

Appendix

Table A1: Diagnostic Read codes used to identify patients with COPD and comorbidities from primary care data

Condition	Read Codes	Definition
COPD	H3... H31* H32* H36.. H37.. H38.. H39.. H3y.. H3y0. H3y1. H3z.. (Not h3101 H31y0 H3122)	Recorded between 1 st April 2000 and 31 st March 2008
CHD	G3... G30* G31* G32* G33.. G330* G33z* G34.. G340* G342. G343. G344. G34y* G35* G36* G38* G3y.. G3z.. Gyu3*	Recorded on or before date of primary care COPD diagnosis
Heart failure	G58* G1yz1 662f. 662g. 662h. 662i.	Recorded on or before date of primary care COPD diagnosis
Diabetes	C10E* C10F*	Recorded on or before date of primary care COPD diagnosis
Asthma	H33* H333. H33z1	Recorded on or before date of primary care COPD diagnosis
Stroke	G61* G63y0 G63y1 G64* G66 G6760 G6W.. G6X.. Gyu62 Gyu63 Gyu64 Gyu65 Gyu66 Gyu6F Gyu6G G65* F4236 (Not G617. and G655.)	Recorded on or before date of primary care COPD diagnosis
Hypertension	G2... G20* G24* G2y.. G2z.. (Not G24z1)	Recorded on or before date of primary care COPD diagnosis
CKD	1Z12. 1Z13. 1Z14. 1Z15. 1Z16. 1Z1B. 1Z1C. 1Z1D. 1Z1E. 1Z1F. 1Z1G. 1Z1H. 1Z1J. 1Z1K. 1Z1L.	Recorded on or before date of primary care COPD diagnosis
Osteoporosis	N330*	Recorded on or before date of primary care COPD diagnosis
Depression	E0013 E0021 E112* E113* E118. E11y2 E11z2 E130. E135. E2003 E291. E2B.. E2B1. Eu204 Eu251 Eu32* Eu33* Eu341 Eu241 Eu412	Recorded on or before date of primary care COPD diagnosis
Dementia	Eu02* E00* Eu01* E02y1 E012* Eu00* E041. Eu041 F110. F111. F112. F116.	Recorded on or before date of primary care COPD diagnosis

Table A2: Codes and definitions used to identify admissions for COPD, AECOPD, and selected comorbidities from SMR01 admissions data and cancer incidence from SMR06 data

Condition	Diagnostic position	ICD10	ICD9	Definition
Prior COPD admission	Any	J40X, J41, J42X, J43, J44, J47X	490, 491, 492, 494, 496	Continuous inpatient stay (CIS) admission date prior to date of diagnosis in primary care (with 10 year look back from date of diagnosis)
First AECOPD after diagnosis	Any	J440, J441	n/a	First episode admission date within CIS after date of COPD diagnosis
AECOPD readmission	Any	J440, J441	n/a	Episode admission date within CIS, 14 days or more after date of discharge from previous CIS AECOPD admission
Liver disease (moderate to severe)	Any	I85, I864, K704, K711, K721, K729, K765, K766, K767 Dagger codes: B65, K70, K71, K74 with asterix code I982	570, 456.0, 456.1, 572.8, 572.3, 572.2 Dagger code: any ICD9 code with asterix code 456.2	Any admission date before date of COPD diagnosis in primary care (with 10 year look back from date of diagnosis)
Pneumonia	Any	J100, J110, J12, J13X, J14X, J15, J16, J18, J850, J851 Dagger codes: A022, A212, A221, A420, A430, A548 with asterix code J170 Dagger codes: B012, B052, B068, B250 with asterix code J171 Dagger codes: B371, B380, B381, B382, B39, B440, B441 with asterix code J172 Dagger codes: B583, B65, B778 with asterix code J173 Dagger codes: A698, A70, A78, I00 with asterix code J178	480, 481, 482, 483, 484, 485, 486, 487, 513.0, 514.9 Dagger codes: 002.0, 003.2, 039.1, 052.9, 083.0, 104.8, 127.0, 130.9 with asterix code 484.8 Dagger code 390.9 with Asterix code 517.1 Dagger code 022.1 with asterix code 484.5 Dagger code 021.9 with asterix code 484.4 Dagger code 033 with asterix code	Any admission date before COPD diagnosis in primary care (with 10 year look back from date of diagnosis)

			484.3 Dagger code 078.5 with asterix code 484.1 Dagger code 055.1 with asterix code 484.0 Dagger code 056.7 with asterix code 480.8 Dagger code 117.3 with asterix code 484.6 Dagger codes 112.4, 114.9, 115 with asterix code 484.7 Dagger code 073 with asterix code 484.2	
Respiratory failure	Any	J96	799.1	Any admission date before COPD diagnosis in primary care (10 year look back from date of diagnosis)
Cor pulmonale	Any	I27.9	416.9	Any admission date before COPD diagnosis in primary care (with 10 year look back from date of diagnosis)
Cancer	All	Tumour site ICD10	Tumour site ICD9	Any date of incidence before COPD diagnosis in primary care (with 10 year look back from date of diagnosis)

Table A3: Read codes, data sources and definitions for covariates derived from primary care data

