

Online Supplementary Files

Prenatal, early-life and childhood exposure to air pollution and lung function: the ALSPAC cohort

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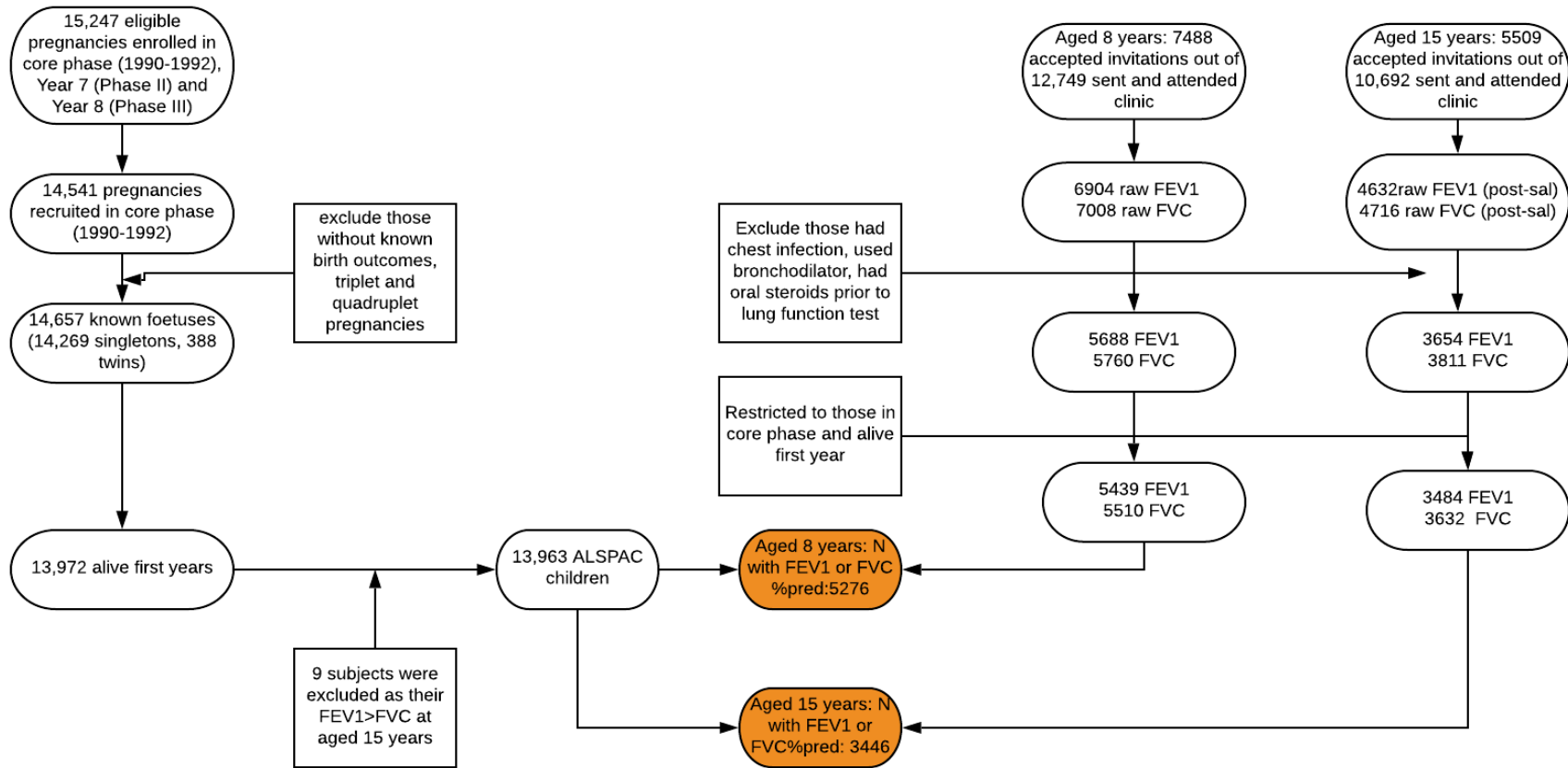
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Figure E1 –flowchart of study populations



Supplementary text on Bayesian profile regression model

We applied the Bayesian profile regression model to a population of 13,963 children tested in order to measure their lung function. The population was partitioned in two groups taking into account the age of the measurements (8 and 15 years old age).

Eighteen covariates were considered in the model. Nine were confounders and treated as fixed effects in the model, and eight were continuous covariates mainly related to environmental factors.

We had six response variables (continuous), three related to the 8 years old group and three related to the 15 years old group.

In order to fit the Bayesian profile regression model, we needed to remove all the NAs from the outcome variables and the confounders. After filtering out the missing values we had a total of 4,214 observations for 8 years old and 2,772 for 15 years old.

We have assumed that the response variable model was Normal, as well as the covariates one. We used the default values for all hyperparameters for the 8 years old group. For the 15 years old one, we used all the default values except for $p(\alpha)$ in this case following a *Gamma* (1,2) distribution.

The other specification for the hyperparameters were:

Dirichlet conjugate priors with $a_j = -2$, this setting allowed the parameter for random variation for the covariates and

$$p(\alpha) \equiv \text{Gamma}(2,1)$$

$$p(\theta_c) \equiv t_7(0,2.5)$$

$$p(\beta) \equiv t_7(0,2.5)$$

Where *Gamma* (α, β) $\equiv \frac{\beta^\alpha}{\Gamma(\alpha)} x^{\alpha-1} e^{-\beta x}$ and

$$t_v(\mu, \sigma) \equiv \frac{\Gamma(v + 1/2)}{\Gamma(v/2)\sqrt{\pi v\sigma}} \left[1 + \frac{1}{v} \left(\frac{x - \mu}{\sigma} \right)^2 \right]^{-\frac{v+1}{2}}$$

We initialised all chains allocating subject randomly to 20 groups. We ran the chain for 10,000 after a burn-in sample of 20,000 iteration for the 8 years old group, and the chain for 20,000 and an initial burn-in of 30,000 iteration for the 15 years old one.

To assess that our MCMC chains have converged to the posterior probability distribution is a very complex problem, in order to verify if there was any evidence against it we used some graphical tools available for diagnostics from the R packages: PReMiuM and coda. In particular, we analysed the traces and the shape of the posterior distribution of the global parameters such as number of cluster (to check if the number we set a priori was big enough to allow for the convergence), alpha and beta and we obtained positive results.

Due to the problem of label switching it is not correct to simply assign each observation to the cluster which maximizes the average posterior probability. In order to deal with it the algorithm choses the partition based on a posterior similarity matrix. At each iteration, a pairwise cluster membership is recorded and construct a score matrix. The average of these matrices over the whole MCMC runs leads to a similarity matrix S used to identify the optimal partition.

In particular, the optimal partition selection is implemented through the PAM (Partitioning Around Medoids Algorithm) on the dissimilarity matrix $1-S$. A final cluster is chosen by maximizing the average silhouette width across these best PAM partitions. For the 8 years group the best partition was composed by three clusters: cluster one (~ 40 children), cluster two (~ 560 children) and cluster three (~3,600 children), the silhouette index associated to the clustering in the best partition is about 0.88 for all the three outcome variables. In the case of the 15 years old group, the number of clusters in the best partition was different for the three outcome variables. For fev1 the number of cluster was 2: cluster 1 (~2000) and cluster 2 (~500) with a silhouette index of about 0.76, for fvc the number of cluster was 3: cluster 1 (~40), cluster 2 (~ 2000), and cluster 3 (~500) with a silhouette index of about 0.76, and for ratio we obtained again 2 clusters: cluster 1 (~500), cluster 2 (~ 2000) with a silhouette index of about 0.77. Since the values of the silhouette index are close to 1 for both the groups across all the outcome variables, it appears that the distance between the clusters is well defined.

