Supplementary Table 1. Cross-sectional associations of DNA methylation age in mid-childhood with total serum IgE, atopic sensitization, environmental allergen sensitization, food allergen sensitization and asthma at mid-childhood, additionally adjusting for chronological age at mid-childhood.

	Mid-childhood DNA methylation age (additionally adjusted for chronological age at mid-childhood)	
Mid-childhood outcomes	**Estimate (95% CI)**	**P value**
Total serum IgE (log-scale)	0.11 (0.02; 0.21)	0.019
	Odds ratio (95% CI)	**P value**
Atopic sensitization	1.21 (1.06; 1.39)	0.005
Environmental allergen sensitization	1.17 (1.02; 1.34)	0.022
Food allergen sensitization	1.28 (1.11; 1.49)	0.001
Current asthma	1.17 (0.99; 1.38)	0.065

Model adjusted for maternal [age at enrollment (continuous), smoking status (never, former, or during pregnancy), education (college / graduate level or not college / graduate level), and atopy history (asthma, eczema or hay fever)], and for child [sex (female or male), race / ethnicity (white, black or others), gestational age (continuous), age at blood draw at mid-childhood (continuous)], and cell type proxies estimated for peripheral blood (percentages of monocytes, granulocytes, CD8T cells, CD4T cells, and B cells).

Supplementary Table 2. Summary statistics and correlation matrix between DNA methylation age, intrinsic epigenetic age acceleration and extrinsic epigenetic age acceleration measured at mid-childhood (N=408).

	Summary statistics		**Spearman correlations**		
Mid-childhood	Mean (SD)	Median (IQR)	DNA methylation age	IEAA (intrinsic)	EEAA (extrinsic)
DNA methylation age	8.8 (1.8)	8.5 (2.5)	1	0.85	0.24
IEAA (intrinsic)	-0.06 (1.6)	-0.3 (2.2)	--	1	0.13
EEAA (extrinsic)	-0.10 (5.8)	0.2 (8.2)	--	--	1

Supplementary Table 3. Associations of DNA methylation age, methylation age for gestational age and age acceleration at birth with total serum IgE, atopic sensitization, environmental allergen sensitization, and food allergen sensitization in mid-childhood.

	“Epigenetic clock” metrics at birth							
	DNA methylation age		**DNAm GA**		**IEAA (intrinsic)**		**EEAA (extrinsic)**	
	Estimate (95% CI)	**P value**	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**
Total serum IgE (log-scale)	-0.52 (-1.59; 0.54)	0.335	0.03 (-0.123; 0.19)	0.692	-0.10 (-1.16; 0.97)	0.856	-0.02 (-0.07; 0.02)	0.295
	Odds ratio (95% CI)	**P value**	**Odds ratio (95% CI)**	**P value**	**Odds ratio (95% CI)**	**P value**	**Odds ratio (95% CI)**	**P value**
Atopic sensitization	0.37 (0.08; 1.55)	0.177	1.13 (0.91; 1.39)	0.271	0.43 (0.10; 1.76)	0.243	0.96 (0.91; 1.02)	0.167
Environmental allergen sensitization	0.40 (0.09; 1.71)	0.223	1.20 (0.97; 1.49)	0.102	0.49 (0.11; 2.02)	0.325	0.97 (0.91; 1.02)	0.252
Food allergen sensitization	0.87 (0.15; 4.72)	0.869	1.01 (0.79; 1.29)	0.946	1.12 (0.21; 5.81)	0.890	0.95 (0.89; 1.01)	0.108
Current asthma	0.55 (0.09; 2.96)	0.494	0.88 (0.70; 1.10)	0.257	0.59 (0.11; 3.00)	0.530	0.96 (0.90; 1.02)	0.212

For DNAmAge and DNAm GA, model adjusted for maternal [age at enrollment (continuous), smoking status (never, former, or during pregnancy), education (college / graduate level or not college / graduate level), and atopy history (asthma, eczema or hay fever)], child [sex (female or male), race / ethnicity (white, black or others), gestational age (continuous)], and cell type proxies estimated for cord blood (percentages of monocytes, granulocytes, CD8T cells, CD4T cells, B cells and nucleated red blood cells).

For IEAA and EEAA, models adjusted for maternal [age at enrollment (continuous), smoking status (never, former, or during pregnancy), education (college / graduate level or not college / graduate level), atopy history (asthma, eczema or hay fever)], child [sex (female or male), race / ethnicity (white, black or others), gestational age (continuous)].

Supplementary Table 4. Associations of DNA methylation age and age acceleration at early-childhood with total serum IgE, atopic sensitization, environmental allergen sensitization, and food allergen sensitization in mid-childhood.