Covariate		Read Code	Other source	Definition
Body mass index		22A* 229* 22K*	Height, weight in screening events table and patient management table; height, weight, BMI in care management table. Spirometry database	Closest to baseline and before censoring date. Where BMI has been calculated from height and weight, the earliest height recorded has been used with the weight closest to baseline
% predicted forced expiratory volume		339a. 339O. 339S.	Care management table Spirometry database	Closest FEV1% predicted to baseline recorded before censoring date. Where FEV1% predicted has been calculated the height used is the earliest recorded height, with FEV1 closest to baseline
Smoking status	Current	67H6. 8H7i. 8HkQ. 8HTK. 9N2k. 745H. 745H0 745H1 745H2 745H4 8B2B. 8B3f. 13p.. 13p0. 13p1. 13p2. 13p3. 13p4. 13p5. 137g. 1372. 1376. 137a. 137b. 137c. 137d. 137e. 137f. 137h. 137.. 137C. 137D. 137E. 137G. 137H. 137J. 137M. 137P. 137Q. 137R. 137V. 137X. 137Y. 137Z. 9N4M.	Smoking cessation therapy prescription Spirometry database	Any evidence of smoking since date of diagnosis (Read code, prescription of smoking cessation drug, specific smoking cessation advice codes)
	Not current/ex	137K. 137L. 137T. 1377. 1379. 137A. 137B. 137F. 137j. 137I. 137N. 137O. 137S.	Spirometry database	Ex-smoker codes and 'not current smoker' codes and no evidence of current smoking
	Never	1371.	Spirometry database	No evidence of smoking before or after diagnosis AND 'Never smoked Read code'
Intervention for respiratory disease prior to diagnosis		BNF 3.1.1, 3.1.2, 3.1.4, 3.2		Evidence of intervention for respiratory disease more than 1 month prior to date of COPD Read code in primary care – prescription of respiratory drugs and/or GP treated exacerbation
GP treated		Oral prednisolone and		Oral prednisolone and

exacerbation	Antibiotics: amoxicillin, cefalexin, ciprofloxacin, clarithromycin, co-amoxiclav, doxycycline, erythromycin		antibiotic prescribed within 7 days of each other and more than 21 days since previous prescription
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Table A4: Associations between characteristics at diagnosis of COPD in primary care and time to first hospital admission for acute exacerbation of COPD, with and without allowance for clustering by practice. The Cox proportional hazards model accounting for clustering includes a term for practice fitted as a random effect (frailty term).

Characteristic at diagnosis of COPD in primary care	Level	Accounting for clustering*		Without accounting for clustering	
		Fully Adjusted Hazard Ratio (95% CI)	p-value	Fully Adjusted Hazard Ratio (95% CI)	p-value
Age (years)	Increase of 1 standard deviation (11.4 years)	1.30 (1.23 to 1.38)	<0.0001	1.31 (1.24 to 1.39)	<0.0001
Sex	Female	0.99 (0.90 to 1.09)	0.82	0.99 (0.90 to 1.09)	0.79
Deprivation	Quintile 1	1.00	0.003	1.00	0.0001
	Quintile 2	0.93 (0.82 to 1.06)		0.90 (0.80 to 1.01)	
	Quintile 3	0.77 (0.66 to 0.89)		0.76 (0.66 to 0.87)	
	Quintile 4	0.83 (0.71 to 0.99)		0.79 (0.68 to 0.92)	
	Quintile 5	0.80 (0.66 to 0.96)		0.74 (0.62 to 0.89)	
COPD severity (% predicted forced expiratory volume)	Mild	1.00	<0.0001	1.00	<0.0001
	Moderate	1.49 (1.22 to 1.82)		1.48 (1.21 to 1.80)	
	Severe	2.58 (2.10 to 3.16)		2.54 (2.07 to 3.11)	
	Very severe	3.51 (2.76 to 4.45)		3.45 (2.72 to 4.37)	
	Unknown	1.59 (1.26 to 1.99)		1.58 (1.26 to 1.99)	
Body mass index (kg/m ²)	Normal	1.00	<0.0001	1.00	<0.0001
	Low	1.48 (1.25 to 1.74)		1.47 (1.25 to 1.73)	
	High	0.84 (0.74 to 0.95)		0.84 (0.74 to 0.95)	
	Unknown	2.40 (2.09 to 2.75)		2.35 (2.05 to 2.69)	
Smoking status	Current smoker	1.00	<0.0001	1.00	<0.0001
	Not current smoker	0.87 (0.78 to 0.97)		0.86 (0.77 to 0.96)	
	Never smoked	0.46 (0.34 to 0.64)		0.47 (0.34 to 0.64)	
	Unknown	0.63 (0.47 to 0.84)		0.67 (0.50 to 0.89)	

Characteristic at diagnosis of COPD in primary care	Level	Accounting for clustering*		Without accounting for clustering	
		Fully Adjusted Hazard Ratio (95% CI)	p-value	Fully Adjusted Hazard Ratio (95% CI)	p-value
Asthma comorbidity		1.13 (0.98 to 1.29)	0.082	1.13 (0.99 to 1.29)	0.078
Other respiratory comorbidity		1.47 (1.26 to 1.72)	<0.0001	1.47 (1.26 to 1.72)	<0.0001
Non-respiratory comorbidity		1.37 (1.23 to 1.52)	<0.0001	1.37 (1.23 to 1.51)	<0.0001
Prior admission with COPD		1.94 (1.74 to 2.17)	<0.0001	1.95 (1.75 to 2.17)	<0.0001
Prior intervention for COPD		1.32 (1.20 to 1.46)	<0.0001	1.34 (1.21 to 1.48)	<0.0001

* Although the random effect across practices was statistically significant throughout, adjustment for practice effects made little difference to estimated hazard ratios and 95% confidence intervals. To aid with model convergence all subsequent modelling was performed without the inclusion of the practice clustering term.