Methods E1 – Comparison of baseline characteristics of participants and non-participants of the 2004 postal survey

Continued participation in the 37-year follow-up was satisfactory with 78.4% of those traced responding to the postal survey. This figure represented 66.7% of the original TAHS cohort. A comparison of baseline characteristics between participants and non-participants revealed that those lost to follow-up were more likely to be male, not have childhood asthma, and be in a lower level of socioeconomic status in 1968.

Methods E2 – Asthma severity categories based on the Australian National Asthma Council (NAC) classification of asthma [1]

Severity	Frequency of symptoms
Asymptomatic asthma	No symptoms in the last year but on asthma medication
Intermittent asthma	Symptoms in the last year but not in the last month, ≤ 3 flare-ups in the last year
Mild persistent asthma	Symptoms in the last month but less than weekly, ≥ 4 flare-ups in the last year but less than monthly
Moderate persistent asthma	Symptoms more than once weekly but not daily, flare-ups more than monthly in the last year
Severe persistent asthma	Symptoms daily and flare-ups more than weekly in the last year

Methods E3 – Asthma symptom score composition based on the European Community Respiratory Health Survey (ECRHS) continuous asthma score framework [2]

ECRHS	TAHS 2004 Postal Survey	Score
Wheeze and breathlessness in the last 12 months?	Have you had wheezing or whistling in the last 12 months? + Have you been breathless at all when the wheezing noise was present?	1
Woken up with a feeling of chest tightness in the last 12 months?	Have you, at any time in the last 12 months, woken up with a feeling of chest tightness in your chest?	1
Attack of shortness of breath at rest in the last 12 months?	Do you ever get short of breath when resting?	1
Attack of shortness of breath after exercise in the last 12 months?	Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?	1
Woken by attack of shortness of breath in the last 12 months?	Have you, at any time in the last 12 months, been woken at night by an attack of shortness of breath?	1
Have you ever had asthma?	Have you, at any time in your life, suffered from attacks of asthma or wheezy breathing?	1
Attacks of asthma in the last 12 months?	How long ago did you have the last attack? [Within the last year]	1
Medication for asthma?	Have you taken any medicine (including inhalers or tablets) for this condition in the last three months?	1

Methods E4 – Details on missing data and multiple imputation methodology

The proportion of missing data in the cofounding variables ranged from 2% for social class to 3% for smoking status. Multiple imputation [3] was performed as a sensitivity analysis for imputing missing values in the confounding variables that were included in the analyses presented in Tables 2, 3 and 4. Multiple imputation by chained equations [4] was adopted using 20 imputations in Stata 13.1 [5] ("mi impute chained" command). In this method, missing data in each incomplete variable was imputed iteratively through a set of univariate conditional distributions. Univariate imputation models were specified such that continuous/discrete variables were imputed using linear regression models, binary variables using logistic regression models, and ordinal variables using ordered logistic regression models. The variables included in the imputation models were the same as those used in the target analysis models to ensure compatibility between imputation and target analysis model [6], and the auxiliary variables gender, height, and childhood lung function for the analyses presented in Tables 2 and 4, and current ICS and ICS + LABA use for the analysis shown in Table 3.

Results E1 – Difference in lung function between remitted, early-onset, late-onset asthma versus control (never asthma)

