Online supplement – Infant lung function and maternal physical activity in pregnancy

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Maternal general activity level

In the PreventADALL study, information on maternal physical activity (PA) in the first half of pregnancy was self-reported by the mothers, approximately at mid-pregnancy. The following questions on leisure time PA were included in the questionnaire:

Question 34: Were you regularly physically active prior to pregnancy?

Physical activity is defined as at least one activity session per week with a duration of at least 20 minutes per session.

- No
- Yes

Question 35: Have you been regularly physically active during the last two weeks?

Physical activity is defined as at least one activity session per week with a duration of at least 20 minutes per session.

- No
- Yes, but I am less active now than before
- Yes, I am equally active as before
- Yes, I am more active now than before

Question 36: Which types of physical activities are usual for you so far in this pregnancy?

Mark all activities that are common for you, both summer and winter activities. For instance, if you like to run in the summer and to ski in the winter, mark both.

	Rarely or never	1-3 times monthly	Once weekly	2-3 times weekly	4-5 times weekly	5-6 times weekly	Every day	More than once daily
Strolling								
Brisk walking								
Jogging								
Bicycling								
Strength training								
Aerobics								
Skiing								
Ball games								
Swimming								
Horse riding								
Yoga/Pilates								
Other								

Question 36 a): Choose the most accurate option compared to the last year preceding your pregnancy:

- I am now far less active than prior to pregnancy
- I am now slightly less active than prior to pregnancy
- I am now equally active as prior to pregnancy
- I am now slightly more active than prior to pregnancy
- I am now far more active than prior to pregnancy

Question 37: What is your average duration of exercise (so far in the pregnancy)?

Do not include the time spent changing clothes, showering, travelling to exercise etc.

- Less than 30 minutes
- 30-60 minutes
- 1-2 hours
- More than 2 hours

Question 37 a): What is the usual intensity of your exercise (so far in the pregnancy)?

Answer for the activity you most commonly perform.

- No sweat or shortness of breath (low intensity)

- Somewhat sweaty and short of breath (moderate intensity)
- Very sweaty and heavy breathing (high intensity)

To estimate the *maternal general activity level* in the first half of pregnancy, women who had regularly performed moderate and/or high intensity exercise were defined as *active*. Strolling was excluded, being a low intensity activity per definition, while all other types of activities were included. All durations and all frequencies except rarely or never were included, and to calculate the estimated minimum number of active minutes per week we used the following numerical assumptions [1]:

Duration: Less than 30 min = 1 min, 30-60 min = 30 min, 1-2 hours = 61 min, more than 2 hours = 121 min.

Frequency, recoded as the estimated number of sessions per week: Rarely or never = 0, 1-3 times monthly = 0.25, 1 times weekly = 1, 2-3 times weekly = 2, 4-5 times weekly = 4, 5-6 times weekly = 5, every day = 7, more than once daily = 8.

To estimate the minimum number of active minutes per week, we added together the frequencies for all types of PA (except strolling) and multiplied by the usual duration of an exercise session. For all *active* women in the PreventADALL cohort, the median estimated minimum number of active minutes per week was 120 minutes [1]. *Active* women with less than 120 active minutes per week according to the estimated minimum number of active minutes were further categorised as *fairly active* and those with 120 active minutes or more as *highly active*. Women who only reported low intensity exercise, or no activities at all were defined as *inactive*.

Calculating the minimum number of active minutes has some limitations. The women were not asked to report the total number of activity sessions per week regardless of the type of

activity, which may result in combined sessions being counted more than once. As an example, a 90 min session two times per week, consisting of 15 min running (warm-up), 60 min strength training and 15 min stretching/yoga would count as two times three sessions, of 1-2 hours each, if the woman reports all these activities as performed two times per week. Although the estimated active minutes per week would be far too many for this exemplified woman, the category *highly active* would still be correct for a person with 180 minutes of running, strength training and stretching of moderate or high intensity every week. In addition, both duration and frequency were reported in ranges, with no upper limit for the highest categories, and no lower limit for a duration less than 30 minutes. Thus, we cannot calculate the exact number of minutes per week. In spite of these limitations, we believe that our subgrouping of the active women into fairly and highly active is a reasonable estimate.