Given the optimal partition, we have then assessed if the algorithm was consistently clustering individuals according with the best partition, in order to ensure narrower credibility intervals.

The boxplots show the posterior distribution for the probabilities of the response and the covariates for the three clusters that form the representative clustering for the 8 years old group and the 15 years old one for all the outcome variables.

With the aim to validate the obtained results we have then defined four pseudo profiles: 1) with the maximum values for all the covariates, 2) with the minimum values for all the covariates, 3) we have considered the maximum value for the covariate pm10_avg_t1 (related to the exposure to the pollutant PM₁₀ in the first in-utero trimester) and NA for all the others, 4) we have considered the minimum value for the covariate pm10_avg_t1 and NA for all the others.

The obtained beanplots show the same distribution for the pseudo profiles related to minimum and maximum values, confirming the uncertainty of the relation with the outcome variables. Moreover, since in the beanplots, we are representing the values of

the outcome variables (instead of the mean) there may be an additional layer of variability to take into account. We have observed the same behaviour between the 8 years old group and the 15 years old one.

Noting that some of the covariates, especially in the 15 years old group, had a similar profile probabilities for all the clusters, we have adopted a variable selection approach, in order to identify the covariates not containing clustering support and exclude them. In the 8 years old group, all the covariates contribute to the clustering for all the outcome variables. In the 15 years old one, the contribution of the covariates for fev1 and ratio is unclear, all of them contribute to fvc.

For further details about the statistical methodology and the PReMiuM package we refer to Liverani *et. al*, 2015.

Reference

Liverani S, Hastie DI, Papathomas MAL, Richardson S. PReMiuM: An R Package for Profile Regression Mixture Models Using Dirichlet Processes. *Journal of Statistical Software* 2015;64.

Table E1 Average PM exposure ($\mu\text{g}/\text{m}^3$) in each time period by child's sex, maternal education and maternal smoking.

	Sex			Education			Maternal smoking		
	boy	girl	p-value	lower	higher	p-value	yes	no	p-value
PM _{10_road}									
T1	0.97	0.96	0.480	0.93	1.01	<0.001	1.00	0.95	0.003
T2	0.96	0.96	0.772	0.93	1.01	<0.001	0.99	0.95	0.006
T3	0.94	0.94	0.945	0.91	0.99	<0.001	0.97	0.93	0.004
WP	0.96	0.96	0.780	0.93	1.00	<0.001	0.99	0.95	0.004
0-6months	0.94	0.94	0.971	0.91	0.99	<0.001	0.97	0.93	0.001
7-12months	0.89	0.90	0.951	0.87	0.93	<0.001	0.92	0.88	0.004
0-7 years	0.97	0.97	0.955	0.95	0.99	<0.001	0.99	0.96	0.007
8-15 years	0.65	0.65	0.535	0.64	0.65	0.185	0.66	0.64	0.039
0-15 years	0.80	0.80	0.827	0.79	0.81	0.003	0.81	0.79	0.039
PM _{10_total}	boy	girl	p-value	lower	higher	p-value	yes	no	p-value
T1	33.5	33.4	0.626	33.3	33.6	0.005	33.6	33.4	0.095
T2	33.0	33.0	0.729	32.8	33.2	<0.001	32.9	33.0	0.261
T3	31.5	31.5	0.823	31.3	31.7	0.002	31.5	31.5	0.816
WP	32.6	32.6	0.904	32.4	32.8	<0.001	32.6	32.6	0.652
0-6months	31.8	31.8	0.506	31.7	32.0	<0.001	32.0	31.7	<0.001
7-12months	31.0	31.0	0.936	30.8	31.2	<0.001	30.9	31.0	0.491
0-7 years	33.0	33.0	0.659	32.9	33.1	<0.001	33.1	32.9	0.007
8-15 years	23.0	23.0	0.717	23.0	23.0	0.630	23.0	22.9	0.004
0-15 years	27.7	27.7	0.926	27.6	27.9	0.016	27.7	27.6	0.016

Table E2. Spearman’s correlation (rho.) between average modelled **PM_{10_road}** exposures for pregnancy trimesters, early infancy (months 1 to 6), and late infancy (months 7-12) and between modelled average PM_{10_road} exposures for later years. All correlations significant at the 0.01 level (2-tailed).

	Trimester 1	Trimester 2	Trimester 3	0-6 months	7-12 months	0-7 years annual average	8-15 years annual average	0-15 years annual average
Trimester 1	1							
Trimester 2	0.93	1						
Trimester 3	0.91	0.92	1					
0-6 months	0.92	0.91	0.93	1				
7-12 months	0.89	0.91	0.92	0.96	1			
0-7 years annual average	0.87	0.88	0.89	0.93	0.94	1		
8-15 years annual average	0.67	0.67	0.69	0.72	0.73	0.85	1	
0-15 years annual average	0.81	0.82	0.83	0.87	0.88	0.97	0.94	1

All correlations two-tailed; p<0.001.

Table E3. Spearman’s correlation (rho.) between average modelled **PM₁₀_other** exposures for pregnancy trimesters, early infancy (months 0 to 6), late infancy (months 7-12) and between modelled average PM₁₀_other exposures for later years. All correlations significant at the 0.01 level (2-tailed).

	Trimester 1	Trimester 2	Trimester 3	0-6 months	7-12months	0-7 years annual average	8-15 years annual average	0-15 years annual average
Trimester 1	1							
Trimester 2	0.84	1						
Trimester 3	0.81	0.82	1					
0-6 months	0.87	0.83	0.86	1				
7-12 months	0.82	0.87	0.87	0.94	1			
0-7 years annual average	0.81	0.81	0.83	0.93	0.94	1		
8-15 years annual average	0.66	0.66	0.68	0.73	0.74	0.85	1	
0-15 years annual average	0.77	0.78	0.79	0.88	0.89	0.97	0.94	1

All correlations two-tailed; $p < 0.001$.

Table E4. Spearman's correlation (rho.) between average modelled **PM₁₀_total** exposures for pregnancy trimesters, early infancy (months 0 to 6), and late infancy (months 7-12) and between modelled average PM₁₀_total exposures for later years. All correlations significant at the 0.01 level (2-tailed).

	Trimester 1	Trimester 2	Trimester 3	0-6 months	7-12months	0-7 years annual average	8-15 years annual average	0-15 years annual average
Trimester 1	1							
Trimester 2	-0.04	1						
Trimester 3	-0.09	0.02	1					
0-6 months	0.44	-0.16	0.10	1				
7-12 months	0.08	0.72	0.22	0.02	1			
0-7 years annual average	0.39	0.37	0.38	0.68	0.60	1		
8-15 years annual average	0.31	0.32	0.37	0.50	0.50	0.88	1	
0-15 years annual average	0.37	0.36	0.39	0.63	0.58	0.98	0.95	1

All correlations two-tailed; $p < 0.001$.

Table E5. Spearman's correlation (rho.) between average modelled PM_{10_road}, PM_{10_other}, PM_{10_total} by pregnancy trimester (T1, T2, T3), early infancy (EI; months 0 to 6), and late infancy (LI; months 7-12). and between modelled average exposures for later years. All correlations significant at the 0.01 level (2-tailed).

