



Do Grandmaternal Smoking Patterns Influence the Etiology of Childhood Asthma?

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Table 1: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by paternal exposure to his mothers' smoking in pregnancy: offspring of smoking mothers. [The non-smoking grandparent is the comparison group throughout].

		PGM-M+	PGM+M+	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	421 (64.3)	426 (65.0)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	124 (18.9)	121 (18.5)	0.96 (0.73, 1.28)	0.99 (0.74, 1.32)	0.97 (0.71, 1.31)	0.99 (0.72, 1.35)
	Late only (42m)	66 (10.1)	57 (8.7)	0.85 (0.58, 1.25)	0.84 (0.57, 1.24)	0.82 (0.54, 1.22)	0.80 (0.53, 1.21)
	Persistent	44 (6.7)	51 (7.8)	1.15 (0.75, 1.75)	1.25 (0.80, 1.93)	1.25 (0.79, 1.97)	1.18 (0.74, 1.86)
Methacholine	<0	58 (19.9)	55 (18.9)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	89 (30.5)	76 (26.1)	0.90 (0.56, 1.45)	0.86 (0.53, 1.39)	0.83 (0.48, 1.41)	0.82 (0.47, 1.43)
	2 nd tertile	72 (24.7)	74 (25.4)	1.08 (0.66, 1.77)	1.02 (0.62, 1.67)	1.10 (0.63, 1.90)	1.09 (0.62, 1.93)
	3 rd tertile	73 (25.0)	86 (29.6)	1.24 (0.77, 2.01)	1.14 (0.70, 1.85)	1.05 (0.61, 1.80)	1.08 (0.61, 1.89)
Lung function (sd scores)	FVC	0.040 (0.940)	0.068 (1.058)	0.028 (-0.102, 0.158)	0.031 (-0.101, 0.163)	0.061 (-0.082, 0.204)	0.090 (-0.055, 0.235)
	FEV 1	-0.036 (1.014)	-0.013 (1.019)	0.023 (-0.109, 0.156)	0.024 (-0.111, 0.159)	0.062 (-0.083, 0.206)	0.095 (-0.052, 0.242)
	FEV 25-75	-0.088 (1.045)	-0.107 (0.998)	-0.019 (-0.152, 0.113)	-0.025 (-0.160, 0.110)	-0.009 (-0.153, 0.136)	0.004 (-0.144, 0.152)
	FEV1:FVC ratio	0.875 (0.069)	0.876 (0.068)	0.001 (-0.008, 0.010)	0.001 (-0.008, 0.010)	0.001 (-0.008, 0.011)	0.002 (-0.008, 0.012)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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g-Table 2: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by paternal exposure to his mothers' smoking in pregnancy: offspring of smoking mothers. [The non-smoking grandparent is the comparison group throughout].

