Supplementary material

Supplementary Material 1: Methods

Box 1: Description of the educational intervention.

The educational intervention consisted of two components during a full day seminar: interactive face-to-face meetings with lectures on COPD management and clinical audits on diagnostic and prescribing behaviour. GPs were invited to participate in workshops on best practices in diagnosing COPD and interpreting spirometry tests as well as appropriate therapeutic management of COPD. This was followed by a clinical audit where GPs were informed of their performance concerning the QOC indicators on an individual level and as a group, in such a way that each GP could consider their clinical performance in comparison to other GPs. The workshop and audit were conducted at three different time-points: baseline (pre-intervention), 12 and 24 months after the audit. Furthermore, continuing professional information on the management of COPD diagnosis and management was offered through a specific application for mobile (COPD APP, version 1.0.8, freely downloadable for smartphone from Apple store or Play store).

Supplementary Table 1: Quality of care indicators with a detailed description and underlying rationale.

QOC indicator macro-categories	Description	Rationale for QOC indicator based on COPD GOLD 2017 guidelines [1]	Rationale for QOC indicator based on other sources
Diagnostic processes	COPD patients with at least one spirometry test recorded anytime in their clinical history	A spirometry test is required to correctly diagnose COPD. Regular assessment of COPD severity through spirometry tests is also essential to assess disease progression and development of complications and/or comorbidities. Decline in FEV_1 can be tracked by spirometry performed at least once a year to identify patients whose COPD is worsening quickly.	Spirometry has been repeatedly identified as the standard for detecting air-flow obstruction as the primary physiological feature of COPD and it has been recommended also in primary care [2]. However, studies suggest that 40-70% of patients diagnosed with COPD have not had diagnostic spirometry [3-5].
	COPD patients with at least one spirometry test recorded in the year prior to data collection (baseline, 12 or 24 months)		Regular spirometry is useful to monitor the course and prognosis of COPD, as well as for evaluating changes in lung function during periods of changing clinical status or in response to alterations in therapy [6[5]].
	COPD patients who are smokers or former smokers, with at least one spirometry test recorded anytime in their clinical history	Not mentioned in guidelines.	Smoking has a significant impact on the development and progression of COPD. A recent review of a statement Consensus of the National Lung Health Education Program (NLHEP) recommends spirometry in adults patients who are smokers or former smokers [6].
Preventative measures	COPD patients with BMI recorded anytime in their clinical history	Not mentioned in guidelines.	Being overweight or obese could worsen the symptoms COPD and obesity is generally associated with a reduced FEV1, especially in men [7-8]. Systematically monitoring and recording BMI could improve overall health status of COPD patients and their symptoms.
	COPD patients with smoking status recorded anytime in their clinical history	Smoking is a modifiable risk factor for COPD. Physicians should systematically identify all smokers at every visit. Therefore, a careful recording of smoking habits of patients is expected.	Targeting of current or former smokers is important, with greater numbers of smokers being confirmed with COPD. Clinical practice guidelines recommend screening all patients for tobacco use at every visit [9].
	COPD patients with documented influenza vaccination recorded in the year prior to data collection (baseline, 12 or 24 months)	Influenza vaccination can reduce serious illness in COPD patients and it is recommended for all patients with COPD. It should be offered and careful recorded by physicians.	Evidences suggest that pneumococcal and influenza vaccinations can prevent community-acquired pneumonia and acute exacerbations in COPD patients [10]. Despite the need to prevent pulmonary infections in COPD patients, vaccination coverage and awareness are low and need to be improved.
	COPD patients with pneumococcal vaccination registration in the last 4 years	Pneumococcal vaccination is recommended for COPD patients ≥65 years and those younger with significant comorbid conditions (especially cardiac diseases).	
Therapeutic processes	COPD patients with prescriptions for drugs targeting COPD recorded in the year prior to data collection (baseline,	COPD can significantly improve with targeted pharmacological therapy. Therefore all COPD patients, independently of severity, should be treated.	An Italian observational study [11], supported the regular use of COPD drugs to improve health status and prognosis among COPD patients, according to clinical guidelines and recommendations.