	PM _{10_road}	PM _{10_other}	PM _{10_total}
PM _{10_other}	T1	0.75	
	T2	0.75	
	T3	0.75	
	0-6m	0.75	
	7-12m	0.75	
	0-7y [#]	0.80	
	8-15y [#]	0.82	
	0-15y [#]	0.82	
PM _{10_total}	T1	0.48	T1 0.61
	T2	0.48	T2 0.61
	T3	0.52	T3 0.66
	0-6m	0.59	0-6m 0.69
	7-12m	0.62	7-12m 0.69
	0-7y [#]	0.85	0-7y [#] 0.96
	8-15y [#]	0.87	8-15y [#] 0.94
	0-15y [#]	0.86	0-15y [#] 0.95

All correlations two-tailed; p<0.00; # annual average

Table E6 Mean Changes in percent predicted of lung function at both aged 8 and 15 years in relation to exposure at different time periods: complete-case (N=1501) analysis based on fully adjusted model*(sex, gestational age, maternal education, home ownership, maternal smoking during pregnancy, passive smoking in childhood, damp and mould presence at home, and season of clinic visit)

PM _{10_road} , per 1 µg/m ³ higher						
time period	% predicted of FEV ₁		% predicted of FVC		% predicted of FEV ₁ /FVC	
	Age 8 years	Age 15 years	Age 8 years	Age 15 years	Age 8 years	Age 15 years
Trimester 1	-0.044 (-0.934 to 0.846)	2.016 (0.815 to 3.216)	0.089 (-0.821 to 0.999)	1.678 (0.528 to 2.828)	-0.084 (-0.611 to 0.444)	0.264 (-0.311 to 0.840)
Trimester 2	-0.073 (-0.934 to 0.787)	1.492 (0.332 to 2.652)	0.032 (-0.847 to 0.912)	1.292 (0.181 to 2.402)	-0.052 (-0.562 to 0.458)	0.127 (-0.428 to 0.683)
Trimester 3	-0.155 (-1.064 to 0.754)	0.779 (-0.448 to 2.006)	-0.076 (-1.006 to 0.854)	0.719 (-0.455 to 1.894)	-0.044 (-0.583 to 0.495)	-0.036 (-0.623 to 0.550)
Whole pregnancy	-0.102 (-1.010 to 0.806)	1.519 (0.292 to 2.745)	0.016 (-0.913 to 0.944)	1.310 (0.135 to 2.484)	-0.068 (-0.606 to 0.470)	0.123 (-0.464 to 0.710)
0-6 Months	-0.196 (-1.113 to 0.720)	0.530 (-0.709 to 1.768)	-0.097 (-1.034 to 0.840)	0.422 (-0.763 to 1.608)	-0.027 (-0.570 to 0.516)	0.042 (-0.550 to 0.635)
7-12 Months	-0.177 (-1.113 to 0.758)	0.618 (-0.646 to 1.881)	0.014 (-0.942 to 0.970)	0.577 (-0.632 to 1.787)	-0.110 (-0.664 to 0.444)	-0.038 (-0.642 to 0.566)
0-7 years	-0.074	0.724	0.001	0.688	0.017	-0.050

	(-1.342 to 1.195)	(-0.990 to 2.438)	(-1.296 to 1.298)	(-0.953 to 2.328)	(-0.734 to 0.769)	(-0.870 to 0.769)
8-15 years	1.578			1.633		-0.233
	(-1.334 to 4.490)			(-1.154 to 4.420)		(-1.625 to 1.159)
0-15 years	1.113			1.100		-0.117
	(-1.166 to 3.391)			(-1.080 to 3.281)		(-1.207 to 0.972)
PM ₁₀ _total, per 10µg/m ³ higher						
	% predicted of FEV ₁		% predicted of FVC		% predicted of FEV ₁ /FVC	
time period	Age 8 years	Age 15 years	Age 8 years	Age 15 years	Age 8 years	Age 15 years
Trimester 1	0.034	1.650	0.156	1.612	-0.105	-0.047
	(-1.212 to 1.280)	(0.047 to 3.252)	(-1.118 to 1.430)	(0.078 to 3.145)	(-0.843 to 0.633)	(-0.814 to 0.720)
Trimester 2	-0.088	1.232	0.389	1.193	-0.360	0.090
	(-1.392 to 1.216)	(-0.411 to 2.876)	(-0.944 to 1.723)	(-0.380 to 2.766)	(-1.133 to 0.412)	(-0.695 to 0.876)
Trimester 3	-0.109	0.272	-0.978	-0.267	0.744	0.562
	(-1.403 to 1.186)	(-1.400 to 1.944)	(-2.301 to 0.345)	(-1.868 to 1.333)	(-0.022 to 1.510)	(-0.236 to 1.361)
Whole pregnancy	-0.148	3.158	-0.397	2.571	0.257	0.572
	(-2.312 to 2.017)	(0.345 to 5.971)	(-2.611 to 1.816)	(-0.123 to 5.264)	(-1.026 to 1.540)	(-0.774 to 1.918)
0-6 Months	0.631	-0.035	0.893	-0.453	-0.259	0.478
	(-1.104 to 2.366)	(-2.344 to 2.274)	(-0.880 to 2.667)	(-2.663 to 1.756)	(-1.287 to 0.769)	(-0.625 to 1.581)
7-12 Months	0.035	2.111	0.283	2.445	-0.056	-0.496

	(-2.020 to 2.091)	(-0.616 to 4.839)	(-1.818 to 2.385)	(-0.164 to 5.055)	(-1.274 to 1.162)	(-1.800 to 0.808)
0-7 years	0.804	1.140	0.913	0.501	-0.021	0.648
	(-2.466 to 4.075)	(-3.291 to 5.570)	(-2.431 to 4.258)	(-3.740 to 4.742)	(-1.960 to 1.917)	(-1.469 to 2.765)
8-15 years		4.642		3.292		1.115
		(-3.025 to 12.308)		(-4.047 to 10.632)		(-2.550 to 4.779)
0-15 years		2.394		1.445		0.883
		(-3.488 to 8.276)		(-4.185 to 7.076)		(-1.928 to 3.694)

Figure E2 Posterior distribution of the parameters for FEV₁ at age 8 years for the representative clustering.

