) (<0.001)
- Examined by a physician for respiratory distress or cough since birth: 682 (94.6%) vs. 1066 (94.3%) (0.814)
- Twins: 4/812 (0.5%) vs. 18/1582 (1.1%) (0.117)

**Maternal characteristics**

- Age, years: 33±3.9 vs. 32±4.3 (<0.001)
- Nullipara: 516/812 (63.5%) vs. 913/1579 (57.8%) (0.007)
- Pre-pregnancy BMI, kg·m^{-2}: 24.4±3.27 (n=799) vs. 25.0±3.86 (n=1554) (<0.001)
- Weight gain until 18 weeks GA, kg: 4.4±3.02 (n=791) vs. 4.8±3.29 (n=1543) (0.006)
- Regular physical activity before pregnancy: 667/812 (82.1%) vs. 1071/1348 (79.5%) (0.126)
- IVF pregnancies: 68/807 (8.4%) vs. 123/1571 (7.8%) (0.612)
- Hypertensive disorders of pregnancy: 68/807 (8.4%) vs. 157/1569 (10.0%) (0.460)
- Any nicotine use in pregnancy: 90/812 (11.1%) vs. 164/1582 (10.4%) (0.590)
- Any smoking in pregnancy: 30/812 (3.7%) vs. 74/1582 (4.7%) (0.264)
- Current smoking in mid-pregnancy: 1/812 (0.1%) vs. 13/1582 (0.8%) (0.013)
- Any snus## in pregnancy: 63/812 (7.8%) vs. 102/1582 (6.4%) (0.231)
- Current snus in mid-pregnancy: 0/812 (0%) vs. 7/1582 (0.4%) (0.036)

**Maternal sociodemographic factors**

- Country of origin: 684 (84.2%) vs. 759 (55.8%) (<0.001)
- Norway: 53 (6.5%) vs. 439 (32.3%) (0.007)
- Sweden: 6 (0.7%) vs. 22 (1.6%) (0.126)
- Other Nordic country: 69 (8.5%) vs. 139 (10.2%) (0.007)
- Rest of the world: 6 (0.7%) vs. 22 (1.6%) (0.126)
- Education: 809 (n=812) vs. 1353 (n=1359) (<0.001)
- High school only or less: 45 (5.6%) vs. 196 (14.5%) (0.007)
- Higher education <4 years: 226 (27.9%) vs. 464 (34.3%) (0.007)
- Higher education ≥4 years: 517 (63.9%) vs. 654 (48.3%) (0.007)
- PhD: 21 (2.6%) vs. 39 (2.9%) (0.971)
- Married/cohabitant: 791/812 (97.4%) vs. 1332/1367 (97.4%) (0.971)
- Living environment: 812 (n=812) vs. 1359 (n=1359) (<0.001)
- City: Densely populated 390 (48.0%) vs. 452 (33.3%) (0.007)
- Less densely populated 320 (39.4%) vs. 506 (37.2%) (0.007)
- Suburb: 78 (9.6%) vs. 267 (19.6%) (0.007)
- Village or countryside: 24 (3.0%) vs. 134 (9.9%) (0.007)

**Family history of atopic diseases¶¶**

- Maternal atopic disease: 328/812 (40.4%) vs. 573/1359 (42.2%) (0.418)
- Asthma: 140/812 (17.2%) vs. 231/1359 (17.0%) (0.884)
- Atopic dermatitis: 135/812 (16.6%) vs. 296/1359 (21.8%) (0.004)
- Allergic rhinitis: 177/812 (21.8%) vs. 268/1359 (19.7%) (0.240)
- Parental atopic disease: 284/757 (37.5%) vs. 467/1400 (33.4%) (0.053)
- Asthma: 101/757 (13.3%) vs. 178/1400 (12.7%) (0.784)
- Atopic dermatitis: 73/757 (9.6%) vs. 147/1400 (10.5%) (0.406)
- Allergic rhinitis: 203/757 (26.8%) vs. 307/1400 (21.9%) (0.026)
- Parental atopic disease: 498/773 (64.4%) vs. 862/1345 (64.1%) (0.877)