Boys		PGM-M+	PGM+M+	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
		N (% affected)	N (% affected)				
Wheezing trajectory	Never	208 (58.3)	204 (61.5)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	90 (25.2)	66 (19.9)	0.75 (0.52, 1.08)	0.77 (0.52, 1.12)	0.78 (0.52, 1.16)	0.80 (0.53, 1.20)
	Late only (42m)	33 (9.2)	32 (9.6)	0.99 (0.59, 1.67)	0.96 (0.56, 1.63)	0.88 (0.50, 1.55)	0.84 (0.47, 1.49)
	Persistent	26 (7.3)	30 (9.0)	1.18 (0.67, 2.06)	1.30 (0.73, 2.30)	1.28 (0.70, 2.36)	1.24 (0.67, 2.31)
Methacholine (0 plus tertiles)	f8lf126<0	28 (18.5)	30 (18.9)				
	1 st tertile	41 (27.2)	39 (24.5)	0.89 (0.45, 1.75)	0.93 (0.42, 1.66)	0.91 (0.42, 1.94)	0.96 (0.43, 2.12)
	2 nd tertile	43 (28.5)	42 (26.4)	0.91 (0.47, 1.78)	0.84 (0.42, 1.65)	1.07 (0.51, 2.28)	1.06 (0.48, 2.33)
	3 rd tertile	39 (25.8)	48 (30.2)	1.15 (0.59, 2.24)	1.05 (0.53, 2.06)	1.09 (0.52, 2.32)	1.20 (0.55, 2.64)
Lung function	FVC	-0.039 (0.965)	-0.060 (1.090)	-0.020 (-0.204, 0.163)	-0.009 (-0.196, 0.178)	0.020 (-0.183, 0.224)	0.042 (-0.165, 0.249)
	FEV ₁	-0.064 (1.017)	-0.119 (1.060)	-0.055 (-0.240, 0.130)	-0.051 (-0.241, 0.139)	-0.015 (-0.217, 0.188)	0.012 (-0.192, 0.217)
	FEV ₂₅₋₇₅	-0.048 (1.038)	-0.128 (1.003)	-0.081 (-0.262, 0.101)	-0.093 (-0.279, 0.092)	-0.074 (-0.270, 0.122)	-0.058 (-0.257, 0.142)
	FEV ₁ :FVC ratio	0.872 (0.068)	0.871 (0.072)	-0.001 (-0.013, 0.012)	-0.002 (-0.014, 0.011)	-0.001 (-0.015, 0.012)	-0.001 (-0.015, 0.013)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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g- Table 3: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by paternal exposure to his mothers' smoking in pregnancy: offspring of smoking mothers. [The non-smoking grandparent is the comparison group throughout]

Girls		PGM-M+	PGM+M+	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	213 (71.5)	222 (68.7)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	34 (11.4)	55 (17.0)	1.55 (0.97, 2.48)	1.56 (0.97, 2.50)	1.43 (0.87, 2.38)	1.45 (0.87, 2.41)
	Late only (42m)	33 (11.1)	25 (7.7)	0.73 (0.42, 1.26)	0.73 (0.42, 1.29)	0.77 (0.43, 1.39)	0.78 (0.42, 1.43)
	Persistent	18 (6.0)	21 (6.5)	1.12 (0.58, 2.16)	1.18 (0.60, 2.33)	1.27 (0.63, 2.55)	1.12 (0.55, 2.29)
Methacholine	<0	30 (21.3)	25 (18.9)				
	1 st tertile	48 (34.0)	37 (28.0)	0.93 (0.47, 1.83)	0.89 (0.45, 1.78)	0.74 (0.33, 1.62)	0.69 (0.30, 1.57)
	2 nd tertile	29 (20.6)	32 (24.2)	1.32 (0.64, 2.75)	1.28 (0.61, 2.67)	1.08 (0.46, 2.55)	1.15 (0.47, 2.78)
	3 rd tertile	34 (24.1)	38 (28.8)	1.34 (0.66, 2.71)	1.23 (0.60, 2.50)	1.00 (0.44, 2.25)	1.00 (0.42, 2.38)
Lung function	FVC	0.126 (0.906)	0.222 (0.998)	0.096 (-0.085, 0.277)	0.088 (-0.096, 0.271)	0.116 (-0.086, 0.317)	0.142 (-0.064, 0.348)
	FEV 1	-0.005 (1.012)	0.118 (0.953)	0.122 (-0.066, 0.311)	0.119 (-0.072, 0.310)	0.145 (-0.065, 0.354)	0.170 (-0.046, 0.387)
	FEV 25-75	-0.132 (1.054)	-0.082 (0.995)	0.050 (-0.145, 0.245)	0.052 (-0.145, 0.250)	0.053 (-0.166, 0.272)	0.055 (-0.170, 0.281)
	FEV1:FVC ratio	0.879 (0.070)	0.883 (0.062)	0.004 (-0.008, 0.017)	0.005 (-0.008, 0.017)	0.004 (-0.010, 0.018)	0.003 (-0.011, 0.018)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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g-Table 4: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by maternal exposure to her mothers' smoking in pregnancy: offspring of smoking mothers. [The non-smoking grandparent is the comparison group throughout]

