

On-line supplement

Interaction between asthma and smoking increases risk of adult airway obstruction

Aanerud M et al

List of investigators in the Early life Working Group in ECRHS

Chair: Cecilie Svanes. Members: Shyamali Dharmage, Melbourne, Australia; Thorarinn Gislason, Reykjavik; Maria Gunnbjørnsdottir, Uppsala; Joachim Heinrich, Neuherberg; Deborah Jarvis, London; Benedicte Leynaert, Paris; Dora Ludvigsdottir, Reykjavik; Roberto de Marco, Verona; Francoise Neukirch, Paris; Chantal Raheison, Paris; Jordi Sunyer, Barcelona; Simona Villani, Pavia, Matthias Wjst, Neuherberg.

List of Principal Investigators and Senior Scientific Teams in ECRHS

Belgium: South Antwerp & Antwerp City (P Vermeire, J Weyler, M Van Sprundel, V Nelen). Estonia: Tartu (R Jogi, A Soon). France: Paris (F Neukirch, B Leynaert, R Liard, M Zureik), Grenoble (I Pin, J Ferran-Quentin). Germany: Erfurt (J Heinrich, M Wjst, C Frye, I Meyer). Iceland: Reykjavik (T Gislason, E Bjornsson, D Gislason, T Blondal, KB Jorundsdottir). Italy: Turin (M Bugiani, P Piccioni, E Caria, A Carosso, E Migliore, G Castiglioni), Verona (R de Marco, G Verlato, E Zanolin, S Accordini, A Poli, V Lo Cascio, M Ferrari), Pavia (A Marinoni, S Villani, M Ponzio, F Frigerio, M Comelli, M Grassi, I Cerveri, A Corsico). Netherlands: Groningen & Geleen (J Schouten, M Kerkhof). Norway: Bergen (A Gulsvik, E Omenaas, C Svanes, B Laerum). Spain: Barcelona (JM Antó, J Sunyer, M Kogevinas, JP Zock, X Basagana, A Jaen, F Burgos), Huelva (J Maldonado, A Pereira, JL Sanchez), Albacete (J Martinez-Moratalla Rovira, E Almar), Galdakao (N Muniozguren, I Urritia), Oviedo (F Payo). Sweden: Uppsala (C Janson, G Boman, D Norback, M Gunnbjørnsdottir), Goteborg (K Toren, L Lillienberg, AC Olin, B Balder, A Pfeifer-Nilsson, R Sundberg), Umea (E Norrman, M Soderberg, K Franklin, B Lundback, B Forsberg, L Nystrom). Switzerland: Basel (N Künzli, B Dibbert, M Hazenkamp, M Brutsche, U Ackermann-Liebrich). United Kingdom: Norwich (D Jarvis, B Harrison), Ipswich (D Jarvis, R Hall, D Seaton)

Centres taking part at their own expense: Australia: Melbourne (M Abramson, S Dharmage, J Raven, EH Walters). France: Bordeaux (A Tayard, C Raheison), Montpellier (J Bousquet, P Demoly). Germany: Hamburg (K Richter). USA: Portland (M Osborne, S Buist, W Vollmer, L Johnson).

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Table E1. Sensitivity analysis. Association of smoking status and asthma with adult airway obstruction. Excluding individuals with airway obstruction at baseline but not at follow-up (n=18508)

	<i>Adult airway obstruction, Adj</i>			
	<i>%</i>	<i>OR‡</i>	<i>95% CI†</i>	
No asthma, never smoker	0.3	1.00	-	
No asthma, current smoker	1.7	4.89	3.07	7.79
Early-onset asthma, never smoker	8.0	23.48	13.49	40.88
Late-onset asthma, current smoker	10.1	28.25	15.76	50.63
	RERI	-0.21		
Late-onset asthma, never smoker	4.9	10.82	6.20	18.88
Late-onset asthma, current smoker	11.0	27.78	16.31	47.32
	RERI	15.4	*	

‡ Odds ratio adjusted for education, age, height, sex, sample and country. † 95%CI= 95% confidence interval. RERI= Relative Excess due to Interaction.

Early-onset defined as asthma onset before 10 yrs of age, late-onset defined as asthma onset after 10 yrs of age

Table E2. Association of smoking history and asthma with adult airway obstruction

Asthma	Smoking	<i>N_{adult airway obstruction}/total</i>		OR_‡	95% CI_†
No asthma	Never smoker	29/8213	0.3%	1.00	-
	Current smoker	127/7020	1.8%	4.43	(2.88,6.83)
Early-onset asthma	Never smoker	59/679	8.7%	20.34	(12.22,33.87)
	Current smoker	42/387	10.8%	24.16	(14.13,41.33)
Late-onset asthma	Never smoker	56/921	6.1%	11.09	(6.67,18.42)
	Current smoker, started after asthma onset	18/141	12.8%	26.95	(13.74,52.86)
	Current smoker, started before asthma onset	49/410	12.0%	24.36	(14.40,41.21)

n=17771. ‡Odds ratio adjusted for education, age height, sex, sample and centre. † 95%CI= 95% confidence interval. Early onset asthma before 10 years of age, late onset after 10 years of age.

Table E3. Association of smoking history and asthma with adult airway obstruction, former smokers included.