Data are presented as mean±SD unless otherwise stated. GA: gestational age; BW/PW: birth weight/placenta weight; BMI: body mass index; IVF: in vitro fertilisation. ¶: differences between groups analysed with the independent sample t-test (continuous variables), the Chi-squared test (nominal variables) or the Mann–Whitney U-test (ordinal variables); ¶: age in days (~3 months) is based on the date of the lung function measurement and, therefore, is missing when no lung function measurement was registered; +: GA is based on fetal femur length at the routine second trimester ultrasound scan, as different methods were used to measure fetal head size at the study sites; #: partly or exclusively breastfed at 3 months of age (see supplementary table S5 for further information on nutrition at 3 months of age for the included infants); f: the first-born twin from four twin pairs was included while the second twin was consequentially excluded; ##: snus (moist snuff) is a smokeless, ground tobacco, placed between the gum and the lip, increasingly used among Scandinavian women [34]; ¶¶: doctor-diagnosed atopic diseases included asthma, atopic dermatitis, allergic rhinitis and food allergies. Bold represents statistically significant p-values.

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**Variables**

**Primary outcome**
The primary outcome, lower lung function, was defined as a $t_{PTEF}/t_{E}$ ratio <0.25.

**Secondary outcome**
The secondary outcome, $V_t$ corrected for body weight, was recorded as a continuous variable.

**Exposure**
The maternal general activity level was based on self-reported intensity of exercise in the first half of pregnancy [20]. Primarily, we compared infants of inactive mothers to those of all active mothers, and secondarily, to infants of active mothers in the subgroups of fairly active and highly active.

**Covariates**
All multivariable regression models were adjusted for maternal age, education, parity, pre-pregnancy BMI, in utero nicotine exposure and parental atopy. These potential confounders of the association between maternal PA in pregnancy and infant lung function were identified using a directed acyclic graph (DAG) [36] prior to statistical analyses (supplementary figure S1). Only conditions arising before the first half of pregnancy and potentially affecting both the exposure and outcome could be considered as confounders and adjusted for in the regression models.

**Statistical analysis**
Continuous variables are presented as mean (range), mean±SD or mean (95% CI). Categorical variables are presented as n (%).

We used logistic regression models to analyse the association between maternal general activity level and $t_{PTEF}/t_{E}$ <0.25, presented as odds ratios with 95% confidence intervals and p-values. For the continuous $V_t$ corrected for body weight outcome, linear regression models are presented with regression coefficients ($\beta$ estimate), $R^2$, 95% confidence intervals and p-values.

To assess a potential interaction with infant sex, we added the interaction term “maternal PA×infant sex” to our regression models.

We compared the infants included in the present study to all remaining infants in the PreventADALL cohort with the independent sample t-test (continuous variables), the Chi-squared test (nominal variables) or the Mann–Whitney U-test (ordinal variables). p-values <0.05 were regarded as significant.

IBM SPSS statistics version 27, RStudio version 4.1.0 and Microsoft Excel 2016 were used for statistical analyses.

**Results**
The 812 infants (48.8% girls) included in the present study were born at mean (range) GA of 40.1 (35.3–42.3) weeks (table 1). Their mean (range) age at the time of lung function testing was 93 (57–137) days and their weight, 6.3 (4.4–8.9) kg.

Approximately one third of the mothers (290 (35.7%) out of 812) were defined as inactive in the first half of pregnancy. Of the 522 (64.3% out of 812) active mothers, 224 (27.6% out of 812) were fairly active and 298 (36.7% out of 812) were highly active.

Mean±SD (range) $t_{PTEF}/t_{E}$ for the included infants was 0.39±0.08 (0.19–0.63), with the distribution shown in figure 2a. Few had low values; while 47 infants (5.8%) had a $t_{PTEF}/t_{E}$ <0.25, only five (0.6%) had values <0.20. The mean±SD number of TFV loops was 21±14 per infant (supplementary table S1).