The PA questions in the PreventADALL questionnaire were adapted from a questionnaire used in the Norwegian Mother and Child Cohort Study (MoBa), that was validated by comparing the answers with physical activity measured with a position and motion sensor in a subgroup of their pregnant study population [2].

Covariates included in multivariable models

Our DAG [3] (Figure S1), constructed prior to all statistical analyses, identified maternal age, education, parity, pre-pregnancy body mass index (BMI), in-utero nicotine exposure and parental atopy as potential confounders on the association between maternal PA in pregnancy and infant lung function.

Especially in-utero exposure to nicotine [4, 5] and maternal asthma [4, 6] are well documented risk factors for impaired lung function in infants, while some studies have

related a family history of asthma and/or atopy in primary or secondary relatives to lower lung function values in infancy and later wheeze and asthma [7, 8]. An association between maternal atopic dermatitis and higher levels of jogging in pregnancy in the PreventADALL cohort has been described [1] and a univariable model mapping associations with maternal PA in pregnancy, revealed a weak but significant positive association with paternal atopy in the present study cohort, while we observed no significant association with maternal atopy. In addition, maternal allergic rhinitis might potentially affect outdoor activities during the spring and summer. Thus, to adjust for the wider exposure of atopy, we decided to include maternal and paternal atopy (doctor diagnosed asthma, atopic dermatitis, allergic rhinitis and food allergies) combined in one variable (parental atopy) in our multivariable models.

Information on *parental atopy* was missing for 39 (4.8%) of the 812 included infants. To prevent loosing these infants from the multivariable models, we coded missing as a "not-ordered" category in the *parental atopy* variable.

Maternal *pre-pregnancy BMI* is missing for 13 (1.6%) of the 812 infants. We kept these infants in the multivariable models using mean imputation. We gave them a BMI value of 24.42, the mean pre-pregnancy BMI of all mothers included in the present study.

Maternal education: To report their education, the mothers had six alternatives: 1) Preliminary school, 2) High school only, 3) Higher education <4 years, 4) Higher education ≥4 years, 5) PhD and 6) Other. These categories were recoded to 1) High school only or less, 2) Higher education <4 years, 3) Higher education ≥4 years. The group "Other" was recoded to "missing".

In-utero exposure to nicotine: The mothers reported smoking and use of snus at 18 weeks, with the alternatives: 1) Never, 2) Stopped many years ago, 3) Stopped in time before

pregnancy, 4) Stopped when recognized pregnancy and 5) Current smoking or use of snus. These were recoded into: 1) No use of nicotine in pregnancy and 2) Any use of nicotine in pregnancy; including "Stopped when recognized pregnancy" and "Current smoking or use of snus". Most of the mothers in the PreventADALL cohort reporting any use of nicotine in pregnancy stopped their use early in pregnancy [9].

Results of supportive analyses

The mean (SD) respiratory rate (RR) for all included infants was 62.2 (13.3) breaths per minute. The mean (SD) RR was highest for infants of highly active mothers, 63.5 (13.7), significantly higher than for infants of fairly active mothers, 60.7 (12.0), p=0.041 (Figure 4b, Table S3b). RR correlated negatively with V_T/kg (Table S4) but did not explain the whole association between maternal PA and V_T/kg (results not shown).

As shown in Figure S2, infant GA at birth, birth weight, placenta weight, the ratio of birth weight relative to placenta weight (BW/PW), birth mode, infant weight or length at three months of age and infant weight gain did not differ significantly according to maternal general activity level. Small differences, not statistically significant, were observed when active women were further categorised to fairly and highly active.

Table S1 – The mean number of TFV loops per infant. Shown according to maternal general activity level and for all included infants.

TFV loops selected for analyses					
General activity level	**n**	**Mean**	**SD**	**95% CI of mean**	**p-value**
Inactive	290	20.0	13.7	18.4, 21.5	0.036[1]
Active	522	22.1	14.1	20.9, 23.3	
Inactive	290	20.0	13.7	18.4, 21.5	0.089[2]
Fairly active	224	22.6	14.2	20.7, 24.4	
Highly active	298	21.8	14.1	20.2, 23.4	
Total	812	21.3	14.0	20.4, 23.0	

[1] Mean number of TFV loops compared between groups with the independent sample t-test.