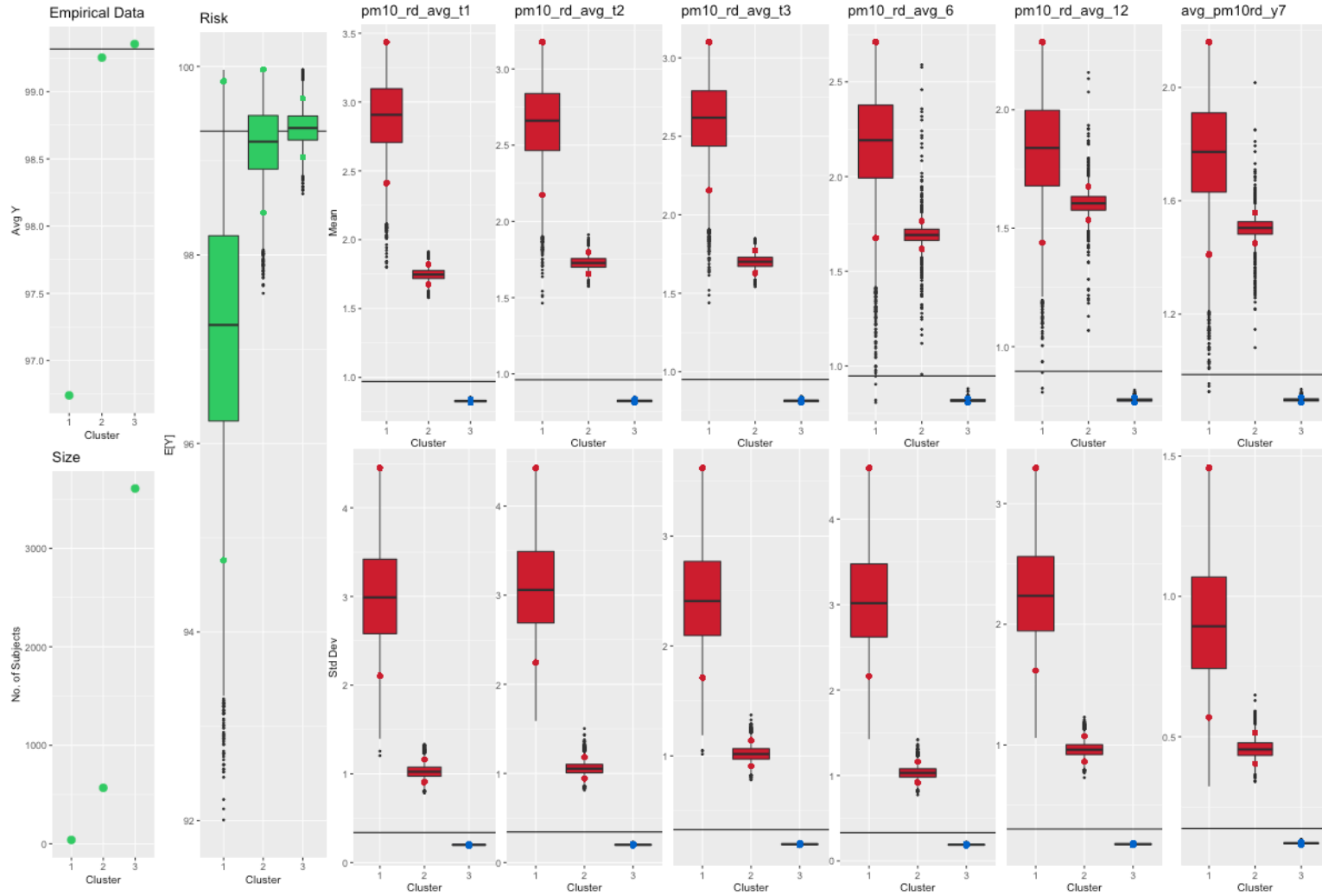


Figure E3 Posterior distribution of the parameters for FVC at age 8 years for the representative clustering.