	"Epigenetic clock" metrics at early-childhood					
	DNA methylation age		**IEAA (intrinsic)**		**EEAA (extrinsic)**	
Mid-childhood outcomes	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**
Total serum IgE (log-scale)	0.16 (-0.38; 0.70)	0.573	0.23 (-0.38; 0.84)	0.461	0.003 (-0.08; 0.08)	0.949
	Odds ratio (95% CI)	**P value**	**Odds ratio (95% CI)**	**P value**	**Odds ratio (95% CI)**	**P value**
Atopic sensitization	1.89 (0.83; 4.77)	0.145	1.71 (0.71; 4.42)	0.241	0.99 (0.88; 1.11)	0.836
Environmental allergen sensitization	1.48 (0.66; 3.62)	0.362	1.87 (0.77; 4.98)	0.182	0.97 (0.86; 1.09)	0.625
Food allergen sensitization	3.40 (0.85; 18.36)	0.108	2.17 (0.62; 10.10)	0.267	0.97 (0.83; 1.13)	0.706
Current asthma	0.64 (0.25; 1.52)	0.332	0.80 (0.32; 1.96)	0.617	1.00 (0.87; 1.14)	0.970

For DNAmAge, models adjusted for maternal [age at enrollment (continuous), smoking status (never, former, or during pregnancy), education (college / graduate level or not college / graduate level), and atopy history (asthma, eczema or hay fever)], child [sex (female or male), race / ethnicity (white, black or others), gestational age (continuous)], and cell type proxies estimated for peripheral blood (percentages of monocytes, granulocytes, CD8T cells, CD4T cells, and B cells).

For IEAA and EEAA, models adjusted for maternal [age at enrollment (continuous), smoking status (never, former, or during pregnancy), education (college / graduate level or not college / graduate level), and atopy history (asthma, eczema or hay fever)], child [sex (female or male), race / ethnicity (white, black or others), gestational age (continuous)].

Supplementary Table 5. Associations of chronological at early and mid-childhood with total serum IgE, atopic sensitization, environmental allergen sensitization, and food allergen sensitization in mid-childhood.

	Chronological age at early-childhood		Chronological age at mid-childhood	
Mid-childhood outcomes	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**
Total serum IgE (log-scale)	0.41 (-0.42; 1.25)	0.334	0.03 (-0.20; 0.26)	0.267

	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Atopic sensitization	3.47 (0.94; 17.7)	0.088	1.12 (0.82; 1.55)	0.463
Environmental allergen sensitization	0.93 (0.24; 3.23)	0.914	1.32 (0.97; 1.81)	0.078
Food allergen sensitization	0.82 (0.14; 3.69)	0.809	0.81 (0.57; 1.13)	0.222
Current asthma	0.15 (0.009; 1.06)	0.113	1.11 (0.80; 1.52)	0.524

Model adjusted for maternal [age at enrollment (continuous), smoking status (never, former, or during pregnancy), education (college / graduate level or not college / graduate level), and atopy history (asthma, eczema or hay fever)], child [sex (female or male), race / ethnicity (white, black or others), gestational age (continuous)].

Supplementary Table 6. Participant characteristics in the 'Genetics of Asthma in Costa Rica' cohort.

Participant characteristics	**N=159**
Maternal	
Current smoking status, N (%)	
Yes	7 (4%)
No	152 (96%)
Asthma history, N (%)*	
Yes	45 (28%)
No	113 (71%)
Child	
Age (years), mean (SD)	9.1 (1.8)
Sex, N (%)	
Female	64 (41%)
Male	95 (59%)
Total serum IgE (kU/L), mean (SD)	840.7 (1016.6)
Atopic sensitization (skin), N (%)	
Yes	144 (91%)
No	15 (9%)
Atopic sensitization (blood), N (%)*	
Yes	136 (86%)
No	23 (14%)
Asthma, N (%)†	
Yes	98 (62%)
No	44 (28%)