		MGM-M+	MGM+M+	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	618 (65.0)	571 (65.0)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	173 (18.2)	158 (18.0)	0.99 (0.77, 1.26)	0.97 (0.75, 1.24)	0.96 (0.73, 1.25)	1.05 (0.80, 1.39)
	Late only (42m)	92 (9.7)	79 (9.0)	0.93 (0.67, 1.28)	0.88 (0.63, 1.22)	0.89 (0.63, 1.26)	0.86 (0.60, 1.23)
	Persistent	68 (7.1)	71 (8.0)	1.13 (0.80, 1.61)	1.13 (0.79, 1.63)	1.13 (0.77, 1.67)	1.04 (0.69, 1.56)
Methacholine	<0	86 (20.2)	75 (20.7)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	103 (24.2)	115 (31.7)	1.28 (0.85, 1.93)	1.29 (0.85, 1.95)	1.30 (0.83, 2.05)	1.45 (0.89, 2.35)
	2 nd tertile	123 (28.9)	74 (20.4)	0.69 (0.45, 1.05)	0.68 (0.44, 1.05)	0.76 (0.48, 1.22)	0.76 (0.46, 1.25)
	3 rd tertile	114 (26.8)	99 (27.3)	1.00 (0.66, 1.50)	0.93 (0.61, 1.41)	0.79 (0.50, 1.26)	0.86 (0.52, 1.41)
Lung function (sd scores)	FVC	0.070 (0.984)	0.046 (1.027)	-0.024 (-0.136, 0.088)	-0.015 (-0.129, 0.100)	0.026 (-0.100, 0.152)	0.028 (-0.104, 0.160)
	FEV 1	-0.005 (1.015)	-0.038 (1.031)	-0.033 (-0.148, 0.081)	-0.015 (-0.132, 0.102)	0.055 (-0.073, 0.184)	0.068 (-0.066, 0.201)
	FEV 25-75	-0.092 (1.037)	-0.118 (0.980)	-0.026 (-0.139, 0.087)	-0.001 (-0.116, 0.114)	0.050 (-0.075, 0.176)	0.059 (-0.073, 0.191)
	FEV1:FVC ratio	0.876 (0.068)	0.875 (0.066)	-0.000 (-0.008, 0.007)	0.001 (-0.007, 0.009)	0.004 (-0.005, 0.012)	0.005 (-0.004, 0.013)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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Table 5: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by maternal exposure to her mothers' smoking in pregnancy: male offspring of smoking mothers. [The non-smoking grandparent is the comparison group throughout].