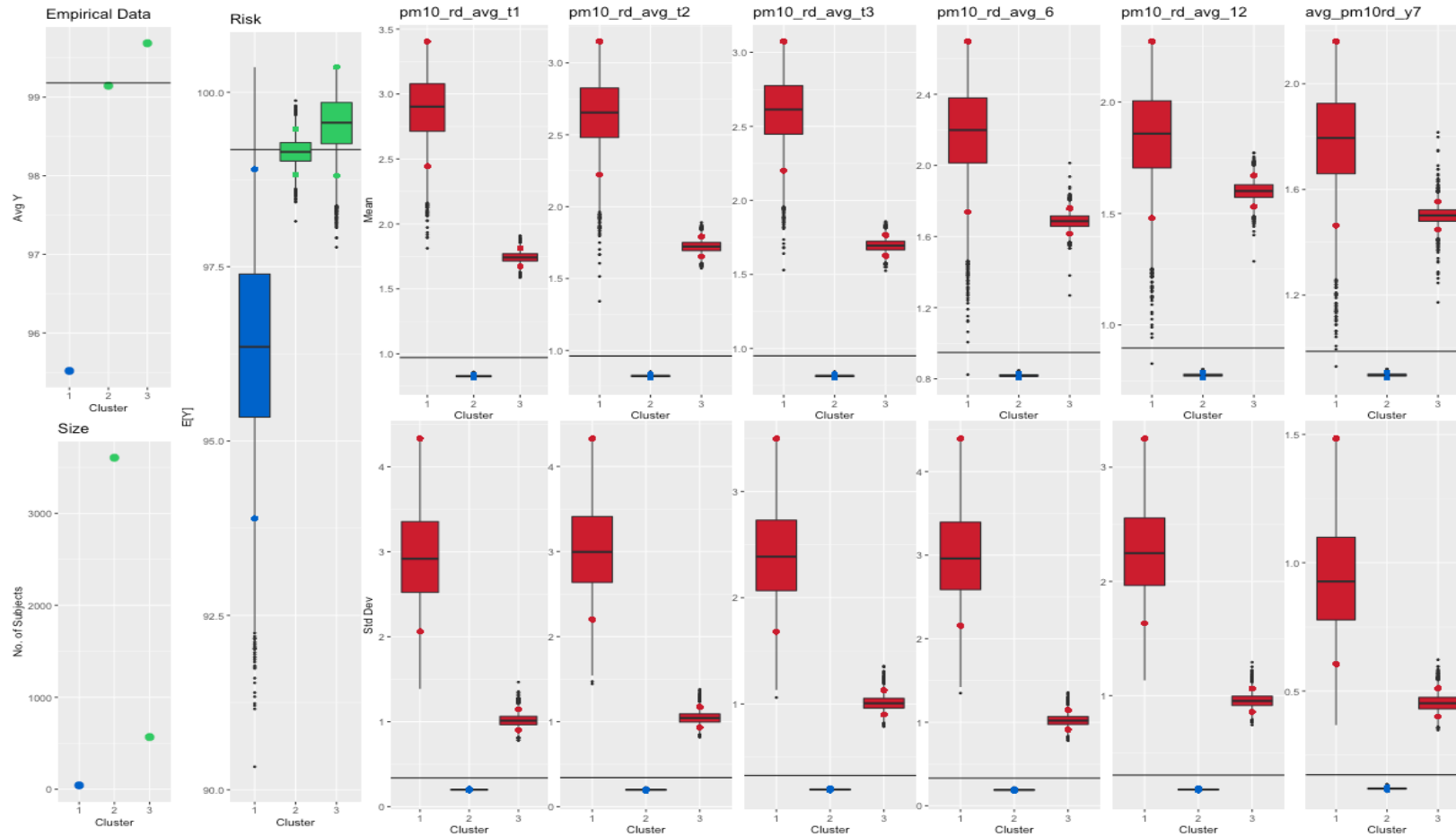
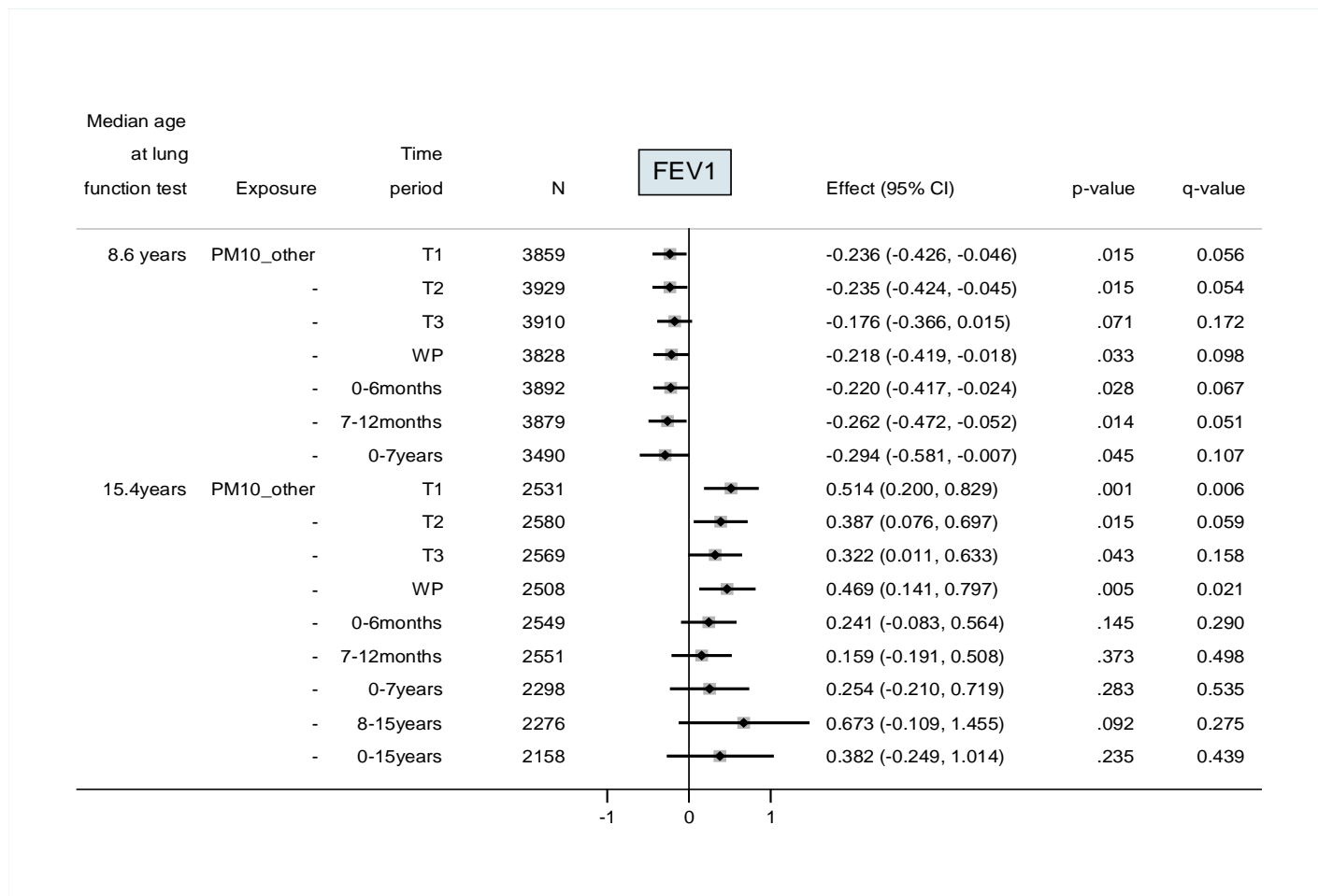
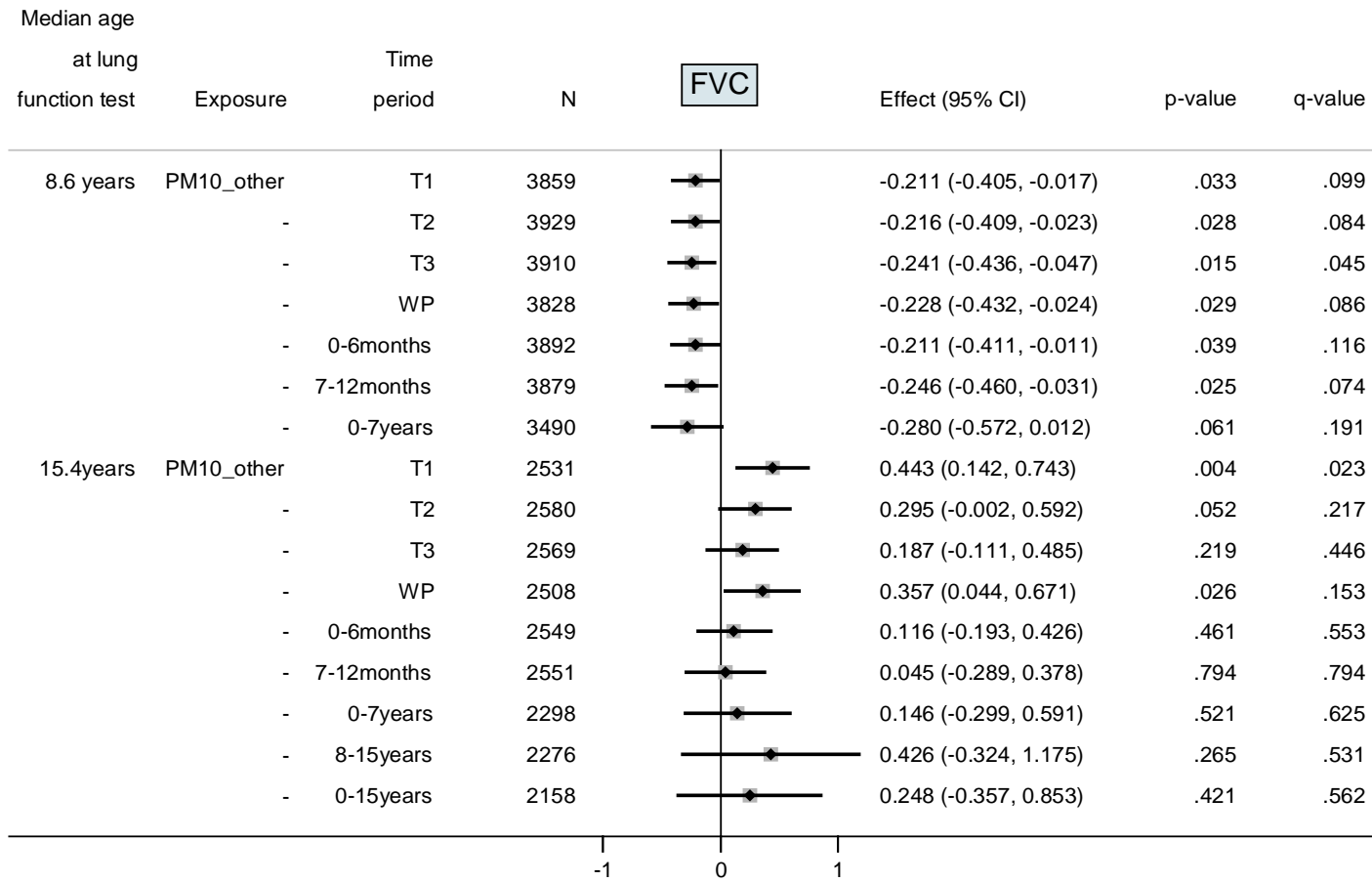