*number of missing = 1

†number of missing = 17

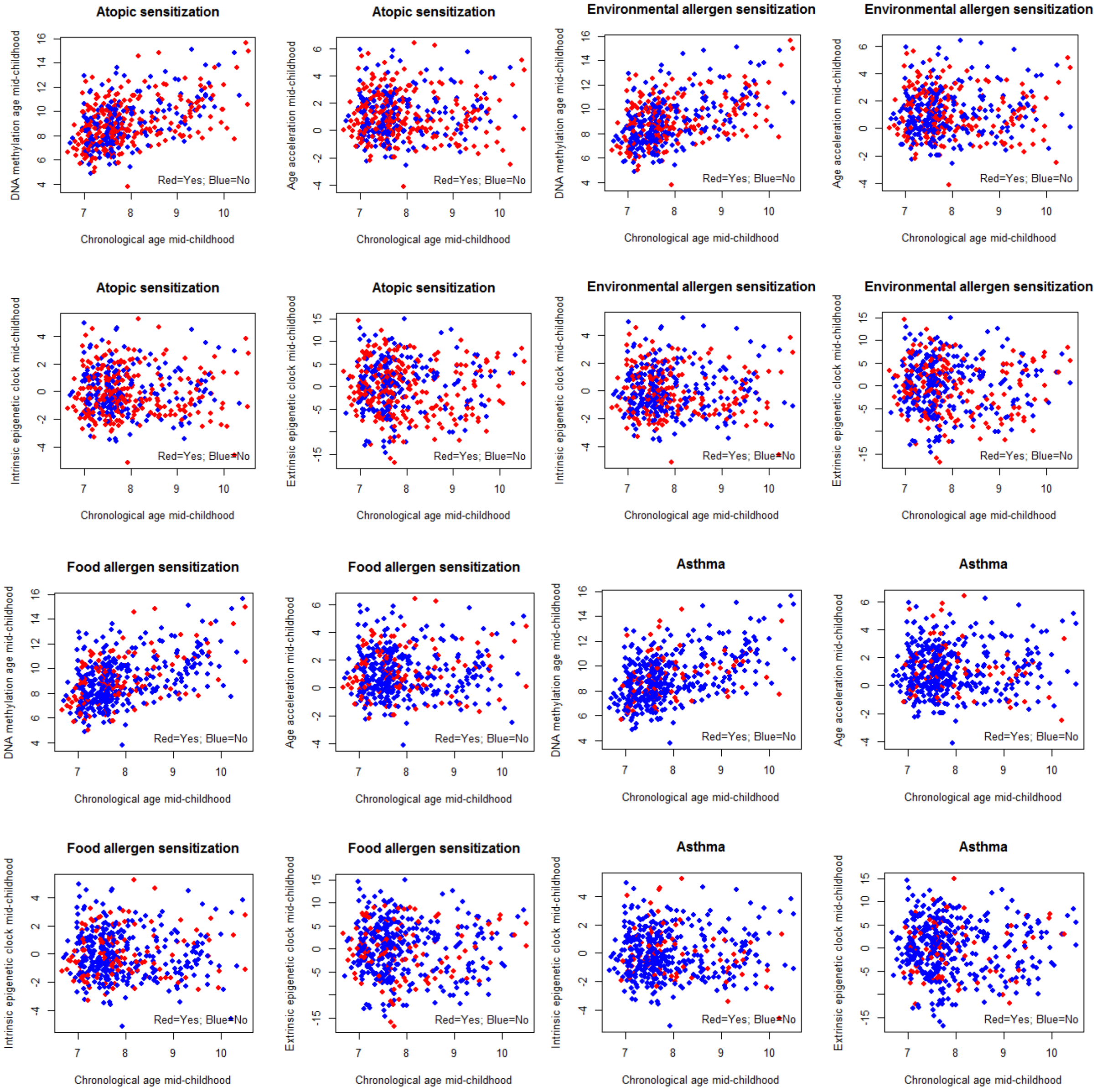
Supplementary Table 7. Replication: associations of DNA methylation age and age acceleration at mid-childhood with total serum IgE and atopic sensitization in mid-childhood in the ‘Genetics of Asthma in Costa Rica’ cohort.

	Costa Rica cohort					
	DNA methylation age		**IEAA (intrinsic)**		**EEAA (extrinsic)**	
Mid-childhood outcomes	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**	**Estimate (95% CI)**	**P value**
Total serum IgE (log-scale)	0.01 (-0.03; 0.05)	0.512	0.01 (-0.03; 0.06)	0.492	0.03 (-0.02; 0.08)	0.214
	Odds ratio (95% CI)	**P value**	**Odds ratio (95% CI)**	**P value**	**Odds ratio (95% CI)**	**P value**
Atopic sensitization (skin)	1.18 (1.04; 1.38)	0.019	1.19 (1.05; 1.37)	0.010	1.18 (1.05; 1.35)	0.009
Atopic sensitization (IgE)	1.07 (0.98; 1.17)	0.165	1.07 (0.98; 1.18)	0.139	1.09 (0.99; 1.21)	0.074
Asthma	1.07 (1.00; 1.15)	0.066	1.09 (1.01; 1.18)	0.027	1.08 (1.00; 1.17)	0.064

