

#### Methods E1: Statistical selection of cut-off points (Youden and Liu Indexes)

Two statistically-selected cut-off points, the Youden and Liu Indexes, were calculated using the TAHS dataset. The Youden Index, also known as the Youden J statistic, defines the optimal cut-off as the point which maximises the sum of the sensitivity and specificity (1, 2). In contrast, the Liu Index defines the optimal cut-off as the point which maximises the product of the sensitivity and specificity (3). Both statistical approaches place equal weighting to sensitivity and specificity.

#### Methods E2: Selection of the symptomatic sample

The symptomatic sample was a subset of the original whole TAHS sample. Symptomatic individuals were identified by positive responses to one or more survey-based questions related to respiratory symptoms in the last 12 months (wheeze, shortness of breath or chest tightness). These questions have been validated and used in other population-based observational studies including the European Community Respiratory Health Survey (ECRHS).

Symptomatic sample defined as a positive response to one or more of the following:

- Have you had wheezing or whistling in your chest in the last 12 months?, or
- Have you had an attack of shortness of breath at rest in the last 12 months?, or
- Have you had an attack of shortness of breath after exercise in the last 12 months?, or
- Have you woken due to a feeling of tightness in your chest in the last 12 months?, or
- Have you been woken at night by an attack of shortness of breath in the last 12 months?

Table E1. Comparison of bronchodilator reversibility between the reference population and disease subgroups

	$\Delta FEV_1$ (ml)		$\Delta FEV_{1initial}$		$\Delta FEV_{1predicted}$	
	Mean Diff. (95%CI)	p-value	Mean Diff. (95%CI)	p-value	Mean Diff. (95%CI)	p-value
Reference Sample	Baseline	-	Baseline	-	Baseline	-
Current Asthma	+55.5 (33.2, 79.7)	<0.001	+2.6 (1.7, 3.4)	<0.001	+1.6 (0.9, 2.4)	<0.001
COPD	+48.8 (18.1, 79.4)	0.002	+3.6 (2.5, 4.7)	<0.001	+1.5 (0.6, 2.4)	0.002
ACO	+155.7 (118.5, 193.0)	<0.001	+9.7 (8.3, 11.1)	<0.001	+4.7 (3.6, 5.8)	<0.001
Current Asthma	Baseline	-	Baseline	-	Baseline	-
COPD	-18.2 (-64.7, 28.2)	0.44	+0.6 (-1.4, 2.6)	0.55	-0.4 (-0.8, 1.0)	0.56
ACO	+111.7 (54.9, 168.5)	<0.001	+8.1 (5.3, 10.8)	<0.001	+3.3 (1.6, 5.0)	<0.001
COPD	Baseline	-	Baseline	-	Baseline	-
ACO	+129.9 (57.9, 202.0)	0.001	+7.5 (3.8, 11.1)	<0.001	3.7 (1.6, 5.8)	0.001

COPD: chronic obstructive pulmonary disease. ACO: asthma-COPD overlap

Table E2. Comparison of bronchodilator reversibility in participants with adult asthma (current asthma OR ACO) by inhaled corticosteroids (ICS) use

	$\Delta FEV_1$ (ml)		$\Delta FEV_{1initial}$		$\Delta FEV_{1predicted}$	
	Mean Diff. (95%CI)	p-value	Mean Diff. (95%CI)	p-value	Mean Diff. (95%CI)	p-value
No ICS use	Baseline	-	Baseline	-	Baseline	-
Current use	+60.5 (29.2, 91.8)	<0.001	+3.3 (2.0, 4.6)	<0.001	+1.8 (0.8, 2.7)	<0.001

MD: Mean Difference

Table E3: Youden Cut-off Points and corresponding diagnostic parameters

Diagnostic utility of GINA BDR cut-off point:	Youden Cut-off	Sensitivity (95% CI)	Specificity (95% CI)
Asthma:			
$\Delta$ FEV <sub>1</sub> (ml) ULN	205.0 ml	82%	56%
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	4.3%	51%	64%
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	4.1%	51%	62%
Asthma-COPD overlap			
$\Delta$ FEV <sub>1</sub> (ml) ULN	110.0 ml	93%	54%
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	6.2%	79%	79%
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	4.3%	81%	65%

