# Current asthma contributes as much as smoking to chronic bronchitis in middle age: a prospective population-based study

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## Online data supplement

## Methods E1: Additional Clinical Definitions

***Skin Prick Tests (SPT)*** were performed for eight aeroallergens (Hollister-Stier, EBOS Groups Pty Ltd, Australia): *Dermatophagoides Pteronyssinus*, Cat Pelt, *Cladosporioides*, *Alternaria Tenuis*, *Penicillium* mix, *Aspergillus fumigatus*, Perennial Rye Grass and 8 Mixed Grasses. A wheal size of at least 3mm greater than the negative control (saline) was regarded as indicating sensitivity. Histamine was used as the positive control.

Second hand smoke (SHS) exposure in middle-age was derived from three 2004 postal survey questions. First, ***SHS exposure inside the house***, was defined by an affirmative response to "Not counting yourself, how many people in your household currently smoke regularly (most days of the week) inside the house?" Second, ***SHS exposure at the workplace***, was defined by an affirmative response to the question "Do people smoke regularly (most days of the week) in the room where you work (not counting yourself)?" Third, ***'SHS exposure in middle-age'***, was defined by the response to "On average, how many hours per day are you exposed to other people's tobacco smoke (work and home)?"

The ***socio-economic status*** variable was based on the participant's occupation in 2004, and coded according to the Australian Standard Classification of Occupations (ASCO) four-digit codes.[28] These codes were grouped into five major skill groups: i) Managers/ Professionals; ii) Associate Professionals; iii) Tradespersons and Advanced Clerical; iv) Intermediate clerical and production; v) Elementary clerical, labourers and related workers. The same methodology was used for paternal occupation in 1968. The participants' highest attained ***educational level*** was considered separately.

Parental respiratory symptoms were derived from the baseline 1968 survey when participants were seven-years old. ***Parental productive cough*** was defined by an affirmative answer to the question, "Do you usually clear or bring up some phlegm (sputum) from your chest in the mornings or sometime during the day?" ***Parental bronchitis*** was defined by an affirmative response to the question "Do you suffer from chronic bronchitis, or from more than one attack of bronchitis every three years or so". ***Maternal and paternal smoking***

were defined by an affirmative response to the question “Do you smoke every day (or six days out of seven)”, and if yes, then “How much do you smoke?” followed by three options: “more than 20 cigarettes a day; six to 20 cigarettes a day; less than 6 cigarettes a day”.

A history of ***childhood pneumonia, whooping cough and immunization to B. pertussis*** was defined by a “yes” response by parents and/or guardians around age-of-school entry, as recorded by the Tasmanian school medical records.

## Methods E2: Additional Lung Function and Statistical Methods

***Pre- and post-BD spirometry*** was performed using the EasyOneTM ultrasonic Spirometer (ndd, Medizintechnik, AG, Switzerland). Participants were asked not to smoke for 4-6 hours prior to testing. Forced expiratory volume in one second (FEV1) was recorded as the best of three attempts that met American Thoracic Society (ATS) and European Respiratory Society (ERS) criteria (S1). Spirometry was repeated 10 minutes after 200 μg of salbutamol administered via spacer. Only three participants reported taking an inhaled beta-2-agonist within 4 hours of testing and another three took prednisolone within 24 hours of testing.

In order to minimize bias from height and sex, lung function was expressed as z-scores and the lower limit of normal predicted values from the Global Lung Initiative (S2). We did not use the GOLD definition for airflow obstruction (S3), as the lower limit of normal closely approximated a forced expiratory ratio of 0.7 in our population (S4).

For the postal survey data (1968-2004), prevalence estimates were based on the full cohort. ***Multivariable logistic regression*** was used to assess the relationships between adult clinical characteristics, early life factors and adult CB. For the independent relationship analyses, *a priori* and confounding variables were included in the model. For the 2004 analysis, *a priori* factors included male gender, parental history of recurrent bronchitis, highest attained educational level and current participant occupation. Asthma, allergy, smoking were found to confound each other's relationships with adult CB whereas SHS exposure confounded the relationship for personal smoking only. For the 1968 analysis, *a priori* factors included male gender, parental history of bronchitic symptoms and paternal occupation. Childhood asthma and recurrent bronchitis were confounders of each other, and allergy reduced the estimate for the most severe bronchitis category by 9.1%.