Boys		MGM-M+	MGM+M+	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	307 (62.3)	302 (62.9)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	101(20.5)	100 (20.5)	1.01 (0.73, 1.38)	0.97 (0.70, 1.34)	0.99(0.70, 1.41)	1.09 (0.76, 1.57)
	Late only (42m)	45 (9.1)	42 (8.6)	0.95 (0.61, 1.49)	0.88 (0.55, 1.39)	0.87 (0.53, 1.43)	0.82 (0.49, 1.38)
	Persistent	40 (8.1)	44 (9.0)	1.12 (0.71, 1.77)	1.08 (0.67, 1.73)	1.20 (0.71, 2.00)	1.06 (0.62, 1.80)
Methacholine (0 plus tertiles)	<0	45 (19.7)	38 (19.1)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	57 (24.9)	59 (29.7)	1.23 (0.70, 2.16)	1.24 (0.69, 2.21)	1.27 (0.67, 2.40)	1.54 (0.76, 3.11)
	2 nd tertile	65 (28.4)	46 (23.1)	0.84 (0.47, 1.49)	0.85 (0.47, 1.54)	1.04 (0.54, 1.99)	1.03 (0.50, 2.11)
	3 rd tertile	62 (27.1)	56 (28.1)	1.07 (0.61, 1.88)	0.99 (0.55, 1.77)	0.91 (0.47, 1.75)	0.95 (0.46, 1.94)
Lung function	FVC	-0.040 (1.017)	0.034 (1.087)	0.073 (-0.087, 0.234)	0.093 (-0.073, 0.258)	0.113 (-0.071, 0.298)	0.098 (-0.094, 0.290)
	FEV 1	-0.074 (1.036)	-0.053 (1.084)	0.021 (-0.141, 0.183)	0.048 (-0.120, 0.215)	0.103 (-0.082, 0.288)	0.107 (-0.085, 0.298)
	FEV 25-75	-0.088 (1.027)	-0.108 (1.009)	-0.021 (-0.177, 0.135)	0.011 (-0.149, 0.170)	0.063 (-0.112, 0.238)	0.076 (-0.107, 0.259)
	FEV1:FVC ratio	0.872 (0.069)	0.866 (0.070)	-0.005 (-0.016, 0.005)	-0.005 (-0.016, 0.006)	-0.001 (-0.013, 0.011)	0.001 (-0.012, 0.013)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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g-Table 6: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by maternal exposure to her mothers' smoking in pregnancy: female offspring of smoking mothers. [The non-smoking grandparent is the comparison group throughout].

Girls		MGM-M+	MGM+M+	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	311 (67.9)	269 (68.8)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	72 (15.7)	58 (14.8)	0.93 (0.64, 1.37)	0.93 (0.63, 1.37)	0.91 (0.60, 1.39)	1.00 (0.64, 1.55)
	Late only (42m)	47 (10.3)	37 (9.5)	0.91 (0.57, 1.44)	0.89 (0.56, 1.42)	0.95 (0.58, 1.56)	0.98 (0.58, 1.65)
	Persistent	28 (6.1)	27 (6.9)	1.11 (0.64, 1.94)	1.17 (0.66, 2.08)	1.12 (0.60, 2.08)	1.08 (0.56, 2.08)
Methacholine	<0	41 (20.8)	37 (22.6)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	46 (23.4)	56 (34.2)	1.35 (0.75, 2.44)	1.35 (0.75, 2.45)	1.43 (0.74, 2.74)	1.49 (0.75, 2.99)
	2 nd tertile	58 (29.4)	28 (17.1)	0.53 (0.28, 1.01)	0.51 (0.27, 0.97)	0.53 (0.26, 1.08)	0.55 (0.27, 1.16)
	3 rd tertile	52 (26.4)	43 (26.2)	0.92 (0.50, 1.67)	0.85 (0.46, 1.57)	0.69 (0.35, 1.36)	0.86 (0.42, 1.76)
Lung function	FVC	0.194 (0.932)	0.060 (0.954)	-0.134 (-0.288, 0.020)	-0.137 (-0.294, 0.019)	-0.073 (-0.245, 0.098)	-0.044 (-0.224, 0.137)
	FEV 1	0.074 (0.985)	-0.021 (0.968)	-0.096 (-0.257, 0.065)	-0.089 (-0.252, 0.074)	0.001 (-0.178, 0.180)	0.026 (-0.162, 0.213)
	FEV 25-75	-0.098 (1.051)	-0.130 (0.947)	-0.032 (-0.197, 0.132)	-0.014 (-0.181, 0.153)	0.044 (-0.140, 0.229)	0.042 (-0.152, 0.236)
	FEV1:FVC ratio	0.880 (0.068)	0.886 (0.059)	0.006 (-0.005, 0.016)	0.007 (-0.004, 0.017)	0.009 (-0.003, 0.021)	0.008 (-0.004, 0.021)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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g-Table 7: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by paternal exposure to his mothers' smoking in pregnancy: offspring of non-smoking mothers. [The non-smoking grandparent is the comparison group throughout]