ULN: Upper limit of normal

$\Delta$ FEV<sub>1</sub> ULN: 280 ml,  $\Delta$ FEV<sub>1</sub> % of initial FEV<sub>1</sub> ULN: 9.2%,  $\Delta$ FEV<sub>1</sub> % of pred. FEV<sub>1</sub> ULN: 8.8%

Table E4: Liu Cut-off Points and corresponding diagnostic parameters

Diagnostic utility of GINA BDR cut-off point:	Liu Cut-off	Sensitivity (95% CI)	Specificity (95% CI)
Asthma:			
$\Delta$ FEV <sub>1</sub> (ml) ULN	100.0 ml	54%	56%
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	4.4%	51%	64%
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	4.0%	51%	61%
Asthma-COPD overlap			
$\Delta$ FEV <sub>1</sub> (ml) ULN	115.0 ml	88%	57%
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	6.2%	79%	79%
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	4.3%	65%	73%

ULN: Upper limit of normal

$\Delta$ FEV<sub>1</sub> ULN: 280 ml,  $\Delta$ FEV<sub>1</sub> % of initial FEV<sub>1</sub> ULN: 9.2%,  $\Delta$ FEV<sub>1</sub> % of pred. FEV<sub>1</sub> ULN: 8.8%

Table E5. Basic characteristics of the disease subgroups in the 2012 TAHS study (Symptomatic Sample)

	No Airways Disease (n=661)	Asthma (n=134)	COPD (n=50)	Asthma-COPD overlap (n=41)
Age, years	52.8 (0.8)	53.0 (0.8)	52.8 (0.7)	52.8 (0.7)
BMI, kgm <sup>-2</sup>	29.9 (5.9)	30.4 (6.8)	27.6 (6.9)	29.0 (7.3)
Female, n (%)	344 (52%)	71 (53%)	29 (58%)	19 (46%)
Smoking History, n (%)				
Never	261 (40%)	67 (51%)	6 (12%)	8 (20%)
Former	241 (37%)	52 (39%)	14 (29%)	15 (37%)
Current	151 (23%)	13 (10%)	29 (59%)	18 (44%)
Asthma History				
Early-onset, n (%)	-	66% (50%)	-	22 (54%)
Current ICS use, n (%)	-	68 (51%)	1 (2%)	17 (41%)
Asthma Severity				
Intermittent	-	10 (8%)	-	0 (0%)
Mild persistent	-	31 (26%)	-	8 (30%)
Moderate-severe persistent	-	79 (66%)	-	19 (70%)
Pre-BD Spirometry				
FEV <sub>1</sub> (% predicted)	95.0 (14.0)	91.0 (15.3)	76.0 (17.0)	63.7 (18.6)
FVC (% predicted)	97.4 (12.9)	96.3 (14.8)	99.3 (17.2)	89.1 (18.4)
FEV <sub>1</sub> /FVC (% predicted)	97.2 (7.1)	94.3 (7.3)	75.7 (8.9)	70.3 (11.6)
Post-BD Spirometry				
FEV <sub>1</sub> (% predicted)	98.4 (13.5)	95.6 (14.0)	81.1 (16.7)	71.5 (18.9)
FVC (% predicted)	98.2 (12.5)	97.8 (13.7)	103.1 (16.6)	96.1 (17.3)
FEV <sub>1</sub> /FVC (% predicted)	100.1 (6.6)	97.6 (6.4)	78.0 (8.6)	73.4 (11.8)
BDR Indices				
ΔFEV <sub>1</sub> (ml)	112.9 (136.8)	152.8 (160.5)	161.6 (171.1)	260.5 (191.2)
ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub>	3.9 (4.8)	5.7 (6.8)	7.8 (8.9)	13.9 (11.8)
ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub>	3.5 (4.1)	4.7 (4.9)	5.1 (5.4)	7.8 (5.1)