	12 or 24 months)		
	COPD patients with no use of ICS as monotherapy (without concomitant LABA and/ or LAMA) recorded in the year prior to data collection (baseline, 12 or 24 months)	Based on the GOLD strategy paper, ICS is proposed as an add-on maintenance treatment for COPD patients, who despite treatment with long-acting bronchodilators (LABA and/or LAMA), still have exacerbations. Therefore ICS monotherapy, are not in keeping with current guidelines.	Long-term studies of ICSs as monotherapy for patients with COPD failed to show benefit of ICS monotherapy on pulmonary function [12-14]. In line with these evidences, prescription of ICSs as monotherapy to treat COPD patients is not appropriate.
	Non-occasional use of LABA and/or LAMA (±ICS) (not having only 1 prescription) recorded in the year prior to data collection (baseline, 12 or 24 months)	Therapy with bronchodilators (±ICS) has to be administered long-term among COPD patients. Occasional utilization of these drugs is not expected.	Patients with regular drug use had higher survival than those with occasional use of COPD medications [11].
	No leukotriene receptor antagonist use recorded in the year prior to data collection (baseline, 12 or 24 months)	LTRA have not been tested adequately in COPD patients and the available evidence does not support their use.	LTRA do not currently have a defined role in the treatment of COPD. Meta-analysis suggest neither short-term nor long-term exposure of LTRA can improve lung function decline in COPD [15-16].
	High adherence to LABA and/or LAMA therapy (±ICS) (COPD patients with ≥8 packages of LABA and/or LAMA therapy (±ICS) in the last year measured on the total of COPD patients in treatment with the same respiratory drugs)	A critical point for the effectiveness of COPD pharmacological treatment is adherence, that is important to control COPD symptoms. Monitoring adherence to LABA and/or LAMA (±ICS) is therefore important to ensure effectiveness.	Despite the progressive nature of COPD and the well-known negative effects of poor adherence to prescribed treatment, the level of medication adherence in COPD patients is very low and this has a negative influence on outcomes. Risk of hospitalization or death increased by 58 and 40%, respectively, in COPD patients who were non-adherent to treatments [11-17].

Abbreviations: BMI: body mass index; COPD: chronic obstructive pulmonary disease; ICS: inhaled corticosteroids; LABA: long-acting beta agonist; LAMA: long-acting muscarinic antagonist; LTRA: leukotriene receptor antagonist.

References

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Supplementary Material: Methods

Box 2: Supplementary methods data

Covariates

Information on patient demographic characteristics such as age and gender as well as lifestyle information (e.g. cigarette smoking habits) and body mass index (BMI) were extracted. Information on influenza vaccination and anti-*Streptococcus pneumoniae* vaccination was also collected. Patient medical history was described in terms of cardiovascular disorders, metabolic diseases, nervous system disorders, gastrointestinal disorders, rheumatological diseases, diseases affecting sense organs, other disorders, all of which are described in detail in **Supplementary Material Table 2**. Drugs used for respiratory diseases were identified using the ATC codes for the following drug classes: short-acting beta agonists (SABA), long-acting beta-agonists (LABA), short-acting muscarinic agents (SAMA) and long-acting acting muscarinic agents (LAMA),inhaled corticosteroids (ICS), ICS+LABA, leukotriene receptor antagonists, xanthines, mucolytic drugs and chromones. Phosphodiesterase 4 inhibitors (PDE4i) and LAMA and LABA as fixed combinations were not prescribed in a primary care setting so their use could not be captured. Concerning other drugs of interest as potential concomitant medications, the following drug classes were identified: antibiotics, cardiovascular drugs, drugs for metabolic diseases, systemic corticosteroids, analgesics (i.e. opioids and non-steroidal anti-inflammatory drugs (NSAIDs)), psychiatric drugs (**Supplementary Material Table 3**).

Supplementary Material Table 2: ICD-9 CM codes used to identify comorbidities.