	Control (n = 415)	Remitted (n = 584)	Early-onset (n = 195)	Late-onset (n = 128)	Adjusted Mean Difference±		
					Remitted vs. control	Early-onset vs. control	Late-onset vs. control
Pre-BD (% predicted)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	MD (95% CI)	MD (95% CI)	MD (95% CI)
FEV$_1$	98.0 (12.6)	95.5 (12.5)	87.0 (16.5)	90.1 (15.2)	**-2.8 (-4.5,-1.0)†**	**-11.4 (-14.3,-8.6)‡**	**-7.6 (-10.7,-4.4)‡**
FVC	100.0 (12.0)	98.5 (12.0)	94.8 (13.3)	96.1 (12.8)	**-1.7 (-3.4,-0.0)***	**-5.1 (-7.5,-2.6)‡**	**-4.3 (-7.2,-1.4)†**
FEV$_1$/FVC	97.5 (7.2)	96.5 (7.9)	91.0 (11.0)	92.7 (9.6)	-0.9 (-2.0,0.1)	**-6.8 (-8.5,-5.1)‡**	**-3.9 (-5.9,-1.9)‡**
FEF$_{25-75}$	95.0 (26.3)	89.8 (26.5)	73.2 (29.9)	77.1 (27.7)	**-5.4 (-9.1,-1.6)†**	**-23.3 (-28.4,-18.2)‡**	**-15.0 (-21.4,-8.6)‡**
Post-BD (% predicted)							
FEV$_1$	100.8 (12.1)	98.6 (12.3)	91.4 (15.0)	94.5 (14.2)	**-2.3 (-4.0,-0.6)†**	**-9.6 (-12.1,-7.0)‡**	**-6.3 (-9.2,-3.3)‡**
FVC	100.2 (11.5)	98.8 (11.6)	96.6 (12.7)	97.8 (12.1)	-1.3 (-2.9,0.4)	**-3.6 (-5.9,-1.2)†**	**-3.0 (-5.9,-0.1)***
FEV$_1$/FVC	100.2 (7.1)	99.3 (7.3)	94.2 (10.7)	95.8 (9.2)	-0.9 (-1.9,0.1)	**-6.0 (-7.7,-4.4)‡**	**-3.4 (-5.2,-1.4)†**
FEF$_{25-75}$	105.4 (27.9)	100.1 (27.8)	82.9 (30.9)	89.0 (29.8)	**-6.1 (-9.9,-2.3)†**	**-23.8 (-29.2,-18.5)‡**	**-13.9 (-20.7,-7.0)‡**
Reversibility, %Δ	3.0 (5.2)	3.5 (4.5)	6.1 (7.8)	5.5 (6.4)	+0.6 (-0.1,1.3)	**+3.2 (2.0,4.4)‡**	**+2.1 (0.8,3.4)†**

Definition of abbreviations: BD = bronchodilator; MD = mean difference; CI = confidence interval

* P < 0.05

† P < 0.01

‡ P < 0.001

± Adjusted for smoking status, social class, family history of obstructive lung, childhood lung infections. Complete-case analysis.

Results E2 – Difference in lung function between early-onset and late-onset adult asthma

	Early-onset (n = 191)	Late-onset (n = 127)	Unadjusted mean difference	Adjusted mean difference†		
				Complete-case analysis	Multiple imputation	Multiple imputation (auxiliary variables)‡
Pre-BD (% predicted)	Mean (SD)	Mean (SD)	MD (95% CI)	MD (95% CI)	MD (95% CI)	MD (95% CI)
FEV$_1$	87.2 (16.5)	90.1 (15.2)	-2.8 (-6.4,0.8)	-2.7 (-6.3,0.9)	-2.9 (-6.6,0.7)	-2.9 (-6.5,0.8)
FVC	95.0 (13.3)	96.1 (12.8)	-1.1 (-4.1,1.9)	+0.1(-3.0,3.2)	-0.3 (-3.4,2.8)	-0.3 (-3.4,2.8)
FEV$_1$/FVC	91.1 (10.9)	92.7 (9.6)	-1.6 (-3.9,0.8)	**-2.8(-5.3,-0.3)***	**-2.5 (-4.9,-0.1)***	**-2.5 (-4.9,-0.1)***
FEF$_{25-75}$	73.6 (29.9)	77.1 (27.7)	-3.5 (-10.1,3.0)	-7.0 (-14.5,0.5)	-6.4 (-13.7,0.9)	-6.3 (-13.6,1.0)
Post-BD (% predicted)						
FEV$_1$	91.6 (15.0)	94.5 (14.2)	-3.0 (-6.3,0.4)	-2.4 (-5.8,0.9)	-2.7 (-6.1,0.6)	-2.7 (-6.0,0.7)
FVC	96.8 (12.6)	97.8 (12.1)	-1.1 (-3.9,1.8)	+0.3 (-2.9,3.4)	-0.0 (-3.0,3.0)	+0.0 (-3.0,3.0)
FEV$_1$/FVC	94.2 (10.7)	95.8 (9.2)	-1.6 (-3.9,0.7)	**-2.6 (-5.0,-0.1)***	**-2.6 (-5.0,-0.2)***	**-2.6 (-5.0,-0.2)***
FEF$_{25-75}$	83.2 (31.0)	89.0 (29.8)	-5.8 (-12.7,1.1)	**-8.7 (-16.6,-0.7)***	**-8.9 (-16.6, -1.1)***	**-8.7 (-16.4, -1.0)***
Reversibility, %Δ	6.0 (7.7)	5.5 (6.4)	+0.4 (-1.2,2.1)	+0.9 (-0.8,2.5)	0.8 (-0.8, 2.3)	0.8 (-0.8,2.3)