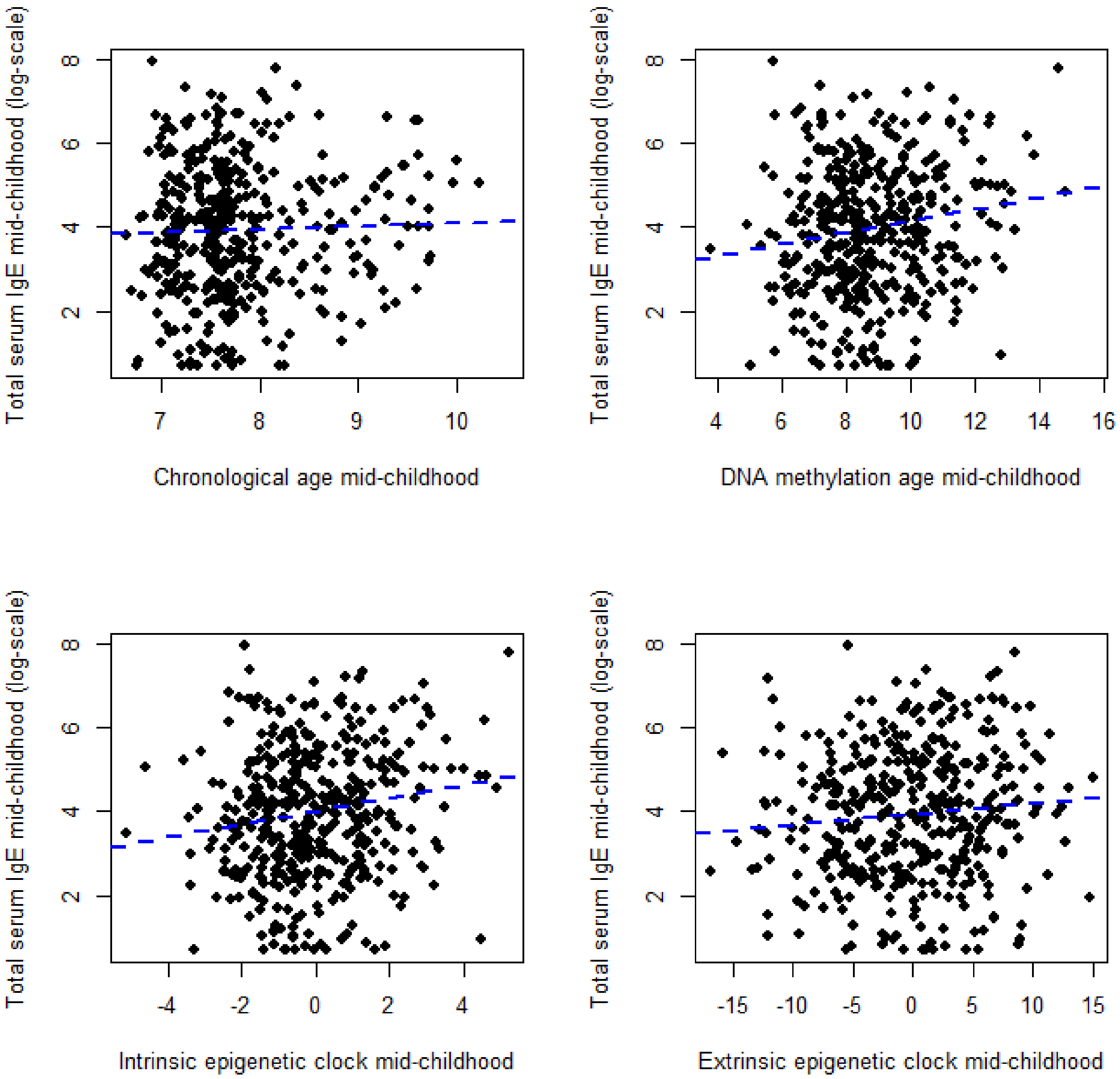
For DNAmAge, models adjusted for maternal [current smoking status (yes / no), asthma history (yes / no)], child [sex (female or male)], plate and cell type proxies estimated for peripheral blood (percentages of monocytes, granulocytes, CD8T cells, CD4T cells, and B cells).

For IEAA and EEAA, models adjusted for maternal [current smoking status (yes / no), asthma history (yes / no)], child [sex (female or male)] and plate.