Data presented as mean (SD) unless otherwise indicated. ICS: inhaled corticosteroid

Complete data were obtained in 875 (99%) for smoking history, 201 (89%) for current ICS use, 147 (84%) for asthma severity

No 'reference sample' is provided in this table as all participants, by definition, had symptoms

**Sensitivity Analysis #1: 1 month asthma definition, ICS users excluded. (Tables E6 to E8)**

Table E6. [1 month definition, ICS users excluded] Areas under the ROC curve (AUC) of BDR measures as diagnostic classifiers for current doctor-diagnosed asthma and asthma-COPD overlap

		AUC (95%CI)	
		Asthma	Asthma-COPD overlap
General Sample (Whole cohort)	$\Delta$ FEV <sub>1</sub> (ml)	57% (50-64%)	79% (70-88%)
	$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub>	59% (51-66%)	86% (78-95%)
	$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub>	57% (50-65%)	79% (70-88%)
Symptomatic Sample		Asthma	Asthma-COPD overlap
	$\Delta$ FEV <sub>1</sub> (ml)	54% (47-62%)	76% (66-85%)
	$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub>	55% (47-62%)	83% (73-92%)
	$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub>	55% (47-63%)	76% (66-86%)

Table E7. [1 month definition, ICS users excluded] General sample: Diagnostic parameters of BDR cut-off points for current doctor-diagnosed asthma and asthma-COPD overlap

Cut-offs for Bronchodilator Reversibility (BDR):	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Diagnostic odds ratio (95% CI)
Asthma:							
ΔFEV <sub>1</sub> (ml) ULN	14% (7-24%)	92% (91-93%)	5% (2-9%)	97% (97-98%)	1.82 (1.00, 3.28)	0.93 (0.85, 1.02)	1.95 (0.98, 3.86)
ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	21% (14-32%)	93% (92-94%)	7% (4-11%)	97% (97-98%)	2.90 (1.83, 4.57)	0.85 (0.75, 0.96)	3.41 (1.92, 6.05)
ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	14% (8-24%)	94% (93-95%)	6% (3-11%)	97% (97-98%)	2.28 (1.26, 4.14)	0.92 (0.84, 1.01)	2.49 (1.25, 4.95)
ΔFEV <sub>1</sub> 12% of initial +200ml	6% (2-13%)	97% (96-98%)	6% (2-14%)	97% (96-98%)	1.99 (0.75, 5.29)	0.97 (0.92, 1.03)	2.04 (0.73, 5.76)
ΔFEV <sub>1</sub> 15% of initial +400ml	1% (0-8%)	99% (99-99%)	4% (0-21%)	97% (96-98%)	1.47 (0.20, 10.72)	1.00 (0.97, 1.02)	1.47 (0.20, 11.07)
Asthma-COPD overlap:							
ΔFEV <sub>1</sub> (ml) ULN	44% (27-63%)	92% (91-93%)	6% (3-10%)	99% (99-100%)	5.75 (3.62, 9.14)	0.61 (0.43, 0.86)	9.48 (4.24, 21.18)
ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	60% (41-77%)	93% (92-94%)	8% (4-12%)	100% (99-100%)	8.15 (5.74, 11.56)	0.43 (0.27, 0.70)	18.86 (8.35, 42.59)
ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	40% (23-59%)	94% (93-95%)	6% (3-11%)	99% (99-100%)	6.57 (3.96, 10.88)	0.64 (0.46, 0.88)	10.28 (4.54, 23.28)
ΔFEV <sub>1</sub> 12% of initial +200ml	44% (27-63%)	97% (96-98%)	14% (7-24%)	99% (99-100%)	15.72 (9.53, 25.94)	0.58 (0.41, 0.82)	27.29 (11.95, 62.32)
ΔFEV <sub>1</sub> 15% of initial +400ml	12% (4-30%)	99% (99-99%)	12% (2-30%)	99% (99-99%)	12.68 (4.07, 39.52)	0.89 (0.77, 1.03)	14.27 (3.99, 51.03)