		PGM-M-	PGM+M-	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	2470 (76.2)	1501 (74.5)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	394 (12.2)	257 (12.8)	1.07 (0.91, 1.27)	1.08 (0.91, 1.28)	1.05 (0.88, 1.26)	1.02 (0.85, 1.22)
	Late only (42m)	264 (8.1)	172 (8.5)	1.07 (0.88, 1.31)	1.10 (0.90, 1.35)	1.11 (0.90, 1.37)	1.07 (0.87, 1.33)
	Persistent	115 (3.6)	86 (4.3)	1.23 (0.92, 1.64)	1.25 (0.93, 1.67)	1.14 (0.84, 1.54)	1.08 (0.79, 1.47)
Methacholine	<0	316 (18.1)	220 (20.7)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	478 (27.4)	285 (26.9)	0.86 (0.68, 1.07)	0.86 (0.68, 1.08)	0.84 (0.66, 1.07)	0.85 (0.66, 1.08)
	2 nd tertile	478 (27.4)	261 (24.6)	0.78 (0.62, 0.99)	0.80 (0.63, 1.01)	0.77 (0.60, 0.98)	0.77 (0.60, 0.99)
	3 rd tertile	475 (27.2)	295 (27.8)	0.89 (0.71, 1.12)	0.91 (0.72, 1.14)	0.95 (0.75, 1.20)	0.95 (0.75, 1.22)
Lung function (sd scores)	FVC	0.005 (1.001)	-0.011 (0.984)	-0.016 (-0.077, 0.046)	-0.016 (-0.078, 0.046)	-0.013 (-0.077, 0.052)	-0.014 (-0.081, 0.052)
	FEV 1	0.022 (0.984)	0.014 (1.009)	-0.008 (-0.070, 0.054)	-0.012 (-0.075, 0.051)	-0.023 (-0.088, 0.042)	-0.025 (-0.091, 0.042)
	FEV 25-75	0.034 (0.998)	0.049 (1.021)	0.015 (-0.048, 0.077)	0.012 (-0.051, 0.075)	0.000 (-0.065, 0.066)	0.001 (-0.066, 0.068)
	FEV1:FVC ratio	0.885 (0.063)	0.886 (0.066)	0.001 (-0.003, 0.005)	0.001 (-0.003, 0.005)	0.000 (-0.004, 0.004)	0.000 (-0.004, 0.004)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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e-Table 8: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by paternal exposure to his mothers' smoking in pregnancy: male offspring of non-smoking mothers. [The non-smoking grandparent is the comparison group throughout]

Boys		PGM-M-	PGM+M-	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	1216 (72.6)	736 (72.3)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	227 (13.6)	141 (13.9)	1.03 (0.82, 1.29)	1.03 (0.82, 1.30)	0.96 (0.76, 1.23)	0.95 (0.74, 1.21)
	Late only (42m)	155 (9.3)	92 (9.0)	0.98 (0.75, 1.29)	0.99 (0.75, 1.31)	1.00 (0.76, 1.34)	0.94 (0.71, 1.26)
	Persistent	77 (4.6)	49 (4.8)	1.05 (0.73, 1.52)	1.06 (0.73, 1.53)	0.92 (0.62, 1.36)	0.88 (0.59, 1.30)
Methacholine	<0	144 (16.3)	99 (19.2)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	246 (27.9)	133 (25.8)	0.79 (0.56, 1.10)	0.78 (0.56, 1.09)	0.75 (0.53, 1.07)	0.77 (0.54, 1.10)
	2 nd tertile	248 (28.1)	127 (24.6)	0.74 (0.53, 1.04)	0.75 (0.54, 1.06)	0.71 (0.50, 1.01)	0.74 (0.52, 1.06)
	3 rd tertile	244 (27.7)	157 (30.4)	0.94 (0.68, 1.30)	0.94 (0.68, 1.31)	0.96 (0.68, 1.35)	0.98 (0.69, 1.40)
Lung function	FVC	-0.003 (0.996)	0.015 (0.963)	0.018 (-0.069, 0.105)	0.016 (-0.072, 0.103)	0.020 (-0.071, 0.111)	0.019 (-0.073, 0.112)
	FEV 1	0.015 (0.986)	0.023 (0.985)	0.008 (-0.079, 0.096)	0.001 (-0.087, 0.089)	-0.019 (-0.110, 0.072)	-0.023 (-0.116, 0.070)
	FEV 25-75	0.030 (1.008)	0.037 (1.008)	0.007 (-0.082, 0.096)	0.002 (-0.087, 0.092)	-0.022 (-0.115, 0.072)	-0.023 (-0.119, 0.072)
	FEV1:FVC ratio	0.875 (0.067)	0.875 (0.069)	-0.000 (-0.006, 0.006)	-0.000 (-0.006, 0.006)	-0.002 (-0.009, 0.004)	-0.003 (-0.009, 0.004)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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g-Table 9: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by paternal exposure to his mothers' smoking in pregnancy: female offspring of non-smoking mothers. [The non-smoking grandparent is the comparison group throughout]