Comorbidites	ICD-9 CM codes
Anxiety	293.84; 300.0*; 300.2*; 308.0; 309.24; 309.28
Arrhythmia	427; 427.0; 427.2; 427.4*; 427.6*; 427.8*; 427.9
Arthritis and arthrosis	711*; 712*; 713*; 714*; 715*; 716*; V13.4; V17.7
Atrial fibrillation	427.3*; 99.61
Cataracts	366*
Cerebrovascular disease	429.2; 43*; 348.1; 772.2; 852*; 747.81; V12.54; 00.62; 99.10; 00.65; 004*; 997.02; V17.1
Chronic kidney disease	583*; 586*; 585*; 588.8; 587
Dementia	290; 290*; 291.2; 294.1*; 331; 331.0; 331.1*; 331.2; 331.82
Depression	296.2*; 296.3*; 296.82; 298.0; 301.12; 311; 307.44; V79.0
Diabetes mellitus	249*; 250*; 357.2; 362.0*; 366.41; 648.0*
GERD	530.81
Gout	274*; V77.5
Heart Failure	398.91; 402.01; 402.11; 402.91; 404.1; 404.3; 404.11; 404.13; 404.91; 404.93; 428*; 429.4
Hyperlipidemia	272*; 440*; 00.55; 39.50; 99.10; 39.90
Hypertension	99791; 401*; 402*; 403*; 404*; 405*
Ischemic heart disease	410*; 411*; 412*; 414*; 429.9
Liver disease	570; 571*; 572*; 573*; 751.69
Osteoporosis	7330*;733.1*; V17.81; V82.81
Parkinson's disease	332*
Peptic ulcer disease	533*; 532*; 531*; 534*; V12.71
Retinopathy	361*; 362* (362.0 excluded);
Schizophrenic disorders	295*; 297*; 298.9
Thyroid disorders	244*; 243*; 242.3*; 242.90; 2421*; 240*; 241*; 242; 2420; 242.2; 242.4; 242.8; 245*; 246*

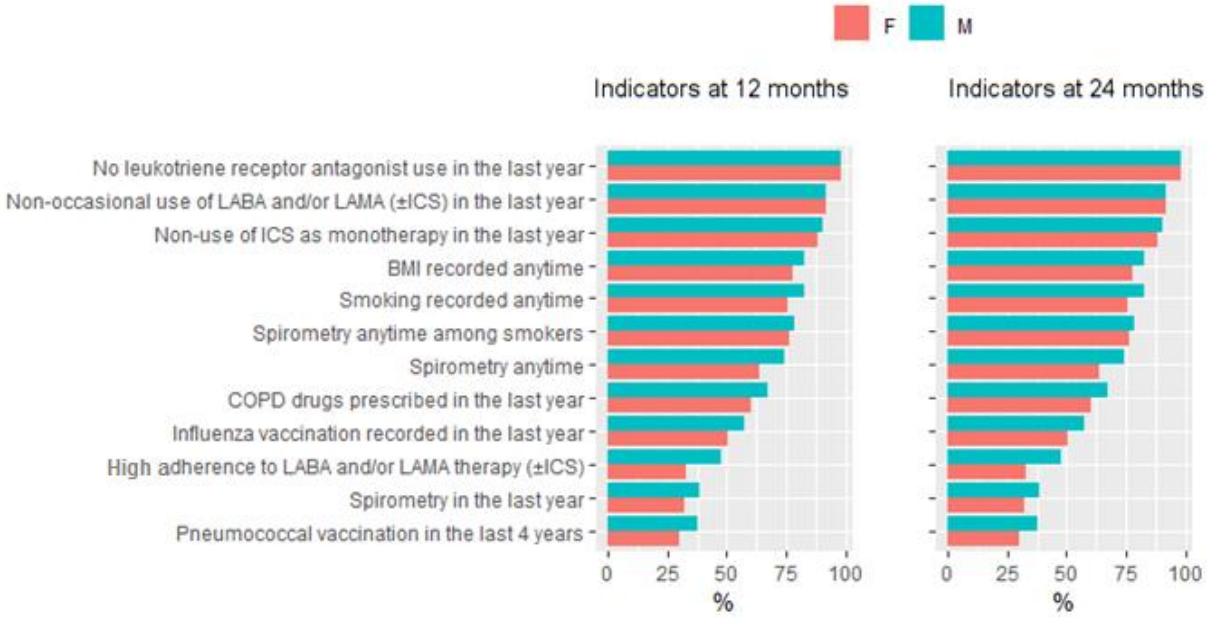
Abbreviations: ICD-9 CM: International Classification of Diseases ^ 9th revision ^ Clinical Modification; GERD: Gastro-esophageal reflux disease.

Supplementary Material Table 3: ATC codes used to identify drug utilization.