ULN: Upper limit of normal. ΔFEV<sub>1</sub> ULN: 280 ml, ΔFEV<sub>1</sub> % of initial FEV<sub>1</sub> ULN: 9.2%, ΔFEV<sub>1</sub> % of pred. FEV<sub>1</sub> ULN: 8.8%

Table E8. [1 month definition, ICS users excluded] Symptomatic sample: Diagnostic parameters of BDR cut-off points for current doctor-diagnosed asthma and asthma-COPD overlap

Cut-offs for Bronchodilator Reversibility (BDR):	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Diagnostic odds ratio (95% CI)
Asthma:							
$\Delta$ FEV <sub>1</sub> (ml) ULN	15% (8-26%)	89% (97-91%)	12% (6-21%)	92% (89-94%)	1.40 (0.76, 2.57)	0.95 (0.86, 1.06)	1.47 (0.72, 3.00)
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	18% (86-91%)	89% (86-91%)	13% (7-22%)	92% (90-94%)	1.61 (0.93, 2.80)	0.92 (0.82, 1.04)	1.75 (0.90, 3.41)
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	15% (8-26%)	92% (89-94%)	15% (7-26%)	92% (90-94%)	1.84 (0.99, 3.42)	0.93 (0.83, 1.03)	1.99 (0.96, 4.10)
$\Delta$ FEV <sub>1</sub> 12% of initial +200ml	6% (2-15%)	95% (93-96%)	11% (3-25%)	91% (89-93%)	1.23 (0.45, 3.36)	0.99 (0.93, 1.05)	1.25 (0.43, 3.63)
$\Delta$ FEV <sub>1</sub> 15% of initial +400ml	2% (0-8%)	98% (96-99%)	6% (0-30%)	91% (90-93%)	0.70 (0.09, 5.20)	1.01 (0.98, 1.04)	0.69 (0.09, 5.33)
Asthma-COPD overlap:							
$\Delta$ FEV <sub>1</sub> (ml) ULN	42% (25-61%)	89% (87-91%)	12% (6-21%)	98% (96-99%)	3.84 (2.28, 6.45)	0.65 (0.47, 0.92)	5.87 (2.52, 13.67)
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	50% (86-91%)	89% (86-91%)	15% (9-24%)	98% (97-99%)	4.43 (2.90, 7.78)	0.56 (0.39, 0.82)	7.86 (3.61, 17.10)
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	42% (25-61%)	92% (89-94%)	15% (7-26%)	98% (96-99%)	5.05 (2.96, 8.62)	0.64 (0.45, 0.89)	7.95 (3.38, 18.69)
$\Delta$ FEV <sub>1</sub> 12% of initial +200ml	46% (28-65%)	95% (93-96%)	24% (13-40%)	98% (97-99%)	9.32 (5.40, 16.06)	0.57 (0.39, 0.82)	16.35 (6.82, 39.18)
$\Delta$ FEV <sub>1</sub> 15% of initial +400ml	13% (4-31%)	98% (96-99%)	17% (4-41%)	97% (95-98%)	5.76 (1.79, 18.57)	0.89 (0.77, 1.04)	6.44 (1.73, 23.94)

ULN: Upper limit of normal.  $\Delta$ FEV<sub>1</sub> ULN: 280 ml,  $\Delta$ FEV<sub>1</sub> % of initial FEV<sub>1</sub> ULN: 9.2%,  $\Delta$ FEV<sub>1</sub> % of pred. FEV<sub>1</sub> ULN: 8.8%