The mean±SD $t_{PTEF}/t_{E}$ was similar among infants of inactive and active mothers: 0.387±0.09 compared to 0.393±0.08 (figure 3 and supplementary table S2); however, as shown in the histogram in figure 2b, the $t_{PTEF}/t_{E}$ distribution appears to be different in the lower tail between the two groups and $t_{PTEF}/t_{E}$ variability greater among infants of inactive mothers.

Infants of inactive mothers had significantly higher odds of having a $t_{PTEF}/t_{E}$ <0.25 compared to infants of all active mothers as well as when compared to the infants of fairly active mothers only, in both univariable and multivariable regression models (table 2).
The mean±SD $V_T$ corrected for body weight for all included infants was 7.05±2.12 mL·kg$^{-1}$, with no significant difference between infants of inactive mothers compared to those of all active mothers (results not shown). However, when active mothers were subdivided into fairly and highly active, $V_T$ corrected for body weight differed significantly between the three groups (figure 4a and supplementary table S3a). Infants of highly active mothers had the lowest mean±SD $V_T$ corrected for body weight of 6.79±2.05 mL·kg$^{-1}$, which was significantly lower than that of the infants of fairly active mothers (7.25±2.13 mL·kg$^{-1}$, p=0.035), while they did not differ significantly from the infants of inactive mothers (7.17±2.16 mL·kg$^{-1}$). A significant association was observed between high maternal activity and lower infant $V_T$ corrected for body weight in both univariable and multivariable models (table 3).

There was no significant interaction between maternal PA in the first half of pregnancy and infant sex, and neither did the association between maternal PA and infant lung function change by including infant sex in the regression models (results not shown).

Discussion
Maternal PA in the first half of pregnancy was significantly associated with lung function in 812 healthy awake 3-month-old infants born after ≥35.0 weeks of pregnancy. Infants of physically inactive mothers...
were more likely to have low \( t_{\text{PTEF/TE}} \) values, with twice the odds of having a \( t_{\text{PTEF/TE}} <0.25 \) compared to infants of active mothers. High maternal activity was associated with lower \( V_T \) corrected for body weight.

The significant association between maternal inactivity in the first half of pregnancy and lower \( t_{\text{PTEF/TE}} \) at 3 months of age is a novel finding, although studies that have examined the fetus during maternal exercise may support our results [37, 38]. Fetal breathing movements, observed as early as the first trimester, are important for development of the lungs and the respiratory system [8, 39]. While maternal exercise can transiently affect both fetal breathing and body movements [37, 38], little is known about potential associations between breathing movements in the fetus and postnatal lung function. In addition, an increased variability in fetal heart rate during maternal exercise may, together with higher blood flow in the umbilical cord and the placental circulation, indicate an improved \( \text{in utero} \) environment in active women and lower the risk of fetal adverse outcomes [38].

Higher odds of low \( t_{\text{PTEF/TE}} \) were observed among infants born to inactive mothers compared to all active and to fairly active mothers. We explored potential associations of PA on lung function values within a normal, healthy infant population, and based upon clinically relevant cut-off values from previous studies, we chose \( t_{\text{PTEF/TE}} <0.25 \) to represent low lung function [1, 3, 7, 25, 26]. Future studies of the PreventADALL cohort may reveal whether maternal inactivity in the first half of pregnancy is associated

### TABLE 2

<table>
<thead>
<tr>
<th>Infants</th>
<th>Inactive versus active</th>
<th>Inactive versus fairly active</th>
<th>Inactive versus highly active</th>
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<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p-value</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Univariable</td>
<td>812</td>
<td>2.14 (1.19–3.90)</td>
<td>0.012</td>
</tr>
<tr>
<td>Multivariable</td>
<td>808</td>
<td>2.07 (1.13–3.82)</td>
<td>0.019</td>
</tr>
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</table>

Multivariable models were adjusted for maternal age, education, parity, pre-pregnancy body mass index, parental atopy and \( \text{in utero} \) exposure to nicotine. Of 812 included infants, the mothers of 290 were defined as inactive, 224 as fairly active and 298 as highly active. Information on maternal education was missing for four infants, resulting in 808 infants (290 of inactive mothers, 222 of fairly active mothers and 296 of highly active mothers) in the multivariable models. Bold indicates statistically significant p-values.