Definition of abbreviations: BD = bronchodilator; MD = mean difference; CI = confidence interval

* P < 0.05

† Adjusted for smoking status, social class, family history of obstructive lung, childhood lung infections

‡ Auxiliary variables were gender, height, childhood lung function

Results E3 – Difference in clinical outcomes between early-onset and late-onset adult asthma

	Early-onset (n = 191)	Late-onset (n = 127)	Unadjusted estimates	Adjusted estimates†		
				Complete-case analysis	Multiple Imputation	Multiple Imputation (auxiliary variables)‡
	Median [IQR]	Median [IQR]	RD (95% CI)	RD (95% CI)	RD (95% CI)	RD (95% CI)
Asthma Score a	4 [2-6]	4 [3-5]	-0.1 (-0.5,0.4)	+0.9 (-0.0,1.8)	**+0.8 (0.0,1.6)***	**+0.8 (0.0,1.7)***
	N (%)	N (%)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Wheeze with dyspnoea (last year) a	109 (57)	78 (61)	0.93 (0.78,1.12)	1.12 (0.88,1.43)	1.12 (0.88,1.42)	1.12 (0.89,1.42)
Woken up with chest tightness (last year) a	98 (51)	56 (44)	1.16 (0.92,1.48)	**1.39 (1.01,1.90)***	1.25 (0.94,1.66)	1.25 (0.94,1.66)
Woken by shortness of breath (last year) a	65 (34)	36 (28)	1.20 (0.85,1.69)	**1.53 (1.02,2.30)***	1.48 (1.00,2.18)	1.48 (1.00,2.19)
Dyspnoea (after exercise) a	57 (30)	52 (41)	0.73 (0.54,0.99)	0.88 (0.61,1.27)	0.85 (0.60,1.21)	0.85 (0.60,1.21)
Dyspnoea (at rest)	17 (9)	15 (12)	0.75 (0.39,1.45)	1.07 (0.51,2.21)	0.96 (0.48,1.90)	0.96 (0.48, 1.90)
Asthma Severity a						
Asymptomatic	36 (22)	20 (20)	-	-	-	-
Intermittent	48 (30)	21 (21)	1.27 (0.60,2.69)	1.82 (0.69,4.78)	2.23 (0.87,5.76)	2.23 (0.86,5.75)
Mild, persistent	31 (19)	26 (26)	0.66 (0.31,1.41)	0.98 (0.38,2.53)	1.11 (0.87,2.79)	1.11 (0.44,2.80)
Moderate, persistent	31 (19)	20 (20)	0.86 (0.39,1.89)	1.28 (0.44,3.68)	1.43 (0.51,4.00)	1.43 (0.51,4.00)
Severe, persistent	16 (10)	13 (13)	0.68 (0.27,1.70)	1.01 (0.34,2.95)	1.08 (0.38,3.08)	1.08 (0.38,3.09)
Asthma Hospitalisation (last year)	4 (2)	0 (0)	-	-	-	-

Definition of abbreviations: RD = rate difference; RR = risk ratio; CI = confidence interval

a Analysis performed using Poisson regression with robust error variance

* P < 0.05

† Adjusted for gender, age, smoking status, social class, family history of obstructive lung disease, childhood lung infections

‡ Auxiliary variables were current ICS use, current ICS+LABA use.