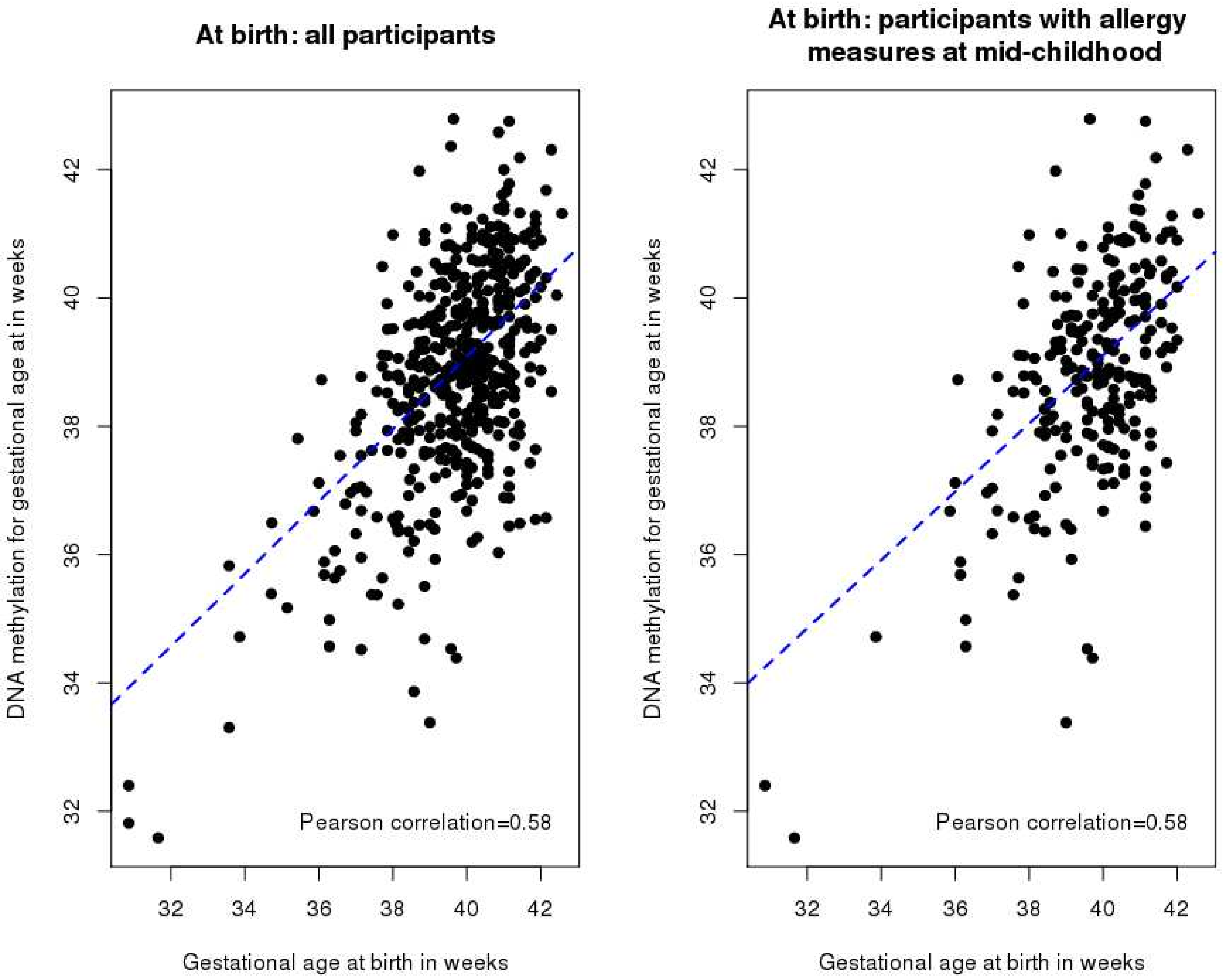
Supplementary Figure 1.



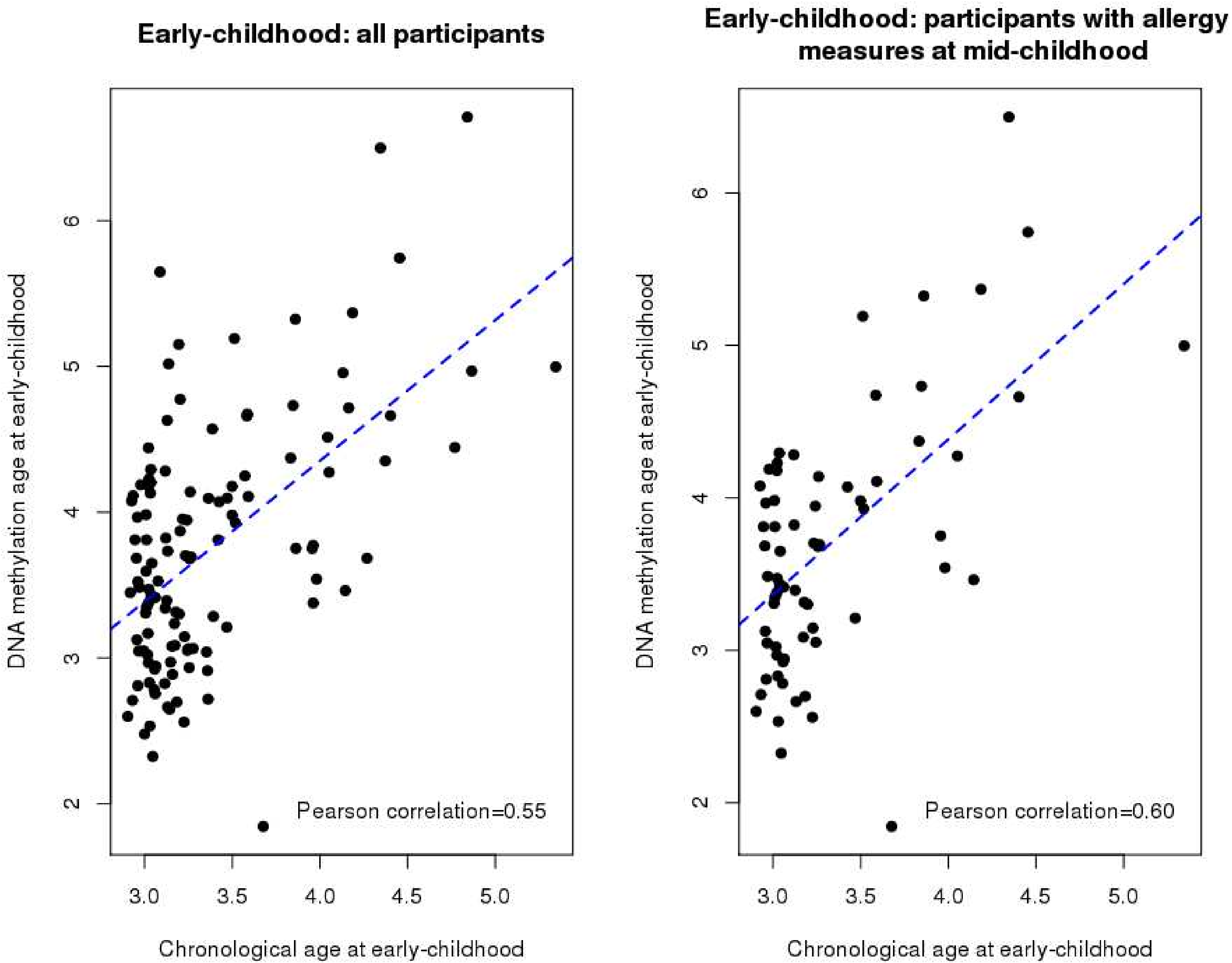
Supplementary Figure 2.