[2] Mean number of TFV loops compared between groups with one-way ANOVA.

Abbreviations: TFV; tidal flow-volume, n; number, SD; standard deviation, CI; confidence interval.

Table S2 – Mean t_{PTEF}/t_E by maternal general activity level in the first half of pregnancy. Showed for infants of a) inactive and active mothers, and b) inactive, fairly active and highly active mothers.

a)

General activity level	n	Mean t_{PTEF}/t_E	SD	95% CI of mean	p-value[1]
Inactive	290	0.387	0.088	0.377, 0.397	0.321
Active	522	0.393	0.081	0.386, 0.400	
Total	812	0.391	0.083	0.385, 0.397	

b)

General activity level	n	Mean t_{PTEF}/t_E	SD	95% CI of mean	p-value[2]
Inactive	290	0.387	0.088	0.377, 0.397	0.594
Fairly active	224	0.393	0.084	0.382, 0.404	
Highly active	298	0.394	0.078	0.385, 0.402	
Total	812	0.391	0.083	0.385, 0.397	

[1] Mean t_{PTEF}/t_E compared between groups with the independent sample t-test.

[2] Mean t_{PTEF}/t_E compared between groups with one-way ANOVA.

Abbreviations: t_{PTEF}/t_E; the ratio of time to Peak Tidal Expiratory Flow to Expiratory time, n; number, SD; standard deviation, CI; confidence interval.

Table S3 - Mean a) V_T/kg and b) RR by maternal general activity level in the first half of pregnancy. Means for the different groups were compared with one-way ANOVA.

a)

General activity level	n	Mean V_T/kg	SD	95% CI of mean	p-value
Inactive	288	7.17	2.16	6.92, 7.42	
Fairly active	224	7.25	2.13	6.97, 7.53	**0.023**
High activity	296	6.79	2.05	6.55, 7.02	
Total	808	7.05	2.12	6.90, 7.20	

b)

General activity level	n	Mean RR	SD	95% CI of mean	p-value
Inactive	290	62.1	13.7	60.5, 63.7	
Fairly active	224	60.7	12.0	59.1, 62.2	0.053
High activity	298	63.5	13.7	61.9, 65.1	
Total	812	62.2	13.3	61.3, 63.1	

Abbreviations: V_T/kg; tidal volume per kg, RR; respiratory rate, n; number, SD; standard deviation, CI; confidence interval.

Table S4 – Pearson correlation for the lung function outcomes, how t_{PTEF}/t_E and V_T/kg correlate with RR.

Correlations with RR	R^2	*r*	95% CI of *r*	p-value
t_{PTEF}/t_E	0.136	0.37	0.31, 0.43	<0.001
V_T/kg	0.189	-0.44	-0.49, -0.38	<0.001

Abbreviations: t_{PTEF}/t_E; the ratio of time to Peak Tidal Expiratory Flow to Expiratory time, V_T/kg; tidal volume per kg, RR; respiratory rate, R^2; the amount of variability explained by the particular exposure by Pearson correlation, *r*; the Pearson correlation coefficient, CI; confidence interval.

Table S5 – Nutrition at three months of age. Shown according to maternal general activity level and for all included infants.

	n (%)*	Exclusive breastfeeding	Only mothers milk (breastfeeding and bottle)	Mothers milk and other food	No mothers milk	p-value
Inactive	245 (84.5%)	140 (57.1%)	24 (9.8%)	66 (26.9%)	15 (6.1%)	0.211
Active	476 (91.2%)	282 (59.2%)	58 (12.2%)	121 (25.4%)	15 (3.2%)	
Inactive	245 (84.5%)	140 (57.1%)	24 (9.8%)	66 (26.9%)	15 (6.1%)	
Fairly active	206 (92.0%)	128 (62.1%)	18 (8.7%)	52 (25.2%)	8 (3.9%)	0.158
Highly active	270 (90.6%)	154 (57.0%)	40 (14.8%)	69 (25.6%)	7 (2.6%)	
Total	721 (88.8%)	422 (58.5%)	82 (11.4%)	187 (25.9%)	30 (4.2%)	

*n (%) represents the number of mothers answering questions on infant nutrition at three months post-partum, with percentage per group.

