

Supplementary materials

Methods

Calculation of costs and HCRU

A cost of €24.13, which included official tariffs and surcharges, was applied to all general practitioner (GP) visits regardless of the year of visit. GP visit costs were sourced from the Dépenses Assurance Maladie Inter-Régimes [DAMIR] database consisting of monthly extractions of data from the larger French National Health Insurance (€24.13 in 2014)¹ and included official tariffs and surcharges. Chronic obstructive pulmonary disease treatment costs were sourced in one of two ways: for products currently on the market, 2015 costs were sourced from the Ministry of Health's public drug database;² for products no longer on the market, costs (at the time of removal) were acquired from the Social Security health insurance database.³ In all instances, treatment costs were calculated by multiplying the product cost by the number of packs prescribed. No discounting or inflation adjustment was applied to the unit cost data. Dispensation fees have been applicable in France since January 1, 2015, and were therefore applied to the data for treatments prescribed from 2015 onwards only, without considering the number or duration of treatment lines received by a patient.

REFERENCES

1. Sherwood A, Maurel F, Colin X. Appraising The Cost Of Physician Visits And Technical Procedures In France In The Age Of Open Data. Paper presented at: ISPOR 18th Annual European Congress; 7-11 November 2015, 2015; Milan, Italy.
2. Ministère Des Affaires Sociales Et De La Santé. Base De Données Publique Des Médicaments. <http://base-donnees-publique.medicaments.gouv.fr/telechargement.php>. Accessed January 2018.
3. Sécurité Sociale: l'Assurance Maladie. Base des Médicaments et Informations Tarifaires. http://www.codage.ext.cnamts.fr/codif/bdm_it/index.php?p_site=AMELI. Accessed January 2018.

Table S1 ICD-10 codes for asthma and respiratory diseases potentially incompatible with COPD

ICD-10 codes	Detail
J45.xx	Asthma
A15.0	Tuberculosis of lung ^a , confirmed by sputum microscopy with or without culture
A15.1	Tuberculosis of lung ^a , confirmed by culture only
A15.2	Tuberculosis of lung ^a , confirmed histologically
A15.3	Tuberculosis of lung ^a , confirmed by unspecified means
A16.0	Tuberculosis of lung ^a , bacteriologically and histologically negative
A16.1	Tuberculosis of lung ^a , bacteriological and histological examination not done
A16.2	Tuberculosis of lung ^a , without mention of bacteriological or histological confirmation
E84.xx	Cystic fibrosis
G47.35	Congenital central alveolar hypoventilation syndrome
J47.xx	Bronchiectasis
J84.1	Other interstitial pulmonary diseases with fibrosis
J84.0	Alveolar and parietoalveolar conditions
J98.2	Interstitial emphysema
J98.3	Compensatory emphysema
J98.0	Diseases of bronchus, not elsewhere classified
Q31.0	Web of larynx
Q31.1	Congenital subglottic stenosis
Q31.3	Laryngocele
Q31.8	Other congenital malformations of larynx
Q32.1	Other congenital malformations of trachea
Q32.4	Other congenital malformations of bronchus
Q33.xx	Congenital malformations of lung

^aTuberculosis: bronchiectasis, fibrosis of lung, pneumonia, pneumothorax. COPD, chronic obstructive pulmonary disease; ICD-10, International Classification of Disease, 10th Edition.

Table S2 Factors potentially associated with initiation of different long-acting bronchodilator-based therapies in exploratory segmentation analysis

Cluster	Long-acting bronchodilator-based therapy	Variable	Sample	Frequency in the cluster (%)	p-value
1	LAMA+LABA	Male gender	133	72.3	0.001
1		0 exacerbations pre-index	170	92.4	0.014
2	LAMA or LABA	COPD 0 days ^a	1,791	58.4	<0.001
2		Age 50–<60 years	832	27.1	<0.001
2		Eosinophils tested - Yes	1,098	35.8	<0.001
2		Neutrophils tested - Yes	1,106	36.0	0.002
2		Age <50 years	462	15.1	0.010
2		Vascular comorbidities - Yes	293	9.5	0.013
3	LAMA+ICS or	COPD >0–500 days ^a	189	24.0	<0.001
3	LAMA+LABA+ICS	Ischemic and cardiac comorbidity - Yes	125	15.9	<0.001
3		Age ≥70 years	288	36.6	0.013
4	LABA+ICS	COPD ≥500 days ^a	1,120	36.5	<0.001
4		Female gender	1,296	42.2	<0.001
4		1 moderate exacerbation pre-index	354	11.5	<0.001
4		COPD symptoms - Yes	1,362	44.4	<0.001
4		≥2 exacerbations pre-index	84	2.7	0.012