Drugs for respiratory diseases	**ATC codes**
Chromones	R03BC*
ICS	R03BA*
LABA	R03AC13; R03AC18; R03AC12; R03AC14; R03AC16; R03AC17; R03AC19
LABA/ICS, *fixed combination*	R03AK11; R03AK10; R03AK08; R03AK07; R03AK06
LABA/LAMA, *fixed combination*	R03AL03; R03AL04; R03AL05; R03AL06; R03AL07
LAMA	R03BB04; R03BB05; R03BB06; R03BB07
Leukotriene receptor antagonists	R03DC*
PDE4i	R03DX07
SABA	R03AC02; R03AC03; R03AC04
SABA/ICS, *fixed combination*	R03AK13
Xanthines	R03DA*, R03DB*
Mucolytics	R05CB*
Concomitant drugs	
ACEis	C09A*; C09B*
Anti-arrhythmics of classes I and III	C01B*
Antibiotics	J01A*; J01C*; J01DB*; J01DC*; J01DD*; J01DE*; J01F*; J01MA*
Antidepressants	N06A*
Anti-diabetics	A10*
Anti-lipidaemic drugs	C10*
Anti-osteoporosis drugs	M05BA*; M05BB*; M05BX01; M05BX03; M05BX04
Anti-thrombotics	B01AB*; B01AA03; B01AC*; B01AF*; B01AE07
ARBs	C09C*
BDZs	N05BA*
Beta-blockers	C07*
Calcium channel blockers	C08*
Corticosteroids systemic	H02A*
Digitalis glycosides	CO1AA05; CO1AA08
Diuretics	C03*
Drugs for peptic ulcer and GORD	A02B*
Immunosuppressive drugs	L04A*
NSAIDs	M01A*
Opioids	N02A*
Other anti-hypertensives	C02*
Vasodilatators	C01DA*

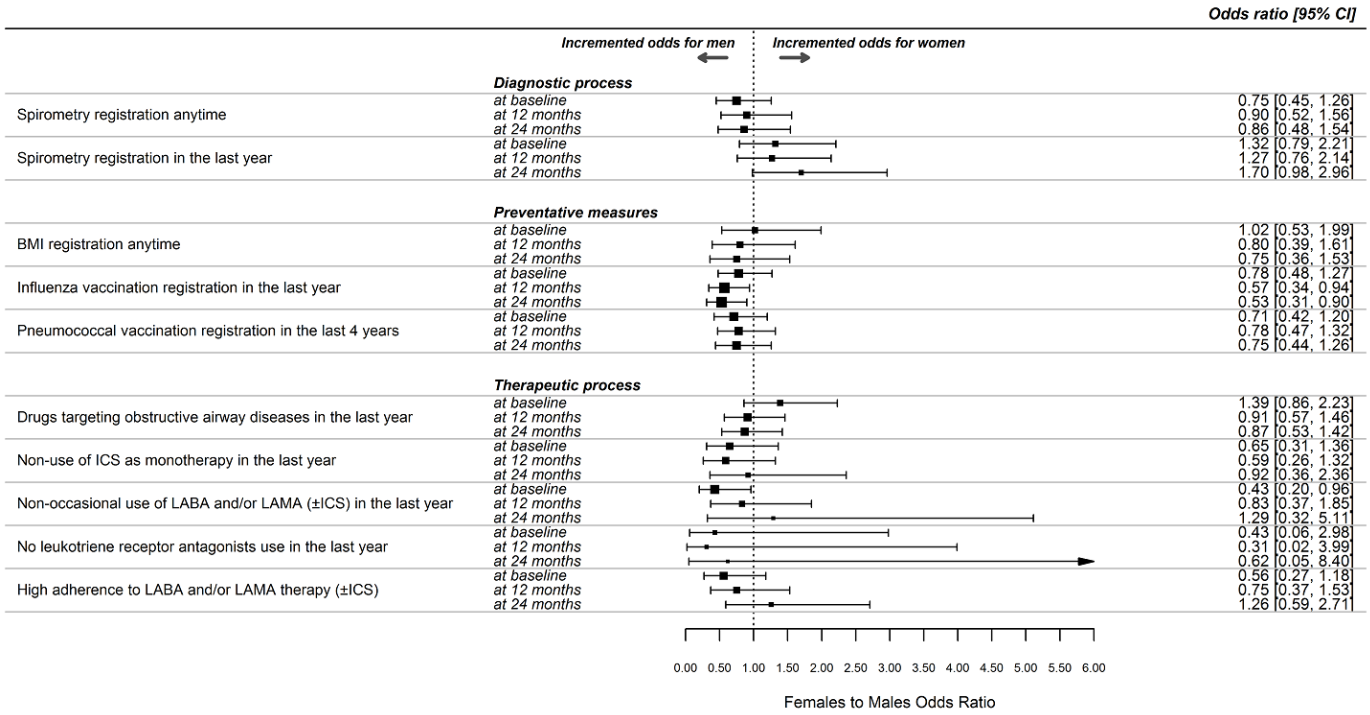
Abbreviations: ACEi: inhibitors of the activity of an angiotensin converting enzyme; ARBs: Angiotensin Receptor Blockers; ATC: Anatomical Therapeutic Chemical (drug classification system); BZDs: Benzodiazepines; GORD: Gastro-oesophageal reflux disease; ICS: Inhaled Corticosteroids; LABA: Long Acting Beta Agonist; LAMA: Long Acting Muscarinic Antagonist; NSAIDs: Nonsteroidal anti-inflammatory drugs; PDE4i: Phosphodiesterase 4 Inhibitor (roflumilast); SABA: short Acting Beta Agonist; SAMA: short Acting Muscarinic Antagonist.