Results E4 – Interaction between early-onset asthma and smoking on post-bronchodilator FEV_1/FVC (% predicted)

		Case-control analysis		Multiple imputation		Multiple imputation (auxiliary variables)	
	Smoking (≥ 1 pack year)	Post-BD FEV_1/FVC	P [Interaction]	Post-BD FEV_1/FVC	P [Interaction]	Post-BD FEV_1/FVC	P [Interaction]
Control (never asthma)	No	Reference		Reference		Reference	
	Yes	-1.96 (-3.36,-0.57)*		-1.87 (-3.23,-0.51)*		-1.88 (-3.24,-0.53)*	
Early-onset	No	-5.16 (-6.97,-3.35)†	P = 0.34	-4.80 (-6.56,-3.04)†	P = 0.23	-4.86 (-6.61,-3.12)†	P = 0.28
	Yes	-8.83 (-11.78,-5.89)†		-8.65 (-11.41,-5.89)†		-8.53 (-11.30,-5.76)†	

Definition of abbreviations: BD = bronchodilator; CI = confidence interval

* P < 0.01

† P < 0.001

‡ Auxiliary variables were gender, height and childhood lung function

Adjusted for smoking status, social class, family history of obstructive lung disease, childhood lung infection

Results E5 – Interaction between late-onset asthma and smoking on post-bronchodilator FEV_1/FVC (% predicted)

		Case-control analysis		Multiple imputation		Multiple imputation (auxiliary variables)	
	Smoking (≥ 1 pack year)	Post-BD FEV_1/FVC	P [Interaction]	Post-BD FEV_1/FVC	P [Interaction]	Post-BD FEV_1/FVC	P [Interaction]
Control (never asthma)	No	Reference		Reference		Reference	
	Yes	-1.94 (-3.34,-0.54)*		-1.90 (-3.26,-0.54)*		-1.88 (-3.24,-0.51)*	
Late-onset	No	-0.65 (-0.34,2.04)	**P = 0.01**	-0.78 (-3.25,1.69)	**P = 0.009**	-0.74 (-3.20,1.72)	**P = 0.008**
	Yes	-7.61 (-10.26,-4.97)†		-7.35 (-9.89,-4.80)†		-7.36 (-9.92,-4.80)†	

Definition of abbreviations: BD = bronchodilator; CI = confidence interval

* P < 0.01

† P < 0.001

‡ Auxiliary variables were gender, height and childhood lung function

Adjusted for smoking status, social class, family history of obstructive lung disease, childhood lung infection

References:

1. Kandane-Rathnayake RK, Matheson MC, Simpson JA, et al. Adherence to asthma management guidelines by middle-aged adults with current asthma. Thorax 2009;**64**(12):1025-31 doi: 10.1136/thx.2009.118430[published Online First: Epub Date]|.
2. Pekkanen J, Sunyer J, Anto JM, et al. Operational definitions of asthma in studies on its aetiology. The European respiratory journal 2005;**26**(1):28-35 doi: 10.1183/09031936.05.00120104[published Online First: Epub Date]|.
3. Rubin D. *Multiple imputation for nonresponse in surveys*. New York: Wiley, 1987.
4. Van Buuren S, Brand JPL, Groothuis-Oudshoorn C, et al. Fully conditional specification in multivariate imputation. Journal of Statistical Computation & Simulation 2006;**76**(12):1049-64
5. StataCorp. Stata Statistical Software: Release 13. College Station, Texas: Stata Corp LP, 2013.
6. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. Stat Med 2011;**30**(4):377-99