For the laboratory study data (2006-2008), multinomial logistic regression models were used. As attendees were enriched for asthma and symptomatic chronic bronchitis, sampling weights were included. Only the three exposures of interest (smoking, asthma, allergy) were included due to the low numbers of adult CB cases in the obstructive subgroup (n=22).

**Table E1. Individual associations between other characteristics and chronic bronchitis in middle age**

| Self-reported clinical characteristics | Self-reported adult CB [N=5,379 (%)] | | | |
|---|---|---|---|---|
| | No [n=5054 (94)] | Yes [n=325 (6)] | Univariable p-for-trend | Adjusted OR (95% CI) [a] |
| **In middle age** | | | | |
| Household smokers | | | <0.001 | |
| None | 4252 (86) | 229 (72) | | 1 |
| One | 507 (10) | 62 (19) | | 1.27 (0.93, 1.75) |
| Two | 116 (2) | 15 (5) | | 1.04 (0.58, 1.85) |
| Three | 56 (1) | 13 (4) | | 1.89 (0.98, 3.64) |
| SHS exposure at work | 251 (5) | 40 (13) | | 1.63 (1.12, 2.37) [d] |
| Heating type | | | 0.007 | |
| Not coal/wood/gas | 2008 (41) | 111 (35) | | 1 |
| Gas | 875 (18) | 50 (16) | | 1.13 (0.80, 1.60) |
| Coal or wood | 2071 (42) | 156 (49) | | 1.27 (0.98. 1.63) |
| Cooking type | | | 0.053 | |
| Electric stove | 3957 (77) | 271 (81) | | 1 |
| Coal, coke or wood stove | 35 (1) | 2 (1) | | 0.72 (0.44, 1.20) |
| Gas stove | 1169 (23) | 60 (18) | | 0.94 (0.67, 1.31) |
| Highest attained level of education [b] | | | <0.001 | |
| University degree | 886 (19) | 24 (8) | | 1 |
| Trade/ apprenticeship | 1521 (33) | 93 (32) | | 1.49 (0.87, 2.55) |
| Grades 10 or 11 | 1952 (42) | 139 (48) | | 1.80 (1.04, 3.11) [d] |
| Grades 1 to 6 | 299 (6) | 35 (12) | | 1.94 (1.00, 3.76) [d] |
| Current occupation [b] | | | <0.001 | |
| Manager/ professional | 1307 (28) | 52 (18) | | 1 |
| Associate professionals | 518 (11) | 22 (8) | | 0.64 (0.37, 1.13) |
| Trades/ advanced clerical | 908 (19) | 65 (22) | | 1.34 (0.86, 2.08) |
| Intermediate production/ clerical | 904 (19) | 68 (23) | | 1.16 (0.74, 1.81) |
| Labourers/ house person/ elementary clerical | 1021 (22) | 84 (29) | | 1.18 (0.75, 1.47) |
| **In childhood** | | | | |
| Childhood allergy | | | | |
| Eczema | 684 (14) | 55 (18) | | 1.30 (0.96, 1.77) |
| Childhood infection | | | | |
| Pneumonia | 458 (9) | 37 (12) | | 1.18 (0.82, 1.69) |
| Whooping cough | 421 (9) | 36 (11) | | 1.36 (0.94, 1.96) |
| Maternal smoking | | | 0.001 | |
| None to some up to five | 3092 (66) | 175 (59) | | 1 |