Girls		PGM-M-	PGM+M-	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	1254 (80.0)	765 (76.7)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	167 (10.7)	116 (11.6)	1.14 (0.88, 1.47)	1.15 (0.89, 1.48)	1.16 (0.89, 1.51)	1.10 (0.84, 1.43)
	Late only (42m)	109 (7.0)	80 (8.0)	1.20 (0.89, 1.63)	1.25 (0.92, 1.70)	1.26 (0.92, 1.71)	1.24 (0.90, 1.70)
	Persistent	38 (2.4)	37 (3.7)	1.60 (1.01, 2.53)	1.65 (1.02, 2.65)	1.56 (0.95, 2.58)	1.42 (0.86, 2.36)
Methacholine	<0	172 (19.9)	121 (22.2)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	232 (26.8)	152 (27.9)	0.93 (0.68, 1.27)	0.94 (0.69, 1.29)	0.94 (0.68, 1.31)	0.94 (0.67, 1.31)
	2 nd tertile	230 (26.6)	134 (24.6)	0.83 (0.60, 1.14)	0.84 (0.61, 1.16)	0.83 (0.59, 1.16)	0.81 (0.57, 1.14)
	3 rd tertile	231 (26.7)	138 (25.3)	0.85 (0.62, 1.16)	0.87 (0.64, 1.20)	0.95 (0.68, 1.33)	0.95 (0.67, 1.33)
Lung function	FVC	0.013 (1.007)	-0.035 (1.004)	-0.048 (-0.136, 0.039)	-0.046 (-0.135, 0.043)	-0.039 (-0.131, 0.054)	-0.046 (-0.141, 0.049)
	FEV 1	0.030 (0.982)	0.006 (1.041)	-0.024 (-0.112, 0.065)	-0.024 (-0.113, 0.066)	-0.026 (-0.119, 0.066)	-0.028 (-0.122, 0.067)
	FEV 25-75	0.038 (0.988)	0.059 (1.033)	0.021 (-0.067, 0.109)	0.022 (-0.067, 0.110)	0.018 (-0.075, 0.110)	0.022 (-0.072, 0.117)
	FEV1:FVC ratio	0.895 (0.057)	0.897 (0.060)	0.002 (-0.004, 0.007)	0.001 (-0.004, 0.007)	0.001 (-0.005, 0.006)	0.001 (-0.005, 0.007)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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g-Table 10: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by maternal exposure to her mothers' smoking in pregnancy: offspring of non-smoking mothers. [The non-smoking grandparent is the comparison group throughout]