^aDuration from first recorded ICD-10 code for COPD to index date in days. COPD, chronic obstructive pulmonary disease; ICD-10, International Classification of Disease, 10th Edition; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; LAMA, long-acting muscarinic antagonist.

Table S3 Exploratory logistic regression model comparing initiation of a particular COPD maintenance therapy over another

Variable	OR	95% CI	p-value
LABA (ref. LAMA)			
Abnormal sputum (ref: No)	0.24	0.07–0.81	0.02
Age	1.00	0.99–1.01	NS
Atopy (ref: No)	<0.001	<0.001	NS
Time interval between first recorded COPD ICD-10 code and index date (years)	1.00	0.97–1.03	NS
Cardiovascular comorbidities (ref: No)	0.97	0.71–1.33	NS
Cough (R05) (ref: No)	1.16	0.96–1.41	NS
Diabetes (ref: No)	1.45	1.12–1.89	0.005
Fatigue (ref: No)	1.01	0.77–1.33	NS
GERD (ref: No)	0.98	0.76–1.27	NS
Gender (ref: Male)	1.03	0.86–1.25	NS
Ischemic and/or cardiac comorbidities (ref: No)	0.71	0.52–0.96	0.03
Number of exacerbation	1.17	0.96–1.43	NS
Shortness of breath (ref: No)	1.63	1.22–2.16	0.0008
Wheezing (ref: No)	>999.99 ^a	<0.001	NS
LABA+ICS (ref. LAMA)			
Abnormal sputum (ref: No)	0.79	0.43–1.44	NS
Age	1.01	1.00–1.01	0.01
Atopy (ref: No)	2.25	0.25–20.34	NS
Time interval between first recorded COPD ICD-10 code and index date (years)	1.08	1.06–1.10	<0.0001
Cardiovascular comorbidities (ref: No)	0.80	0.62–1.02	NS
Cough (R05) (ref: No)	1.30	1.12–1.50	0.0006
Diabetes (ref: No)	1.16	0.95–1.43	NS
Fatigue (ref: No)	0.97	0.79–1.20	NS
GERD (ref: No)	0.79	0.65–0.96	0.02
Gender (ref: Male)	1.24	1.08–1.43	0.002
Ischemic and/or cardiac comorbidities (ref: No)	1.00	0.80–1.24	NS
Number of exacerbations	1.31	1.13–1.52	0.0004
Shortness of breath (ref: No)	0.94	0.73–1.19	NS

Triple therapy (ref. dual therapy)^b			
Abnormal sputum (ref: No)	0.40	0.18–0.88	0.02
Age	1.00	0.99–1.01	NS
Atopy (ref: No)	0.58	0.06–5.41	NS
Cardiovascular comorbidities (ref: No)	1.16	0.78–1.72	NS
Cough (R05) (ref: No)	1.55	1.20–1.99	0.0006
Diabetes (ref: No)	1.26	0.91–1.74	NS
Time interval between first recorded COPD ICD-10 code and index date (years)	1.05	1.01–1.08	0.007
Fatigue (ref: No)	1.63	1.08–2.45	0.02
GERD (ref: No)	0.91	0.66–1.25	NS
Gender (ref: Male)	1.68	1.33–2.12	<0.0001
Ischemic and/or cardiac comorbidities (ref: No)	0.73	0.54–0.98	0.04
Number of exacerbations	1.24	0.96–1.60	NS
Shortness of breath (ref: No)	0.60	0.43–0.83	0.002

^aThe OR for wheezing is very large owing to low numbers of patients experiencing this symptom; ^btriple therapy: LAMA+LABA+ICS, dual therapy: LAMA+LABA, LAMA+ICS or LABA+ICS. CI, confidence interval; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; ICD-10, International Classification of Disease, 10th Edition; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; LAMA, long-acting muscarinic antagonist; NS, non-significant; OR, odds ratio