Figure E4A-C: Mean Changes in percent predicted of lung function at both aged 8 and 15 years in relation to per 1 $\mu\text{g}/\text{m}^3$ higher **PM₁₀_other** at different time periods, main model* (sex, gestational age, maternal education, home ownership, maternal smoking during pregnancy, passive smoking in childhood, damp and mould presence at home, and season of clinic visit)





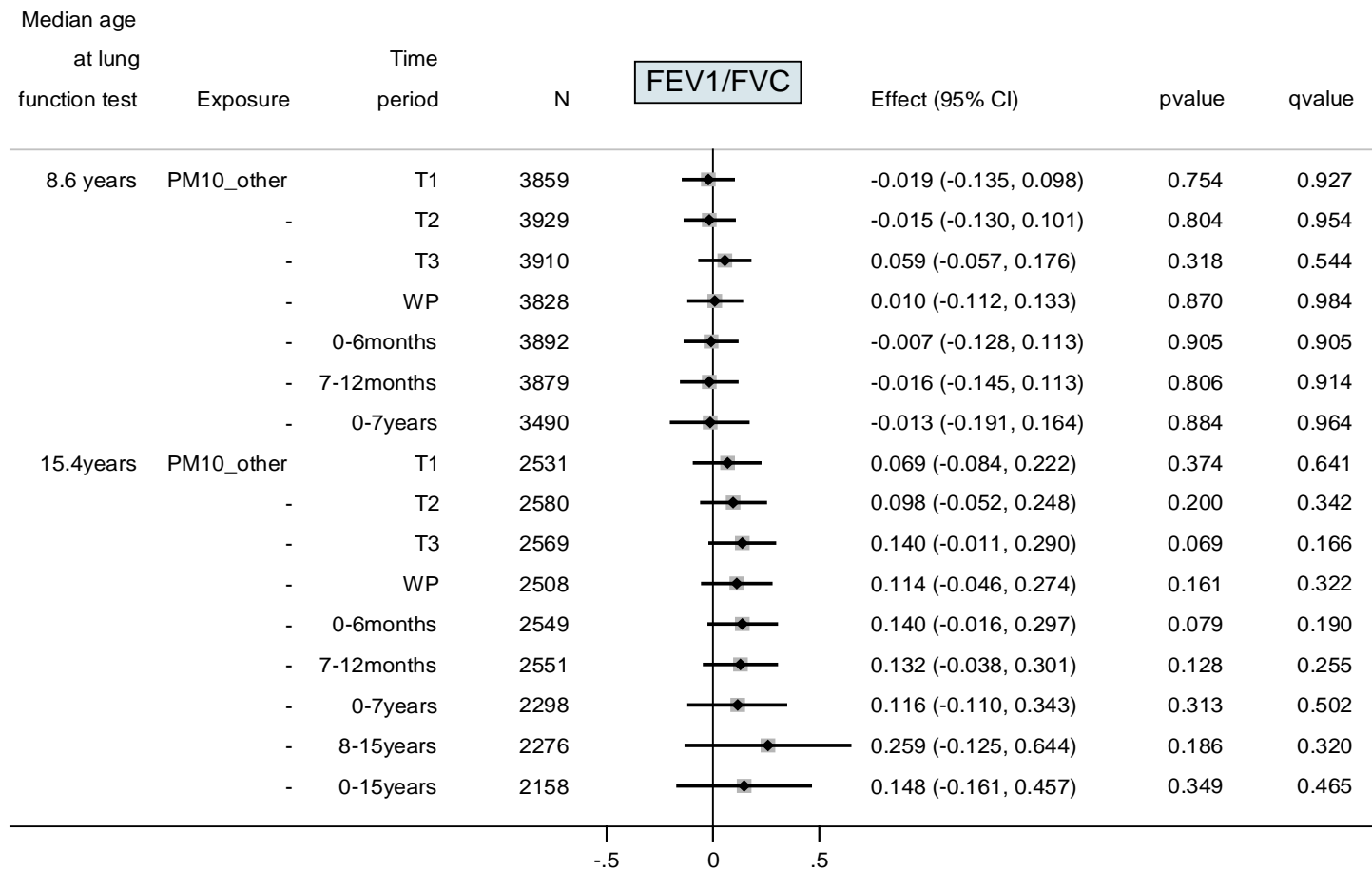


Table E7 Mean Changes in percent predicted of lung function at both aged 8 and 15 years in relation to per 10µg/m³ higher **PM₁₀_total** at different time periods: co-adjusting PM₁₀_total exposures in preceding time periods based on main model*(sex, gestational age, maternal education, home ownership, maternal smoking during pregnancy, passive smoking in childhood, damp and mould presence at home, and season of clinic visit)

	% predicted of FEV ₁ at aged 8 years					
	Main Model	Main Model +T1+T2	Main Model +T1+T2+T3	Main Model +T1+T2+T3+0-6 months	Main Model +T1+T2+T3+0- 6months+7-12 months	Main Model +T1+T2+T3+ 0-7 years
Trimester 1	-0.679 (-1.440 to 0.082)	-0.676 (-1.437 to 0.085) vif:1.20	-0.651 (-1.417 to 0.115) Vif:1.21	-0.662 (-1.542 to 0.219) Vif:1.58	-0.508 (-1.405 to 0.389) Vif: 1.61	-0.893 (-1.860 to 0.073) Vif:1.67
Trimester 2	-0.930 (-1.718 to -0.142)	-0.910 (-1.702 to -0.119) vif: 1.29	-0.904 (-1.700 to -0.108) Vif: 1.29	-0.953 (-1.753 to -0.154) Vif: 1.29	-0.463 (-1.649 to 0.723) Vif:2.81	-0.817 (-1.827 to 0.193) Vif:1.84
Trimester 3	-0.577 (-1.351 to 0.197)		-0.402 (-1.196to 0.392) Vif: 1.17	-0.459 (-1.266 to 0.348) Vif: 1.21	-0.238 (-1.098 to 0.623) Vif:1.35	-0.091 (-1.075 to 0.893) Vif:1.57
0-6months	-0.451 (-1.488 to 0.586)			0.172 (-1.046 to 1.389) Vif:1.48	0.176 (-1.061 to 1.412) Vif:1.51	-
7-12 months	-2.045 (-3.291 to -0.800)				-1.162 (-3.174 to 0.850) Vif:2.64	-
0-7 years	-2.498 (-4.633 to -0.362)					-0.304 (-3.494 to 2.886) Vif:2.19
	% predicted of FVC at aged 8 years					

	Main Model	Main Model +T1+T2	Main Model +T1+T2+T3	Main Model +T1+T2+T3+0-6 months	Main Model +T1+T2+T3+0- 6months+7-12 months	Main Model +T1+T2+T3+ 0-7 years
Trimester 1	-0.468 (-1.244 to 0.308)	-0.473 (-1.249 to 0.303) Vif:1.20	-0.395 (-1.175 to 0.384) Vif:1.21	-0.496 (-1.392 to 0.400) Vif:1.58	-0.361 (-1.274 to 0.552) Vif:1.61	-0.628 (-1.611 to 0.354) Vif:1.67
Trimester 2	-0.610 (-1.414 to 0.194)	-0.572 (-1.379 to 0.235) Vif:1.29	-0.564 (-1.373 to 0.246) Vif:1.29	-0.595 (-1.409 to 0.219) Vif:1.29	-0.141 (-1.348 to 1.066) Vif:2.81	-0.315 (-1.342 to 0.712) Vif:1.84
Trimester 3	-1.312 (-2.100 to -0.525)		-1.202 (-2.009 to -0.394) Vif:1.17	-1.229 (-2.051 to -0.408) Vif:1.21	-1.038 (-1.915 to -0.162) Vif:1.35	-0.817 (-1.818 to 0.184) Vif:1.57
0-6months	-0.195 (-1.251 to 0.862)			0.406 (-0.834 to 1.645) Vif:1.48	0.379 (-0.880 to 1.638) Vif:1.51	-
7-12 months	-1.805 (-3.074 to -0.536)				-1.058 (-3.107 to 0.990) Vif:2.64	-
0-7 years	-2.069 (-4.242to 0.105)					-0.147 (-0.392 to 3.098) Vif:2.19
% predicted of FEV ₁ /FVC at aged 8 years						
	Main Model	Main Model +T1+T2	Main Model +T1+T2+T3	Main Model +T1+T2+T3+0-6 months	Main Model +T1+T2+T3+0- 6months+7-12 months	Main Model +T1+T2+T3+ 0-7 years
Trimester 1	-0.173 (-0.638 to 0.293)	-0.164 (-0.630 to 0.301) Vif:1.20	-0.211 (-0.679 to 0.256) Vif:1.21	-0.099 (-0.638 to 0.439) Vif:1.58	-0.086 (-0.634 to 0.462) Vif:1.61	-0.203 (-0.800 to 0.393) Vif:1.67
Trimester 2	-0.255 (-0.737 to 0.227)	-0.273 (-0.758 to 0.211) Vif:1.29	-0.275 (-0.761 to 0.211) Vif:1.29	-0.292 (-0.781 to 0.197) Vif:1.29	-0.311 (-1.036to 0.413) Vif:2.81	-0.413 (-1.036 to 0.210) Vif:1.84

Trimester 3	0.641 (0.168 to 1.113)	0.696 (0.212 to 1.181) Vif:1.17	0.677 (0.183 to 1.170) Vif:1.21	0.688 (0.162 to 1.213) Vif:1.35	0.623 (0.015 to 1.230) Vif:1.57
0-6months	-0.268 (-0.903 to 0.368)		-0.278 (-1.023 to 0.467) Vif:1.48	-0.260 (-1.015 to 0.496) Vif:1.51	-
7-12 months	-0.140 (-0.903 to 0.622)			0.023 (-1.206 to 1.252) Vif:2.64	-
0-7 years	-0.388 (-1.709 to 0.933)				-0.198 (-2.166 to 1.771) Vif:2.19