Supplementary Figure 3.



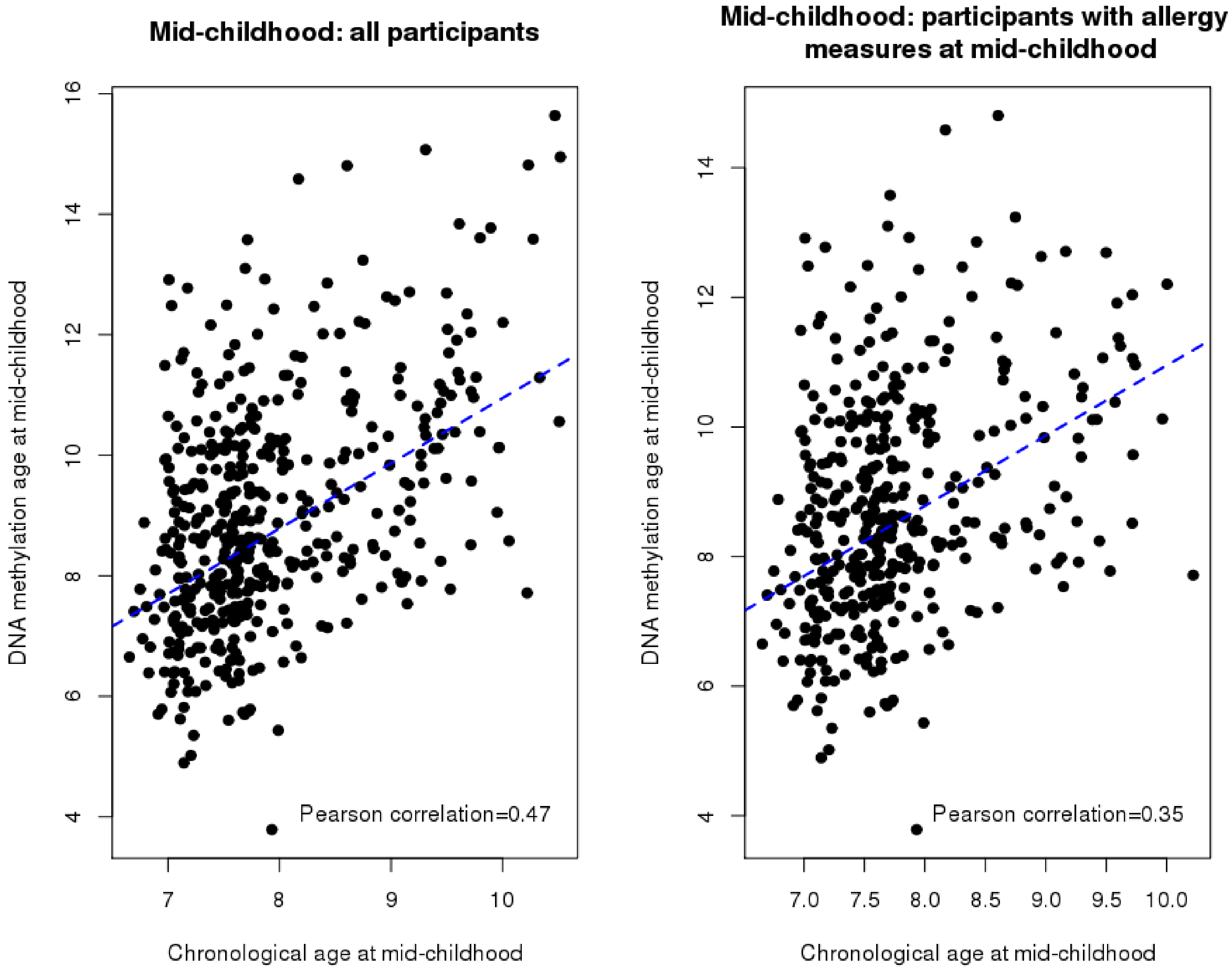
Supplementary Figure 4.