**Sensitivity Analysis #2: 12 month asthma definition, ICS users included (Tables E9 to E11)**

Methods E3: Disease definitions for sensitivity analysis #2. ‘Current doctor-diagnosed asthma’ was defined as asthma-related symptoms and/or healthcare or medication utilisation in the last 12 months in participants who self-reported doctor-diagnosed asthma and did not have post-bronchodilator (BD) airflow obstruction (AO). ‘Post-BD AO’ or ‘chronic obstructive pulmonary disease (COPD)’ was defined as a post-BD FEV<sub>1</sub>/FVC ratio below the lower limit of normal (LLN). ‘Asthma-COPD overlap’ (ACO) was defined by the combined criteria of current doctor-diagnosed asthma and post-BD AO. The three disease categories were therefore mutually exclusive.

Table E9. [12 month definition, ICS users included] Areas under the ROC curve (AUC) of BDR measures as diagnostic classifiers for current doctor-diagnosed asthma and asthma-COPD overlap

		AUC (95%CI)	
		Asthma	Asthma-COPD overlap
General Sample (Whole cohort)	ΔFEV <sub>1</sub> (ml)	58% (55-62%)	78% (72-84%)
	ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub>	61% (57-65%)	85% (79-91%)
	ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub>	59% (55-63%)	78% (71-84%)
Symptomatic Sample		Asthma	Asthma-COPD overlap
	ΔFEV <sub>1</sub> (ml)	57% (52-61%)	75% (68-82%)
	ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub>	58% (54-63%)	82% (76-89%)
	ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub>	58% (53-62%)	75% (68-82%)



Table E10. [12 month definition, ICS users included] General sample: Diagnostic parameters of BDR cut-off points for current doctor-diagnosed asthma and asthma-COPD overlap

Cut-offs for Bronchodilator Reversibility (BDR):	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Diagnostic odds ratio (95% CI)
Asthma:							
ΔFEV <sub>1</sub> (ml) ULN	15% (11-20%)	92% (91-93%)	11% (8-17%)	92% (90-93%)	1.96 (1.40, 2.75)	0.92 (0.87, 0.97)	2.13 (1.44, 3.14)
ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	19% (14-24%)	93% (92-94%)	21% (16-27%)	92% (91-93%)	2.61 (1.93, 3.54)	0.88 (0.82, 0.93)	2.98 (2.07, 4.29)
ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	19% (13-25%)	92% (90-93%)	18% (13-25%)	92% (90-93%)	2.19 (1.56, 3.08)	0.89 (0.83, 0.96)	2.46 (1.63, 3.71)
ΔFEV <sub>1</sub> 12% of initial +200ml	9% (6-13%)	97% (97-98%)	25% (16-35%)	91% (90-93%)	3.46 (2.15, 5.57)	0.94 (0.90, 0.97)	3.70 (2.21, 6.19)
ΔFEV <sub>1</sub> 15% of initial +400ml	5% (3-8%)	99% (99-99%)	35% (19-55%)	91% (90-92%)	5.53 (2.68, 11.40)	0.96 (0.93, 0.99)	5.75 (2.72, 12.16)
Asthma-COPD overlap:							
ΔFEV <sub>1</sub> (ml) ULN	36% (23-49%)	92% (91-93%)	10% (6-15%)	98% (98-99%)	4.74 (3.22, 6.98)	0.69 (0.57, 0.85)	6.83 (3.82, 12.22)
ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	55% (41-67%)	93% (92-94%)	15% (10-20%)	99% (98-99%)	7.66 (5.76, 10.19)	0.49 (0.36, 0.66)	15.72 (8.95, 27.60)
ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	34% (23-47%)	94% (93-95%)	11% (7-17%)	98% (98-99%)	5.32 (3.54, 7.98)	0.71 (0.58, 0.86)	7.53 (4.17, 13.62)
ΔFEV <sub>1</sub> 12% of initial +200ml	40% (28-53%)	97% (97-98%)	5% (16-36%)	99% (98-99%)	14.80 (9.80, 22.35)	0.62 (0.50, 0.77)	23.85 (13.03, 43.67)
ΔFEV <sub>1</sub> 15% of initial +400ml	11% (5-23%)	99% (99-99%)	24% (9-45%)	98% (97-99%)	14.02 (5.84, 33.68)	0.89 (0.81, 0.98)	15.68 (5.99, 41.05)