		MGM-M-	MGM+M-	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	3255 (75.8)	1469 (74.1)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	527 (12.3)	250 (12.6)	1.05 (0.89, 1.24)	1.06 (0.90, 1.25)	1.01 (0.85, 1.20)	0.98 (0.82, 1.17)
	Late only (42m)	351 (8.2)	161 (8.1)	1.02 (0.84, 1.24)	1.02 (0.83, 1.24)	1.01 (0.82, 1.24)	0.98 (0.79, 1.21)
	Persistent	160 (3.7)	102 (5.2)	1.41 (1.09, 1.82)	1.40 (1.08, 1.81)	1.34 (1.02, 1.76)	1.26 (0.95, 1.67)
Methacholine	<0	416 (18.0)	203 (20.1)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	624 (27.0)	277 (27.4)	0.91 (0.73, 1.13)	0.89 (0.71, 1.11)	0.90 (0.71, 1.14)	0.84 (0.66, 1.06)
	2 nd tertile	637 (27.6)	264 (26.1)	0.85 (0.68, 1.06)	0.84 (0.67, 1.05)	0.79 (0.62, 1.00)	0.74 (0.58, 0.95)
	3 rd tertile	631 (27.3)	268 (26.5)	0.87 (0.70, 1.08)	0.87 (0.70, 1.09)	0.86 (0.68, 1.08)	0.81 (0.63, 1.03)
Lung function (sd scores)	FVC	-0.019 (0.994)	0.017 (0.991)	0.036 (-0.024, 0.095)	0.030 (-0.030, 0.090)	0.045 (-0.019, 0.108)	0.045 (-0.020, 0.111)
	FEV 1	-0.002 (0.991)	0.046 (1.004)	0.048 (-0.012, 0.108)	0.038 (-0.023, 0.099)	0.046 (-0.018, 0.109)	0.045 (-0.021, 0.111)
	FEV 25-75	0.017 (0.994)	0.063 (1.021)	0.046 (-0.014, 0.106)	0.036 (-0.025, 0.096)	0.043 (-0.021, 0.107)	0.045 (-0.022, 0.111)
	FEV1:FVC ratio	0.885 (0.063)	0.886 (0.066)	0.001 (-0.003, 0.005)	0.001 (-0.003, 0.005)	0.000 (-0.004, 0.004)	-0.000 (-0.004, 0.004)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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g-Table 11: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by maternal exposure to her mothers' smoking in pregnancy: male offspring of non-smoking mothers. [The non-smoking grandparent is the comparison group throughout]

Boys		MGM-M-	MGM+M-	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	1604 (72.9)	713 (69.5)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	296 (13.5)	155 (15.1)	1.18 (0.95, 1.46)	1.17 (0.94, 1.45)	1.08 (0.86, 1.36)	1.06 (0.84, 1.34)
	Late only (42m)	198 (9.0)	92 (9.0)	1.05 (0.80, 1.36)	1.07 (0.82, 1.40)	1.03 (0.78, 1.36)	0.98 (0.74, 1.30)
	Persistent	103 (4.7)	66 (6.4)	1.44 (1.05, 1.99)	1.45 (1.05, 2.01)	1.40 (0.99, 1.97)	1.29 (0.91, 1.84)
Methacholine	<0	190 (16.7)	85 (17.5)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	308 (27.0)	128 (26.3)	0.93 (0.67, 1.29)	0.88 (0.63, 1.23)	0.87 (0.61, 1.22)	0.79 (0.55, 1.12)
	2 nd tertile	314 (27.5)	141 (29.0)	1.00 (0.73, 1.39)	0.98 (0.71, 1.36)	0.92 (0.65, 1.29)	0.85 (0.60, 1.20)
	3 rd tertile	329 (28.8)	133 (27.3)	0.90 (0.65, 1.25)	0.90 (0.65, 1.25)	0.91 (0.64, 1.28)	0.81 (0.57, 1.16)
Lung function	FVC	-0.007 (0.972)	0.044 (1.002)	0.051 (-0.033, 0.134)	0.049 (-0.036, 0.134)	0.059 (-0.030, 0.147)	0.055 (-0.036, 0.146)
	FEV 1	0.007 (0.976)	0.064 (1.013)	0.057 (-0.028, 0.142)	0.049 (-0.037, 0.134)	0.039 (-0.050, 0.129)	0.039 (-0.052, 0.131)
	FEV 25-75	0.013 (0.985)	0.066 (1.049)	0.054 (-0.032, 0.139)	0.041 (-0.046, 0.128)	0.032 (-0.059, 0.123)	0.041 (-0.052, 0.135)
	FEV1:FVC ratio	0.875 (0.065)	0.876 (0.072)	0.001 (-0.005, 0.006)	0.000 (-0.006, 0.006)	-0.001 (-0.007, 0.005)	-0.001 (-0.007, 0.006)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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e-Table 12: n (%) and effect sizes for each category of wheezing and methacholine challenge and mean (sd) and mean differences for each lung function outcome by maternal exposure to her mothers' smoking in pregnancy: female offspring of non-smoking mothers. [The non-smoking grandparent is the comparison group throughout]