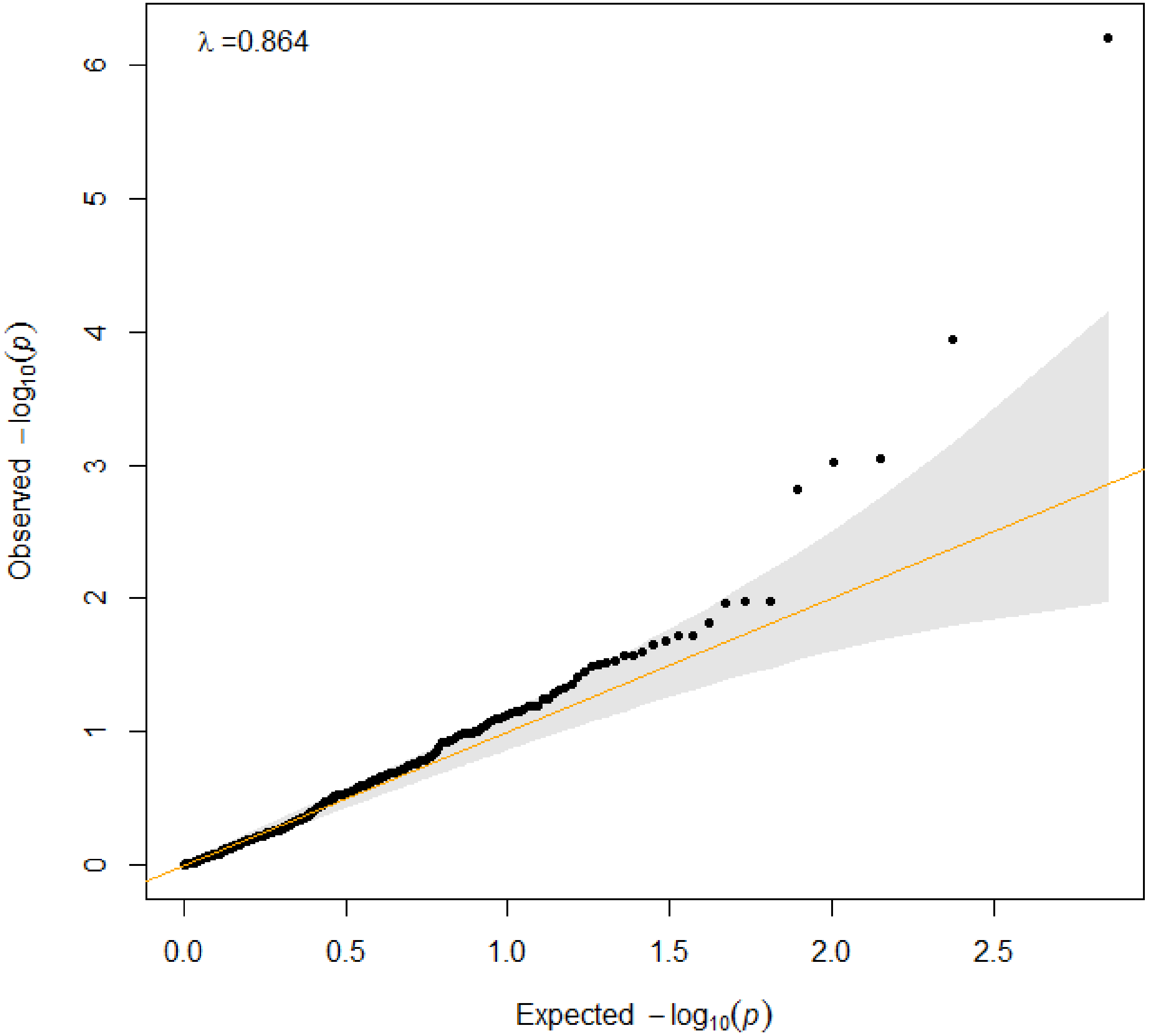
Early-childhood: all participants

Early-childhood: participants with allergy measures at mid-childhood

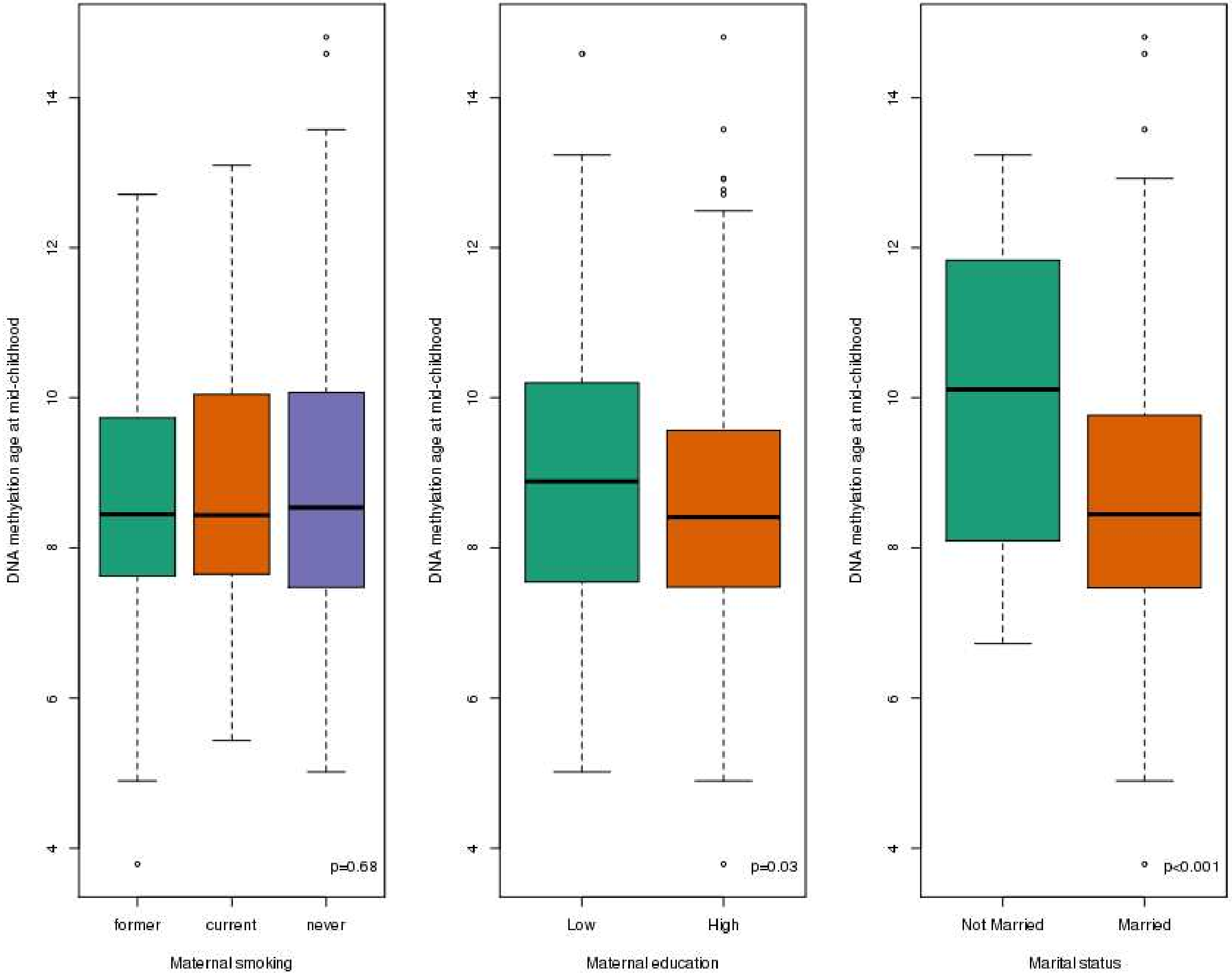
Supplementary Figure 5.



Supplementary Figure 6.



Supplementary Figure 7.



Supplementary Figure legend:

Supplementary Figure 1.
Scatter plot of chronological age vs. DNA methylation age and age acceleration at mid-childhood by atopic sensitization, environmental allergen sensitization, food allergen sensitization and asthma status (red=yes; blue=no).

Supplementary Figure 2.
Scatter plots of DNA methylation age vs. total serum IgE (log-scale) at mid-childhood (Horvath estimate).

Supplementary Figure 3.
Scatter plots of gestational week at delivery vs. DNA methylation for gestational age (in week) (Knight estimate).

Supplementary Figure 4.
Scatter plots of chronological age vs. DNA methylation age at early-childhood visit (Horvath estimate).

Supplementary Figure 5.
Scatter plots of chronological age vs. DNA methylation age at mid-childhood visit (Horvath estimate).

Supplementary Figure 6.
Q-Q plot of the association between chronological age and the 353 methylation sites contributing to the Horvath's DNA methylation age.

Supplementary Figure 7.
DNA methylation age at mid-childhood by maternal smoking status and sociodemographic characteristics (maternal education level; maternal marital status) measured during pregnancy.