FIGURE 4

Infant a) tidal volume \( (V_T) \) corrected for body weight and b) respiratory rate at 3 months of age according to maternal general activity level in three categories. a) Mean \( V_T \) corrected for body weight was compared between groups with one-way ANOVA \((p=0.023)\). Mean \( V_T \) corrected for body weight differed significantly between infants of fairly active and highly active mothers \( \text{mean difference} 0.47 \text{ mL·kg}^{-1}, 95\% \text{ CI 0.026–0.905 mL·kg}^{-1}; p=0.035)\). b) Mean respiratory rate was compared between groups with one-way ANOVA \((p=0.053)\). Mean respiratory rate differed significantly between infants of highly active and fairly active mothers \( \text{mean difference} 2.84, 95\% \text{ CI 0.09–5.59 breaths per min; } p=0.041)\). Symbols represent means and whiskers represent 95% confidence intervals.
While previously shown to affect lung function, were regarded as potential confounders. Complications nor infant factors such as sex, GA, birth weight or breastfeeding [6, 8, 23, 27, 30, 40], the association between maternal PA level in the first half of pregnancy and infant lung function we have only found for high-level PA and lower V_T corrected for body weight. We are unaware of similar findings reported elsewhere. The potential reasons for the association might not catch up as fast, reflected by lower V_T corrected for body weight and normal V_T corrected for body weight at 3 months of age. Infants of inactive mothers were compared to infants of active mothers subdivided into fairly active and highly active. Multivariable models were adjusted for maternal age, education, parity, pre-pregnancy body mass index, parental atopy and in utero exposure to nicotine. β: β estimate. #: information on infant weight at 3 months of age was missing for four out of 812 included infants; therefore, 808 infants could be included in models with tidal volume corrected for body weight as the outcome (288 with inactive, 224 with fairly active and 296 with highly active mothers); additionally, four infants were excluded from the multivariable model due to missing data on maternal education, resulting in 288 infants with inactive mothers, 222 infants with fairly active mothers and 294 infants with highly active mothers. Bold indicates statistically significant p-values.

The large group of healthy infants, with lung function measured in the awake state at a relatively similar age, is a strength of this study. The general activity level was slightly higher for the mothers of the infants included in the present study compared with the whole PreventADALL cohort [20] and some maternal differences related to study sites were observed [33]. Nevertheless, we believe our results are representative of the general Scandinavian population. Prior to analyses, we identified confounders by constructing a DAG based on available knowledge. Apart from nonsignificantly lower birthweight and higher weight gain in the first 3 months of life, no differences in infant characteristics according to maternal PA level were observed, supporting our DAG and findings.
Due to the design of the study, all information on maternal PA was self-reported, with certain limitations arising from the questionnaire. Although our analyses are based on an estimate of active minutes per week, as the women were not asked about the total weekly duration or frequency of exercise, we believe that the classification of active women into fairly and highly active is reasonable. In this study, we addressed the role of PA in the first half of pregnancy for early fetal respiratory development, using detailed PA data collected at enrolment. Information on maternal PA in the second half of pregnancy was limited to changes in PA habits from mid-pregnancy until 34 weeks gestation and after this time no information on maternal PA was available. In addition, to account for potential pregnancy complications that may impact on activity levels, more likely to be present in the last part of pregnancy, would necessitate a larger cohort than ours.

**Conclusion**

Maternal PA in pregnancy was significantly associated with infant lung function, with higher odds of low $f_{PTEF}$/FE in infants of inactive compared to active mothers, and an association between high maternal activity and lower $V_t$. The observed association between maternal inactivity and lower infant lung function may have clinical implications, adding to the importance of advising and supporting pregnant women to adhere to guidelines on PA during pregnancy. Nevertheless, there might be confounders for which we have not adjusted and, potentially, maternal PA level could be a proxy for general health or an unknown factor associated with lung function in the offspring.

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