Girls		MGM-M-	MGM+M-	Model 1: OR (95% CI)	M2: AOR (95% CI)	M3: AOR (95% CI)	M4: AOR (95% CI)
Wheezing trajectory	Never	1651 (78.9)	756 (79.1)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	Early only (6m)	231 (11.0)	95 (9.9)	0.90 (0.70, 1.16)	0.93 (0.72, 1.20)	0.92 (0.70, 1.20)	0.86 (0.65, 1.13)
	Late only (42m)	153 (7.3)	69 (7.2)	0.98 (0.73, 1.33)	0.96 (0.71, 1.30)	0.99 (0.73, 1.35)	0.98 (0.71, 1.35)
	Persistent	57 (2.7)	36 (3.8)	1.38 (0.90, 2.11)	1.35 (0.87, 2.09)	1.24 (0.78, 1.97)	1.19 (0.74, 1.92)
Methacholine	<0	226 (19.4)	118 (22.5)	1.00 Ref	1.00 Ref	1.00 Ref	1.00 Ref
	1 st tertile	316 (27.1)	149 (28.4)	0.90 (0.67, 1.21)	0.91 (0.67, 1.22)	0.94 (0.68, 1.29)	0.88 (0.63, 1.23)
	2 nd tertile	323 (27.7)	123 (23.4)	0.73 (0.54, 0.99)	0.72 (0.53, 0.98)	0.68 (0.49, 0.95)	0.63 (0.45, 0.89)
	3 rd tertile	302 (25.9)	135 (25.7)	0.86 (0.63, 1.16)	0.86 (0.63, 1.17)	0.83 (0.59, 1.15)	0.79 (0.56, 1.12)
Lung function	FVC	-0.031 (1.014)	-0.010 (0.981)	0.022 (-0.063, 0.106)	0.012 (-0.074, 0.097)	0.030 (-0.061, 0.120)	0.026 (-0.068, 0.121)
	FEV 1	-0.012 (1.006)	0.028 (0.995)	0.040 (-0.045, 0.125)	0.028 (-0.058, 0.114)	0.048 (-0.043, 0.139)	0.038 (-0.057, 0.133)
	FEV 25-75	0.021 (1.004)	0.060 (0.994)	0.039 (-0.045, 0.123)	0.030 (-0.055, 0.115)	0.051 (-0.040, 0.142)	0.036 (-0.059, 0.131)
	FEV1:FVC ratio	0.895 (0.060)	0.897 (0.058)	0.001 (-0.004, 0.006)	0.001 (-0.004, 0.006)	0.001 (-0.004, 0.007)	0.000 (-0.005, 0.006)

Model 1: Unadjusted

Model 2: Model 1 + family history of asthma

Model 3: Model 2 + parity + gestation + breastfeeding + maternal education + amount mother smoked during pregnancy

Model 4: Model 3 + paternal smoking during pregnancy + child's passive exposure at ages <2 years and at 2-8 years

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