% predicted of FEV₁ at aged 15 years

	Main Model	Main Model +T1+T2	Main Model +T1+T2+T3	Main Model +T1+T2+T3+0-6 months	Main Model +T1+T2+T3+0- 6months+7-12 months	Main Model +T1+T2+T3+ 0-15 years
Trimester 1	1.303 (0.077 to 2.529)	1.374 (0.145 to 2.602) Vif:1.14	1.480 (0.252 to 2.709) Vif:1.14	1.703 (0.245 to 3.161) Vif:1.59	1.732 (0.251 to 3.212) Vif:1.61	1.608 (0.046 to 3.171) Vif:1.56
Trimester 2	0.610 (-0.622 to 1.843)	0.660 (-0.576 to 1.896) Vif:1.20	0.661 (-0.575 to 1.898) Vif:1.20	0.580 (-0.667 to 1.826) Vif:1.20	-0.134 (-2.022 to 1.754) Vif:2.73	1.158 (-0.409 to 2.725) Vif:1.63
Trimester 3	0.008 (-1.191 to 1.206)		-0.006 (-1.244 to 1.231) Vif:1.14	-0.026 (-1.283 to 1.231) Vif:1.16	-0.404 (-1.771 to 0.963) Vif:1.36	0.260 (-1.291 to 1.810) Vif:1.49
0-6months	0.416 (-1.291 to 2.214)			-0.650 (-2.693 to 1.392) Vif:1.58	-0.887 (-2.958 to 1.183) Vif:1.61	-
7-12 months	1.330 (-0.723 to 3.282)				1.694 (-1.700 to 5.088)	-

							Vif:2.72
0-15 years	1.467 (-3.310 to 6.244)						-2.702 (-9.555 to 4.151) Vif:2.03
% predicted of FVC at aged 15 years							
	Main Model	Main Model +T1+T2	Main Model +T1+T2+T3	Main Model +T1+T2+T3+0-6 months	Main Model +T1+T2+T3+0- 6months+7-12 months	Main Model +T1+T2+T3+ 0-15 years	
Trimester 1	1.173 (0.005 to 2.342)	1.204 (0.033 to 2.376) Vif:1.14	1.303 (0.131 to 2.476) Vif:1.14	1.821 (0.429 to 3.213) Vif:1.59	1.751 (0.339 to 3.163) Vif:1.61	1.633 (0.139 to 3.127) Vif:1.56	
Trimester 2	0.491 (-0.688 to 1.669)	0.555 (-0.623 to 1.734) Vif:1.20	0.563 (-0.617 to 1.743) Vif:1.20	0.515 (-0.675 to 1.705) Vif:1.20	-0.740 (-2.541 to 1.061) Vif:2.73	1.008 (-0.490 to 2.506) Vif:1.63	
Trimester 3	-0.582 (-1.728 to 0.564)		-0.564 (-1.744 to 0.617) Vif:1.14	-0.479 (-1.679 to 0.721) Vif:1.16	-1.041 (-2.346 to 0.263) Vif:1.36	-0.015 (-1.498 to 1.467) Vif:1.49	
0-6months	-0.267 (-1.901 to 1.367)			-1.416 (-3.367 to 0.534) Vif:1.58	-1.755 (-3.731 to 0.220) Vif:1.61	-	
7-12 months	1.236 (-0.723 to 3.194)				2.974 (-0.264 to 6.212) Vif:2.72	-	
0-15 years	0.284 (-4.291 to 4.860)						-3.138 (-9.690 to 3.414) Vif:2.03
%predicted of FEV ₁ /FVC at aged 15 years							
	Main Model	Main Model +T1+T2	Main Model +T1+T2+T3	Main Model +T1+T2+T3+0-6 months	Main Model +T1+T2+T3+0- 6months+7-12 months	Main Model +T1+T2+T3+ 0-15 years	
Trimester 1	0.087 (-0.507 to 0.682)	0.136 (-0.460 to 0.733) Vif:1.14	0.143 (-0.455 to 0.740) Vif:1.14	-0.223 (-0.930 to 0.484) Vif:1.59	-0.098 (-0.816 to 0.620) Vif:1.61	-0.103 (-0.872 to 0.665) Vif:1.56	
Trimester 2	0.147	0.134	0.134	0.093	0.803	0.177	

	(-0.448 to 0.742)	(-0.466 to 0.734) Vif:1.20	(-0.467 to 0.735) Vif:1.20	(-0.512 to 0.697) Vif:1.20	(-0.112 to 1.719) Vif:2.73	(-0.593 to 0.948) Vif:1.63
Trimester 3	0.606 (0.027 to 1.185)		0.550 (-0.052 to 1.152) Vif:1.14	0.424 (-0.185 to 1.034) Vif:1.16	0.677 (0.013 to 1.340) Vif:1.36	0.233 (-0.530 to 0.996) Vif:1.49
0-6months	0.796 (-0.031 to 1.622)			0.956 (-0.034 to 1.947) Vif:1.58	1.089 (0.084 to 2.093) Vif:1.61	-
7-12 months	0.072 (-0.924 to 1.067)				-1.675 (-3.321 to -0.028) Vif:2.72	-
0-15 years	1.325 (-1.014 to 3.664)					0.648 (-2.724 to 4.019) Vif:2.03

Figure E5 Mean Changes in percent predicted of FVC at aged 8 years in relation to per 10 $\mu\text{g}/\text{m}^3$ higher **PM₁₀_total** at different time periods by sex, maternal education and smoking, main model*