ULN: Upper limit of normal. ΔFEV<sub>1</sub> ULN: 280 ml, ΔFEV<sub>1</sub> % of initial FEV<sub>1</sub> ULN: 9.2%, ΔFEV<sub>1</sub> % of pred. FEV<sub>1</sub> ULN: 8.8%

Table E11. [12 month definition, ICS users included] Symptomatic sample: Diagnostic parameters of BDR cut-off points for current doctor-diagnosed asthma and asthma-COPD overlap

Cut-offs for Bronchodilator Reversibility (BDR):	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Diagnostic odds ratio (95% CI)
Asthma:							
$\Delta$ FEV <sub>1</sub> (ml) ULN	16% (12-21%)	89% (87-91%)	34% (25-44%)	76% (72-79%)	1.48 (1.01, 2.17)	0.94 (0.88, 1.01)	1.57 (1.01, 2.46)
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	19% (15-25%)	89% (86-91%)	37% (28-47%)	76% (73-79%)	1.74 (1.22, 2.47)	0.91 (0.85, 0.98)	1.91 (1.25, 2.92)
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	15% (10-20%)	92% (90-94%)	38% (28-50%)	76% (72-79%)	1.81 (1.19, 2.76)	0.93 (0.88, 0.99)	1.95 (1.21, 3.14)
$\Delta$ FEV <sub>1</sub> 12% of initial +200ml	10% (7-15%)	95% (93-97%)	42% (28-57%)	76% (72-79%)	2.12 (1.23, 3.63)	0.95 (0.90, 0.99)	2.24 (1.25, 4.01)
$\Delta$ FEV <sub>1</sub> 15% of initial +400ml	5% (3-9%)	98% (97-99%)	50% (28-72%)	75% (72-78%)	2.92 (1.29, 6.64)	0.97 (0.93, 1.00)	3.03 (1.29, 7.08)
Asthma-COPD overlap:							
$\Delta$ FEV <sub>1</sub> (ml) ULN	36% (24-50%)	89% (87-91%)	21% (13-31%)	95% (92-96%)	3.34 (2.17, 5.16)	0.72 (0.58, 0.89)	4.66 (2.48, 8.75)
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	54% (40-67%)	89% (86-91%)	28% (19-38%)	96% (94-97%)	4.87 (3.47, 6.83)	0.52 (0.38, 0.70)	9.41 (5.11, 17.31)
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	36% (24-50%)	92% (90-94%)	26% (17-39%)	95% (93-96%)	4.48 (2.84, 7.06)	0.70 (0.57, 0.86)	6.44 (3.37, 12.27)
$\Delta$ FEV <sub>1</sub> 12% of initial +200ml	42% (29-56%)	95% (93-97%)	42% (28-57%)	95% (93-97%)	9.01 (5.56, 14.59)	0.61 (0.48, 0.77)	14.81 (7.55, 29.05)
$\Delta$ FEV <sub>1</sub> 15% of initial +400ml	12% (6-24%)	98% (97-99%)	25% (14-62%)	93% (91-95%)	6.79 (2.62, 17.58)	0.90 (0.81, 0.99)	7.57 (2.68, 21.45)

ULN: Upper limit of normal.  $\Delta$ FEV<sub>1</sub> ULN: 280 ml,  $\Delta$ FEV<sub>1</sub> % of initial FEV<sub>1</sub> ULN: 9.2%,  $\Delta$ FEV<sub>1</sub> % of pred. FEV<sub>1</sub> ULN: 8.8%

