

TableO2 Gene main effects of *HMOX1* and *GST* polymorphisms on annual decline in FEF<sub>25-75</sub> stratified by sex

Gene-Polymorphism	WOMEN (n=2308)				MEN (n=2057)			
	Gene main effect on decline in FEF <sub>25-75</sub> /year (in mL/s per year) <sup>1</sup>		95% confidence interval	P-value	Gene main effect on decline in FEF <sub>25-75</sub> /year (in mL/s per year) <sup>1</sup>		95% confidence interval	P-value
<b>Heme Oxygenase-1 Single Nucleotide Polymorphisms</b>								
	<i>Alleles</i>	<i>N (whole sample)</i>						
<i>HMOX1</i> rs2071746	AA	1401	ref			ref		
	AT	2089	0.7	-4.6 to 6.1	0.093 <sup>c</sup>	1.1	-5.8 to 7.9	0.109 <sup>c</sup>
	TT	763	5.7	-1.2 to 12.7		7.1	-1.8 to 15.9	
<i>HMOX1</i> rs735266	AA	1669	ref			ref		
	AT	2022	-1.0	-6.1 to 4.1	0.365 <sup>c</sup>	3.3	-3.3 to 9.8	0.054 <sup>a</sup>
	TT	595	2.5	-4.7 to 9.8		9.5	0.0 to 19.0	
<i>HMOX1</i> rs5995098	CC	2021	ref			ref		
	CG	1876	-1.7	-6.7 to 3.2	0.217 <sup>c</sup>	0.2	-6.2 to 6.5	0.062 <sup>c</sup>
	GG	427	4.1	-4.1 to 12.2		9.7	-0.9 to 20.2	
<b>Heme Oxygenase-1 Haplotypes<sup>2</sup></b>								
	<i>No of alleles</i>	<i>N</i>						
Haplotype AAC	0	798	ref			ref		
	1	2178	-3.6	-10.0 to 2.7	0.181 <sup>b</sup>	-5.1	-13.2 to 3.0	0.139 <sup>b</sup>
	2	1389	-4.9	-11.7 to 2.0		-6.9	-15.5 to 1.8	
Haplotype ATC	0	3925	ref			ref		
	1	431	6.0	-1.9 to 13.9	0.123 <sup>a</sup>	-1.4	-11.2 to 8.3	0.704 <sup>a</sup>
	2	9	28.9	-79.0 to 136.9		-9.0	-61.8 to 43.9	
Haplotype TTC	0	3873	ref			ref		
	1	478	1.8	-5.6 to 9.3	0.488 <sup>c</sup>	5.6	-3.9 to 15.1	0.321 <sup>b</sup>
	2	14	14.7	-26.1 to 55.5		-25.7	-78.9 to 27.6	
Haplotype TTG	0	2057	ref			ref		
	1	1895	-2.0	-6.9 to 2.9	0.210 <sup>c</sup>	0.1	-6.2 to 6.3	0.032 <sup>c</sup>
	2	413	4.0	-4.2 to 12.2		11.3	0.6 to 22.0	
<b>Heme Oxygenase-1 Promoter Repeat Polymorphism</b>								
	<i>long allele</i>	<i>N</i>						
	( <i>&gt;=33 repeats</i> )							
<i>HMOX1</i> (GT) <sub>n</sub>	no	3919	ref			ref		
	yes	446	4.0	-3.7 to 11.7	0.310	-2.7	-12.7 to 7.4	0.603
<b>Glutathione S-Transferase Polymorphisms</b>								
	<i>complete</i>							
<i>GSTM1</i> deletion <sup>3</sup>	no	2032	ref			ref		
	yes	2319	-3.6	-8.3 to 1.0	0.128	2.9	-3.1 to 9.0	0.341
<i>GSTT1</i> deletion <sup>3</sup>	no	3554	ref			ref		
	yes	797	4.4	-1.5 to 10.2	0.145	-6.2	-14.3 to 1.8	0.126
<i>GSTP1</i> Val/Ile Polymorphism	Ile / Ile	2061	ref			ref		
	Ile/Val	1892	-4.2	-9.0 to 0.7	0.089 <sup>b</sup>	-3.7	-10.0 to 2.6	0.159 <sup>a</sup>
	Val/Val	401	-3.4	-12.0 to 5.3		-6.1	-16.7 to 4.5	

<sup>a</sup> under an additive genetic model

<sup>b</sup> under a dominant genetic model

<sup>c</sup> under a recessive genetic model

<sup>1</sup> Negative values represent accelerations of the natural decline, positive values attenuations, compared to the reference group

Estimates from a multivariable linear regression of annual change in FEF<sub>25-75</sub> on genetic variants adjusted for:

PM10 exposure at baseline, annual change in PM10, sex, age, age squared, height and atopy at baseline, smoking status at follow-up, cigarettes per day in smokers at both surveys, pack-years up to baseline and between surveys, parental smoking, workplace-exposure to dust and fumes at each survey, baseline BMI, change in BMI and the interaction between the two, level of education and its change, nationality, season of assessment and clustering within area.

<sup>2</sup> Determined from rs2071746, rs735266 and rs5995098 SNPs (in this sequence) using PHASE software v2.1

<sup>3</sup> Deletions are homozygous gene deletions (null vs. non-null)