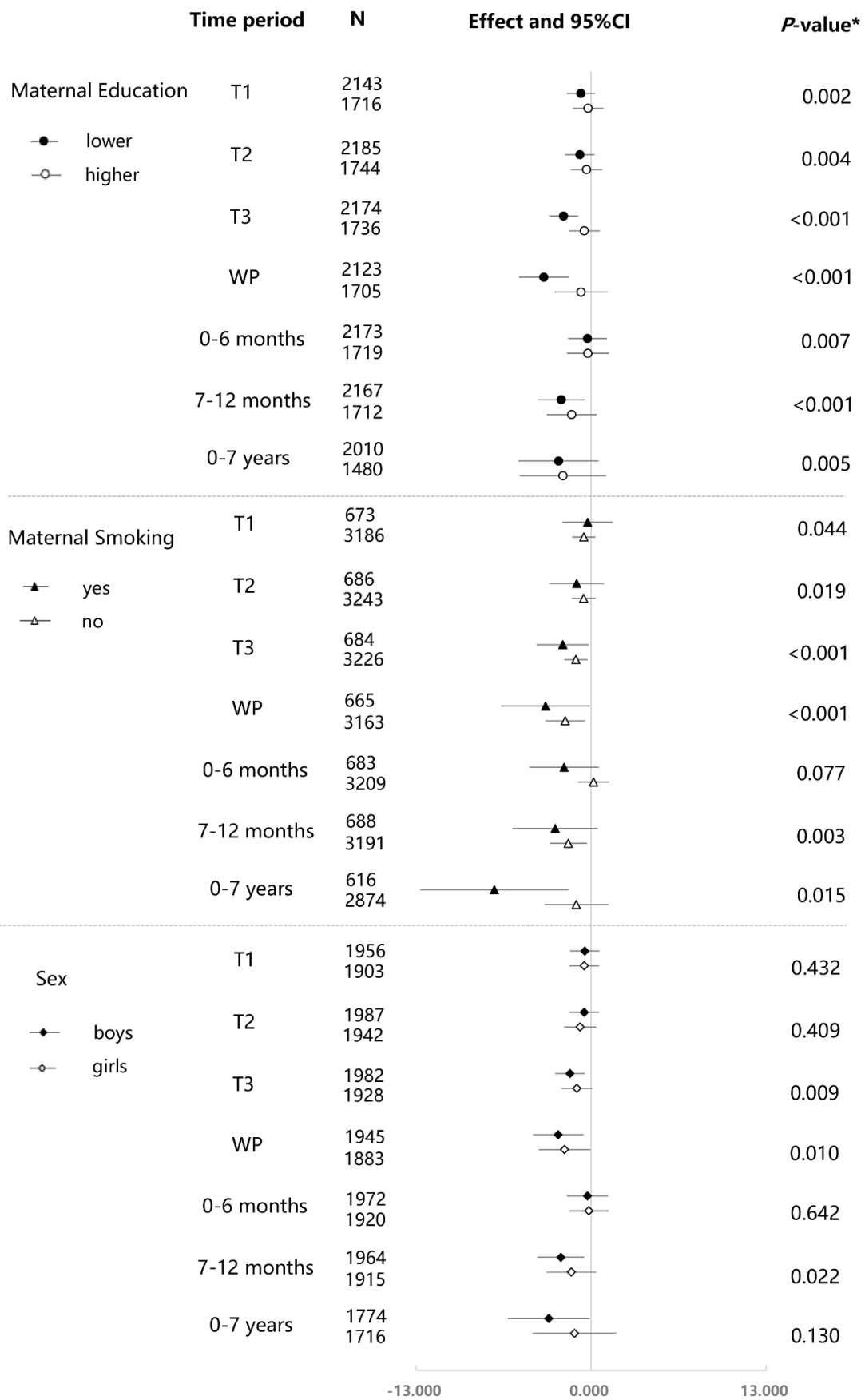


Table E8 Mean Changes in percent predicted of lung function at both aged 8 and 15 years in relation to per $1\mu\text{g}/\text{m}^3$ higher **PM_{10_road}** at different time periods: sensitivity analyses based on fully adjusted model*(sex, gestational age, maternal education, home ownership, maternal smoking during pregnancy, passive smoking in childhood, damp and mould presence at home, and season of clinic visit)

Available as additional data in a large spreadsheet labelled as Table E6.1

Table E9 Mean Changes in percent predicted of lung function at both aged 8 and 15 years in relation to per $10\mu\text{g}/\text{m}^3$ higher **PM_{10_total}** at different time periods: sensitivity analyses based on main model(sex, gestational age, maternal education, home ownership, maternal smoking during pregnancy, passive smoking in childhood, damp and mould presence at home, and season of clinic visit)

Available as additional data in a large spreadsheet labelled as Table E6.2

Table E10 Associations between air pollution in different time periods and lung function growth in litres/year from age 8 to 15 years

	PM₁₀_total, per 10 µg/m³	N	Effect(95%CI)	PM₁₀_road, per 1 µg/m³	N	Effect(95%CI)	PM₁₀_other, per 1µg/m³	N	Effect(95%CI)
FEV₁ growth	Trimester 1	2129	0.009 (0.002 to 0.016)	Trimester 1	2129	0.007 (0.002 to 0.012)	Trimester 1	2129	0.002 (0.001 to 0.004)
	Trimester 2	2176	0.007 (0.000 to 0.014)	Trimester 2	2176	0.005 (0.000 to 0.010)	Trimester 2	2176	0.002 (-0.000 to 0.003)
	Trimester 3	2168	0.000 (-0.007 to 0.007)	Trimester 3	2168	0.003 (-0.002 to 0.008)	Trimester 3	2168	0.001 (-0.001 to 0.002)
	Whole pregnancy	2112	0.015 (0.003 to 0.027)	Whole pregnancy	2112	0.006 (0.001 to 0.011)	Whole pregnancy	2112	0.002 (0.000 to 0.004)
	0-6 months	2155	-0.003 (-0.012 to 0.006)	0-6 months	2155	0.003 (-0.002 to 0.008)	0-6 months	2155	0.000 (-0.001 to 0.002)
	7-12 months	2161	0.007 (-0.004 to 0.018)	7-12 months	2161	0.002 (-0.003 to 0.008)	7-12 months	2161	0.000 (-0.002 to 0.002)
	0-7 years	1945	-0.002 (-0.021 to 0.017)	0-7 years	1945	0.003 (-0.004 to 0.010)	0-7 years	1945	0.000 (-0.002 to 0.003)
	8-15 years	1924	0.017 (-0.016 to 0.050)	8-15 years	1924	0.009 (-0.003 to 0.022)	8-15 years	1924	0.003 (-0.001 to 0.007)
	0-15 years	1820	0.001 (-0.026 to 0.027)	0-15 years	1820	0.006 (-0.004 to 0.016)	0-15 years	1820	0.001 (-0.003 to 0.004)
	FVC growth	Trimester 1	2195	0.010 (0.002 to 0.017)	Trimester 1	2195	0.005 (-0.0002 to 0.010)	Trimester 1	2195
Trimester 2		2243	0.006 (-0.002 to 0.014)	Trimester 2	2243	0.004 (-0.001 to 0.009)	Trimester 2	2243	0.001 (-0.000 to 0.003)
Trimester 3		2234	-0.004 (-0.012 to 0.003)	Trimester 3	2234	0.002 (-0.004 to 0.007)	Trimester 3	2234	0.000 (-0.002 to 0.002)
Whole pregnancy		2177	0.010 (-0.002 to 0.023)	Whole pregnancy	2177	0.004 (-0.001 to 0.010)	Whole pregnancy	2177	0.001 (-0.000 to 0.003)
0-6 months		2220	-0.007	0-6 months	2220	0.002	0-6 months	2220	0.000

		(-0.018 to 0.003)			(-0.004 to 0.007)			(-0.002 to 0.002)
7-12 months	2226	0.006 (-0.006 to 0.018)	7-12 months	2226	0.002 (-0.004 to 0.007)	7-12 months	2226	-0.000 (-0.002 to 0.002)
0-7 years	2005	-0.008 (-0.029 to 0.012)	0-7 years	2005	0.002 (-0.006 to 0.010)	0-7 years	2005	-0.000 (-0.003 to 0.003)
8-15 years	1982	0.004 (-0.032 to 0.040)	8-15 years	1982	0.006 (-0.007 to 0.020)	8-15 years	1982	0.002 (-0.002 to 0.007)
0-15 years	1877	-0.008 (-0.037 to 0.020)	0-15 years	1877	0.005 (-0.006 to 0.016)	0-15 years	1877	0.000 (-0.003 to 0.004)

Table E11 Comparisons of characteristics, exposures and lung function between those remained and those lost to follow-up in this study

	Participated at age 8 years			Participated at age 15 years			Participated at both ages 8 and 15 years (n=2364)	Participated at age 8 but drop-out at age 15 years(n=2912)	p-value
	yes (N=5276)	no (n=8687)	p-value	yes (n=3446)	no (n=10517)	p-value			
preterm birth - yes	5.8%	6.2%	0.308	5.0%	6.4%	0.004	4.7%	6.7%	0.002
Maternal education level - lower	55.9%	70.7%	<0.001	53.8%	68.6%	<0.001	51.3%	59.8%	<0.001
Home ownership - rented	13.0%	27.2%	<0.001	12.0%	24.5%	<0.001	11.0%	14.7%	<0.001
Damp and mould presence at home - yes	48.0%	47.4%	0.550	50.3%	46.6%	<0.001	49.0%	47.2%	0.209
smoking in pregnancy - yes	18.2%	29.5%	<0.001	15.7%	28.3%	<0.001	14.5%	21.3%	<0.001
Exposure to passive smoke - yes	55.5%	73.6%	<0.001	51.7%	71.1%	<0.001	49.9%	60.2%	<0.001
PM₁₀_road exposure in 1st trimester (mean(SD))	0.96 (0.70)	0.97 (0.72)	0.626	0.96 (0.68)	0.97 (0.72)	0.610	0.95(0.67)	0.97(0.72)	0.457
PM₁₀_road exposure in 2nd trimester(mean(SD))	0.96 (0.70)	0.96 (0.72)	0.615	0.96 (0.69)	0.96 (0.72)	0.931	0.96(0.69)	0.96(0.71)	0.999
PM₁₀_road exposure in 3rd trimester(mean(SD))	0.94 (0.68)	0.94(0.70)	0.994	0.94 (0.66)	0.94(0.70)	0.954	0.94(0.65)	0.94(0.71)	0.687
FEV₁ in L at aged 8 years (mean(SD))							1.70(0.26)	1.69(0.26)	0.608
FVC in L at aged 8 years (mean(SD))							1.92(0.31)	1.93(0.31)	0.736