**Sensitivity Analysis #3: 12 month asthma definition, ICS users excluded (Tables E12 to E14)**

Methods E4: Disease definitions for sensitivity analysis #3. ‘Current doctor-diagnosed asthma’ was defined as asthma-related symptoms and/or healthcare or medication utilisation in the last 1 month in participants who self-reported doctor-diagnosed asthma and did not have post-bronchodilator (BD) airflow obstruction (AO). ‘Post-BD AO’ or ‘chronic obstructive pulmonary disease (COPD)’ was defined as a post-BD FEV<sub>1</sub>/FVC ratio below the lower limit of normal (LLN). ‘Asthma-COPD overlap’ (ACO) was defined by the combined criteria of current doctor-diagnosed asthma and post-BD AO. The three disease categories were therefore mutually exclusive.

Table E12. [12 month definition, ICS users excluded] Areas under the ROC curve (AUC) of BDR measures as diagnostic classifiers for current doctor-diagnosed asthma and asthma-COPD overlap

		AUC (95%CI)	
		Asthma	Asthma-COPD overlap
General Sample (Whole cohort)	ΔFEV <sub>1</sub> (ml)	59% (54-64%)	77% (68-85%)
	ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub>	61% (56-66%)	83% (75-92%)
	ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub>	60% (55-65%)	76% (68-84%)
Symptomatic Sample		Asthma	Asthma-COPD overlap
	ΔFEV <sub>1</sub> (ml)	57% (52-62%)	74% (65-82%)
	ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub>	58% (53-64%)	80% (71-89%)
	ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub>	58% (53-64%)	73% (64-82%)

Table E13. [12 month definition, ICS users excluded] General sample: Diagnostic parameters of BDR cut-off points for current doctor-diagnosed asthma and asthma-COPD overlap

Cut-offs for Bronchodilator Reversibility (BDR):	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Diagnostic odds ratio (95% CI)
Asthma:							
ΔFEV <sub>1</sub> (ml) ULN	13% (9-19%)	93% (91-94%)	10% (6-15%)	94% (93-95%)	1.75 (1.13, 2.69)	0.94 (0.88, 1.00)	1.86 (1.13, 3.05)
ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	18% (12-24%)	93% (92-94%)	14% (10-20%)	95% (94-95%)	2.55 (1.75, 3.70)	0.89 (0.82, 0.95)	2.88 (1.85, 4.50)
ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	13% (9-19%)	94% (93-95%)	13% (8-19%)	94% (93-95%)	2.23 (1.44, 3.46)	0.92 (0.87, 0.98)	2.42 (1.47, 3.99)
ΔFEV <sub>1</sub> 12% of initial +200ml	7% (4-12%)	97% (97-98%)	15% (8-26%)	94% (93-95%)	2.77 (1.49, 5.15)	0.95 (0.91, 1.00)	2.91 (1.50, 5.64)
ΔFEV <sub>1</sub> 15% of initial +400ml	3% (1-7%)	99% (99-99%)	21% (7-42%)	94% (93-95%)	4.04 (1.53, 10.67)	0.98 (0.95, 1.00)	4.14 (1.53, 11.25)
Asthma-COPD overlap:							
ΔFEV <sub>1</sub> (ml) ULN	34% (21-51%)	93% (91-94%)	6% (3-11%)	99% (98-99%)	4.58 (2.84, 7.41)	0.71 (0.56, 0.90)	6.45 (3.16, 13.19)
ΔFEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	51% (36-67%)	93% (92-94%)	10% (6-15%)	99% (99-100%)	7.43 (5.21, 10.59)	0.52 (0.37, 0.73)	14.23 (7.20, 28.14)
ΔFEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	31% (19-48%)	94% (93-95%)	7% (4-13%)	99% (98-99%)	5.37 (3.20, 8.90)	0.73 (0.58, 0.91)	7.37 (3.54, 15.35)
ΔFEV <sub>1</sub> 12% of initial +200ml	34% (21-51%)	97% (97-98%)	17% (9-27%)	99% (99-99%)	13.37 (7.93, 22.53)	0.67 (0.53, 0.86)	19.82 (9.42, 41.68)
ΔFEV <sub>1</sub> 15% of initial +400ml	11% (5-26%)	99% (99-100%)	18% (5-40%)	99% (98-99%)	14.85 (5.30, 41.63)	0.79 (1.01)	16.64 (5.32, 52.02)