| | | | | | |
|---|---|---|---|---|---|
| | days per week | | | | |
| | Light regular (1-5 cigs/day) | 256 (5) | 16 (5) | | 1.09 (0.64, 1.87) |
| | Moderate (6-20 cigs/day) | 1079 (23) | 81 (27) | | 0.98 (0.74, 1.32) |
| | Heavy (>20 cigs/day) | 258 (6) | 26 (9) | | 1.02 (0.64, 1.63) |
| Paternal smoking | | | | 0.095 | |
| | None to some up to five days per week | 1882 (41) | 108 (37) | | 1 |
| | Light regular (1-5 cigs/day) | 183 (4) | 11 (4) | | 0.92 (0.48, 1.77) |
| | Moderate (6-20 cigs/day) | 1591 (35) | 107 (47) | | 0.86 (0.64, 1.15) |
| | Heavy (>20 cigs/day) | 900 (20) | 64 (22) | | 0.78 (0.55, 1.11) |
| Childhood lung function | | | | | |
| | $FEV_1$ > LLN | 212 (5) | 12 (5) | | 0.81 (0.44, 1.48) |
| | $FEV_1$/FVC > LLN | 154 (4) | 19 (7) | | 1.89 (1.16, 3.09) [d] |
| Paternal occupation [c] | | | | 0.124 | |
| | Manager/ professional | 1104 (19) | 58 (19) | | 1 |
| | Associate professionals | 320 (7) | 27 (9) | | 1.61 (1.00, 2.59) |
| | Trades/ advanced clerical | 1433 (29) | 94 (31) | | 1.21 (0.86, 1.70) |
| | Intermediate production/ clerical | 1379 (28) | 74 (24) | | 0.97 (0.68, 1.39) |
| | Labourers/ house person/ elementary clerical | 626 (13) | 55 (18) | | 1.59 (1.08, 2.34) [d] |

*Definitions of abbreviations:* CB, chronic bronchitis; CI, confidence interval; $FEV_1$, forced expiratory volume in one second; FVC, forced vital capacity, LLN, lower limit of normal; OR, odds ratio; py, pack-years; SHS, second-hand smoke.

[a] Participant numbers are based on adjustment for parental history, male gender, social class and/or educational level. Models for SHS exposure were additionally adjusted for personal smoking (n=4,931 and n=319). Models for childhood lung function were additionally adjusted for childhood asthma (n=4,268 and n=275).

[b] Estimates from table 2

[c] Estimates from table 4

[d] $p < 0.05$

[e] $p < 0.01$

Exposure to SHS in middle age was associated with adult CB for those exposed at the current workplace (p=0.011), but was borderline for those living with at least three household smokers (p=0.057). Domestic heating with coal or wood were no longer associated with adult CB in the multivariable model. A positive but independent association was also found for lower attained levels of education ($p \leq 0.050$).

Spirometric evidence of airflow obstruction in childhood was associated with a borderline increase in the odds for adult CB [OR 1.67, p=0.051]. There was no interaction between the effects of recurrent childhood bronchitis and personal smoking on adult CB (p=0.130)

A childhood history of eczema, self-reported pneumonia and whooping cough were not associated with adult CB. Regular maternal and paternal smoking when participants were seven-years old was not significant in the multivariable model.

## Supplementary References


S1. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CP, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J. Standardisation of spirometry. *Eur Respir J* 2005;26:319-338.

S2 Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, Enright PL, Hankinson JL, Ip MS, Zheng J, Stocks J. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J* 2012; 40: 1324-1343

S3 Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: Global Initiative for Chronic Obstructive Lung Disease. Updated 2014. http://www.goldcopd.org. Accessed 19.4.14.

S4 Perret JL, Dharmage SC, Matheson MC, Johns DP, Gurrin LC, Burgess JA, Marrone J, Markos J, Morrison S, Feather I, Thomas PS, McDonald CF, Giles GG, Hopper JL, Wood-Baker R, Abramson MJ, Walters EH. The Interplay between the Effects of Lifetime Asthma, Smoking, and Atopy on Fixed Airflow Obstruction in Middle Age. *Am J Respir Crit Care Med* 2013; 187: 42-48.

S5. National Asthma Council. Asthma management handbook 2006. Melbourne: National Asthma Council, 2006.