Asthma	Smoking	<i>N_{adult airway obstruction}/total</i>		OR[‡]	95% CI
No asthma	Never smoker	29/8213	0.3%	1.00	-
	Current smoker	127/7020	1.8%	4.21	(2.74,6.46)
	Former smoker	37/4555	0.8%	1.85	(1.11,3.07)
Early-onset asthma	Never smoker	59/679	8.7%	19.60	(11.86,32.39)
	Current smoker	40/380	10.5%	22.52	(13.20,38.52)
	Former smoker	34/287	11.8%	25.11	(14.36,43.89)
Late-onset asthma	Never smoker	56/921	6.1%	10.85	(6.56,17.96)
	Current smoker, started after asthma onset	17/126	13.5%	28.33	(14.25,56.31)
	Smoker before asthma	50/412	12.1%	23.06	(13.70,38.82)
	Former smoker after asthma	6/91	6.6%	10.58	(5.80,19.28)
	Former smoker before asthma	27/374	7.2%	12.09	(4.41,33.15)

n=23058. Odds ratio adjusted for education, age height, sex, sample, and country. 95% CI = 95% Confidence interval. Early-onset asthma before 10 years of age, late-onset asthma after 10 years of age.

Table E5. Population attributable fractions of adult airway obstruction from asthma and smoking

	N total (%)	N adult airway obstruction (%)	OR	95%CI	AF
Asthma					
No asthma	13884 (91.1)	119 (58.9)	1		
Early-onset asthma	594 (3.9)	34 (16.8)	10.23	(7.77-13.49)	15.2%
Late-onset asthma	761 (5.0)	49 (24.3)	5.83	(4.46-7.61)	20.1%
Early+late	1355 (8.9)	83 (41.1)	7.23	(5.74-9.11)	35.3%
Total	15239 (100)	202 (100)			
Smoking					
Never smoker	6669 (43.4)	51 (24.1)	1		
Current smoker	3784 (24.6)	56 (26.4)	2.45	(1.92-3.12)	29.3%
Former smoker	4908 (32.0)	105 (49.5)	1.34	(1.01-1.78)	6.7%
Current and former smoker	8692 (56.6)	161 (75.9)	1.93	(1.54-2.42)	36.0%
Total	15361 (100)	212 (100)			
Interaction asthma*smoking					
No asthma, never smoker	5892(38.9)	20 (9.9)	1		
No asthma, current smoker	4513 (29.8)	71 (35.1)	4.27	(2.78-6.54)	26.9%
No asthma, former smoker	3403 (22.5)	28 (13.9)	1.85	(1.11-3.06)	6.3%
Early-onset asthma, never smoker	286 (1.9)	11 (5.4)	19.82	(12.01-32.69)	5.2%
Late-onset asthma, current smoker	149 (1.0)	9 (4.5)	22.48	(13.23-38.20)	4.3%
Early-onset asthma, former smoker	154 (1.0)	14 (6.9)	26.80	(15.58-46.09)	6.7%
Late-onset asthma, never smoker	405 (2.7)	19 (9.4)	10.73	(6.50-17.74)	8.5%
Late-onset asthma, current smoker	189 (1.3)	20 (9.9)	23.63	(14.50-38.52)	9.5%
Late-onset asthma, former smoker	166 (1.1)	10 (5.0)	10.57	(6.01-18.61)	4.5%
Any versus none*	9265 (61.1)	182 (90.1)	6.23	(4.20-9.23)	71.9%

OR: Odds ratios estimated from GEE random effects model adjusted for age, sex, sample, country, height and education. 95% CI: 95% confidence interval. AF: Attributable fraction. * Having any risk factor (asthma, either early- or late onset, or smoking, either as current or former smoker, compared to subjects who never smoked and never have had asthma).

Table E6. Association of adult airway obstruction with atopy and smoking, stratified by asthma (n=16108)

		Adult airway obstruction¹				
Atopy	Smoking status[†]	%Adult airway obstruction	Odds ratio²	95% confidence interval		
All	No atopy	Never smoker	0.7%	1.00	-	
		Current smoker	2.6%	3.57	2.38	5.35
	Atopy	Never smoker	3.1%	3.65	2.47	5.41
		Current smoker	3.9%	4.76	3.13	7.24
			<i>RERI⁴</i>	-1.46	-3.15	0.24
No asthma ³	No atopy	Never smoker	0.4%	1.00	-	
		Current smoker	0.5%	1.38	0.62	3.05
	Atopy	Never smoker	1.8%	4.42	2.61	7.51
		Current smoker	1.7%	4.51	2.44	8.35
			<i>RERI⁴</i>	-0.28	-2.53	1.96
Asthma ³	No atopy	Never smoker	4.7%	1.00		
		Current smoker	8.8%	1.80	1.02	3.18
	Atopy	Never smoker	12.9%	2.99	1.59	5.62
		Current smoker	11.3%	2.29	1.25	4.20
			<i>RERI⁴</i>	-1.50	-3.33	0.33

[†]Excluding former smokers. ¹ Adult airway obstruction defined as pre-bronchodilator FEV1/FVC < 70 % and FEV1 < 80 % predicted. ² Odds ratio adjusted for education, age height, sex, sample and centre ³Asthma = early or late onset asthma ⁴ RERI= Relative Excess due to Interaction.

Table E7. Number and percentage of asthma according to adult airway obstruction at baseline and follow-up

Adult airway obstruction†	Total	Ever asthma at baseline		p-value‡
	n	n	%	
No adult airway obstruction	8,049	976	12.1%	0.810
Adult airway obstruction at baseline <u>not</u> at follow-up (1)	67	42	62.7%	
Adult airway obstruction at baseline <u>and</u> at follow-up (2)	97	59	60.8%	
Adult airway obstruction only at follow-up	101	42	41.6%	
Total	8,314	1,119	13.5%	

† Adult airway obstruction defined as pre-bronchodilator FEV1/FVC < 70 % and FEV1 < 80 % predicted ‡p-value from chi² test (comparing distribution of asthmatic in (1) and (2), Pearson chi2(1) = 0.0581)

Figure E1. Smoking intensity for current smokers by asthma status (no asthma, early onset, and late onset)