ULN: Upper limit of normal. ΔFEV<sub>1</sub> ULN: 280 ml, ΔFEV<sub>1</sub> % of initial FEV<sub>1</sub> ULN: 9.2%, ΔFEV<sub>1</sub> % of pred. FEV<sub>1</sub> ULN: 8.8%

Table E14. [12 month definition, ICS users excluded] Symptomatic sample: Diagnostic parameters of BDR cut-off points for current doctor-diagnosed asthma and asthma-COPD overlap

Cut-offs for Bronchodilator Reversibility (BDR):	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Diagnostic odds ratio (95% CI)
Asthma:							
$\Delta$ FEV <sub>1</sub> (ml) ULN	14% (10-21%)	90% (87-92%)	24% (15-34%)	82% (79-85%)	1.38 (0.87, 2.20)	0.96 (0.89, 1.03)	1.45 (0.84, 2.48)
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	18% (13-25%)	90% (87-92%)	28% (19-39%)	83% (80-86%)	1.75 (1.15, 2.68)	0.91 (0.84, 0.99)	1.92 (1.16, 3.19)
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	14% (10-21%)	92% (90-94%)	30% (20-43%)	83% (80-85%)	1.92 (1.18, 3.14)	0.93 (0.86, 0.99)	2.08 (1.19, 3.64)
$\Delta$ FEV <sub>1</sub> 12% of initial +200ml	8% (5-14%)	96% (94-97%)	30% (16-47%)	82% (79-85%)	1.87 (0.95, 3.69)	0.96 (0.91, 1.01)	1.95 (0.94, 4.04)
$\Delta$ FEV <sub>1</sub> 15% of initial +400ml	4% (2-8%)	98% (97-99%)	33% (12-62%)	82% (79-85%)	2.21 (0.77, 6.36)	0.98 (0.95, 1.01)	2.26 (0.76, 6.71)
Asthma-COPD overlap:							
$\Delta$ FEV <sub>1</sub> (ml) ULN	33% (20-50%)	90% (87-92%)	15% (8-25%)	96% (94-98%)	3.18 (1.86, 5.43)	0.75 (0.58, 0.95)	4.27 (1.98, 9.20)
$\Delta$ FEV <sub>1</sub> % of initial FEV <sub>1</sub> ULN	48% (33-65%)	90% (87-92%)	20% (12-31%)	97% (95-98%)	4.70 (3.08, 7.16)	0.57 (0.41, 0.80)	8.17 (3.94, 16.97)
$\Delta$ FEV <sub>1</sub> % of pred. FEV <sub>1</sub> ULN	33% (20-50%)	92% (90-94%)	19% (10-32%)	96% (94-98%)	4.42 (2.53, 7.71)	0.72 (0.57, 0.92)	6.13 (2.80, 13.42)
$\Delta$ FEV <sub>1</sub> 12% of initial +200ml	36% (22-53%)	96% (94-97%)	32% (18-49%)	97% (95-98%)	8.53 (4.74, 15.35)	0.67 (0.51, 0.86)	12.84 (5.71, 28.88)
$\Delta$ FEV <sub>1</sub> 15% of initial +400ml	12% (5-27%)	98% (97-99%)	29% (8-58%)	95% (93-97%)	7.39 (2.45, 22.33)	0.89 (0.79, 1.02)	8.28 (2.45, 27.97)

ULN: Upper limit of normal.  $\Delta$ FEV<sub>1</sub> ULN: 280 ml,  $\Delta$ FEV<sub>1</sub> % of initial FEV<sub>1</sub> ULN: 9.2%,  $\Delta$ FEV<sub>1</sub> % of pred. FEV<sub>1</sub> ULN: 8.8%

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