Difference between groups was analysed with the Chi-squared test (χ^2) and revealed no statistically significant difference in infant nutrition according to maternal general activity level.

Figure S1 – Directed Acyclic Graph (DAG) including variables affecting either one or both of maternal physical activity level and infant lung function. The DAG was constructed to identify possible confounders, prior to statistical analyses.

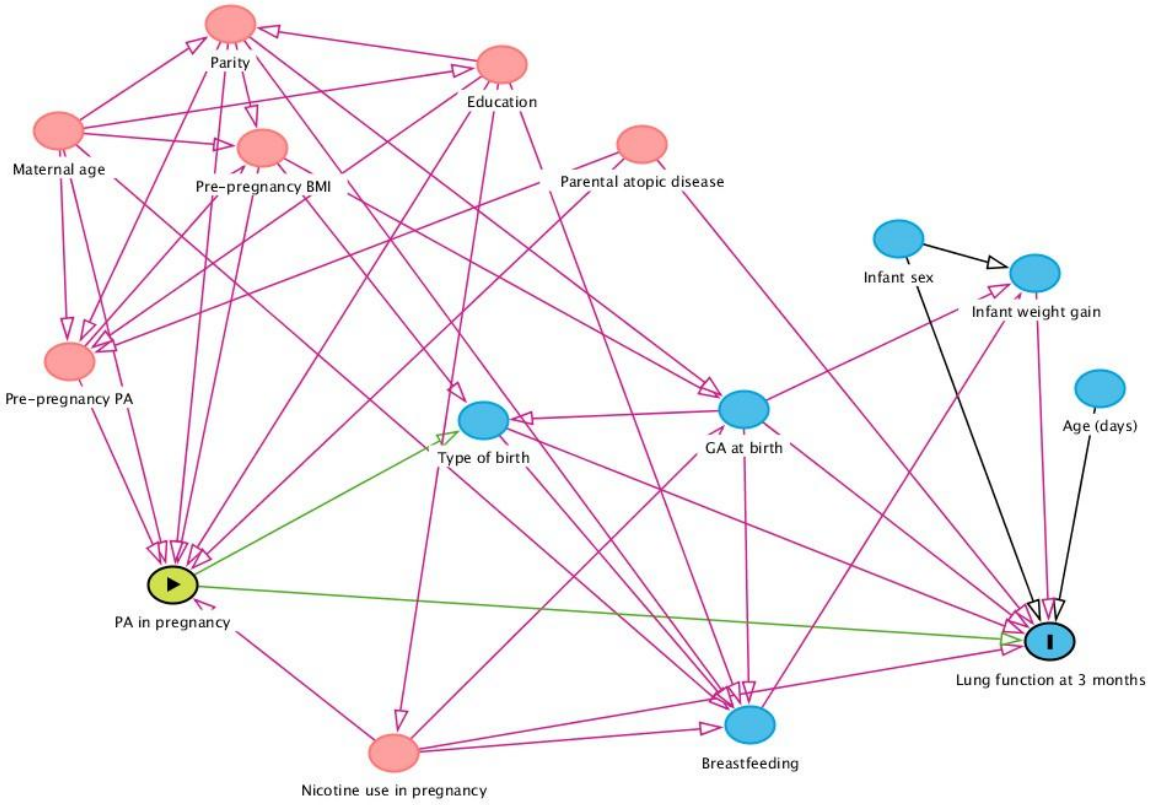
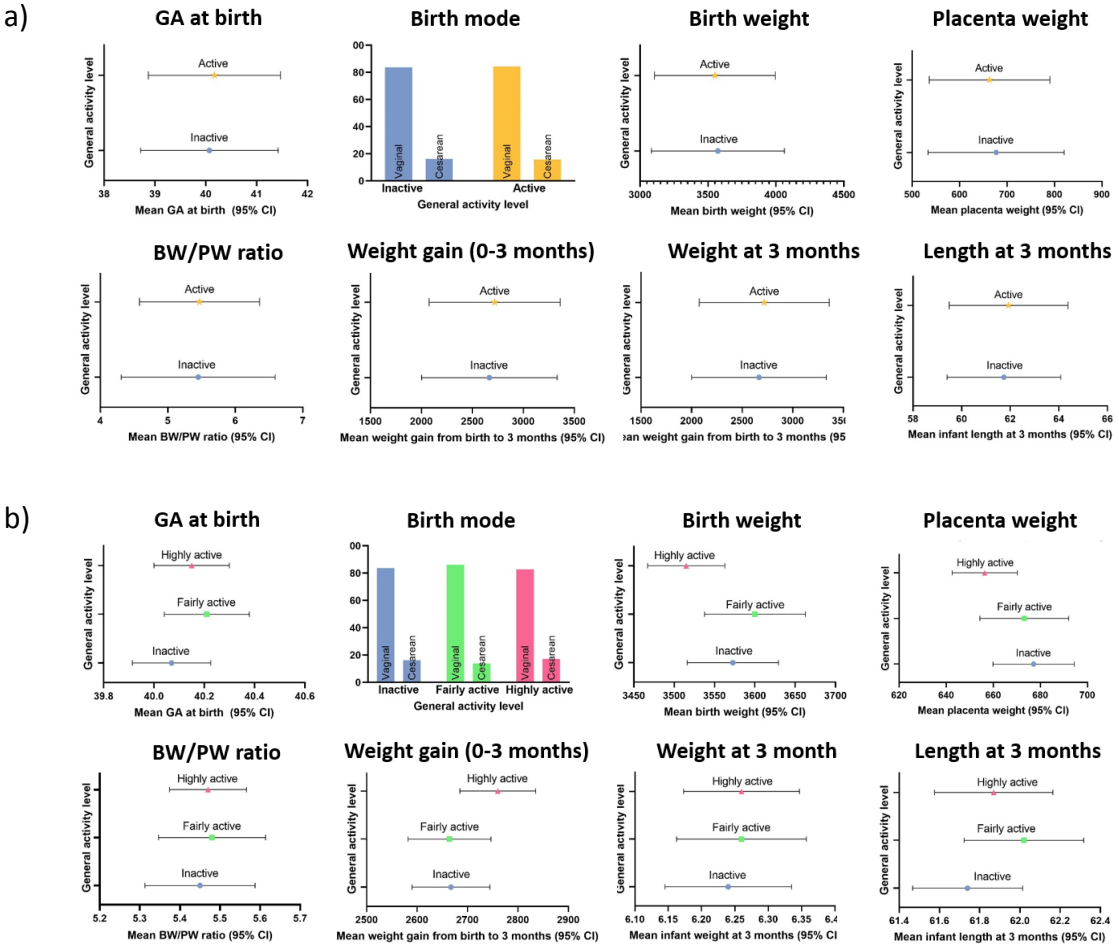


Figure S2 - Infant factors at birth and at three months of age; GA at birth, birth mode, birth weight, placenta weight, the BW/PW ratio, weight gain until three months of age, infant weight and length at three months of age. Shown for infants of a) inactive and active mothers, and b) inactive, fairly active and highly active mothers.



a) Means were compared between infants of inactive and active mothers with the independent sample t-test for continuous outcomes; GA at birth (p=0.305), birth weight (p=0.529), placenta weight (p=0.199), BW/PW ratio (p=0.771), infant weight gain (p=0.281), weight (p=0.676) and length (p=0.272) at three months of age, and with the Chi-squared test (χ^2) for the binary outcome of birth mode (p=0.861).

b) Means were compared between infants of inactive, fairly active and highly active mothers with one-way ANOVA for continuous outcomes; GA at birth (p=0.516), birth weight (p=0.094), placenta weight (p=0.160), BW/PW ratio (p=0.950), infant weight gain (p=0.142), weight (p=0.915) and length (p=0.421) at three months of age, and with the Chi-squared test (χ^2) for the binary outcome of birth mode (p=0.580).

Abbreviations: GA; gestational age, BW/PW ratio; birth weight to placenta weight ratio, CI; confidence interval.

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