Supplementary Figure 1: Gender differences in the individual quality of care indicators after the educational intervention.



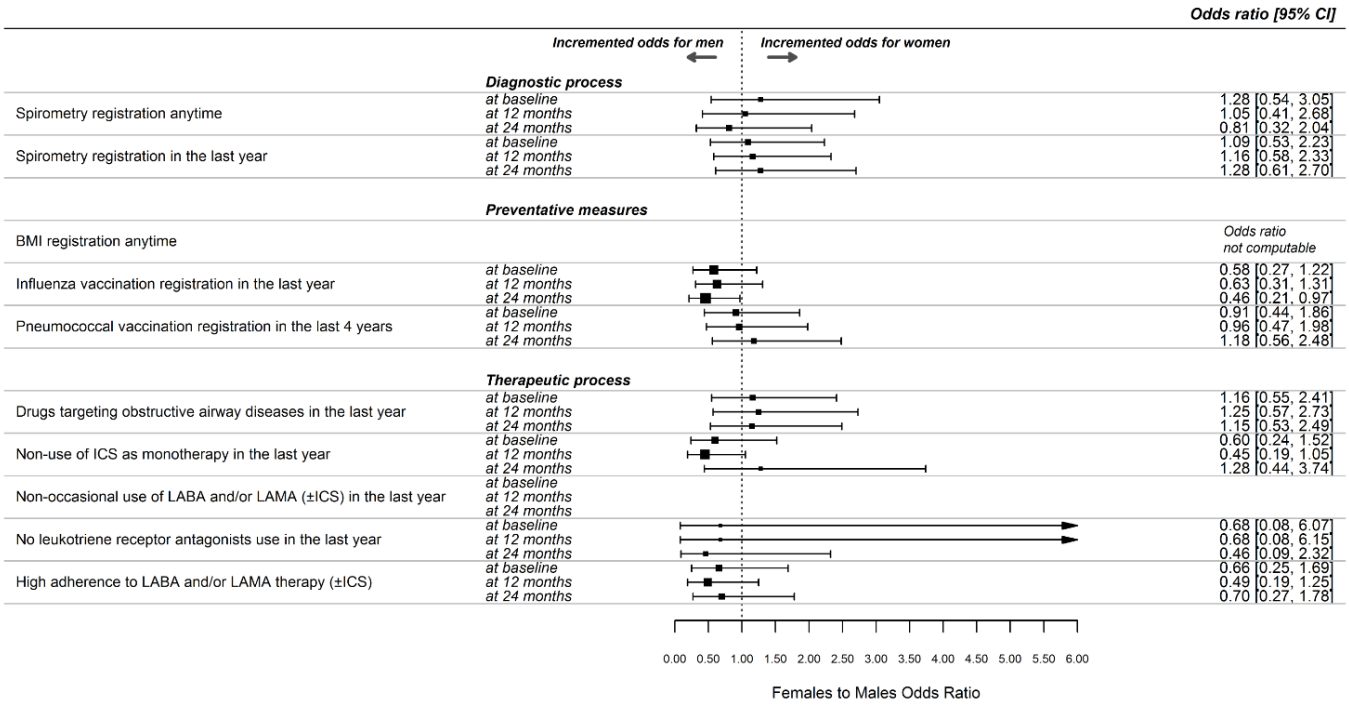
Abbreviations: BMI: body mass index; COPD: chronic obstructive pulmonary disease; F: female; ICS: inhaled corticosteroid; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic agonist; M: male; OR: odds ratio

Supplementary Figure 2. Gender differences in individual quality of care indicators before and after the educational intervention, restricted to current smokers.



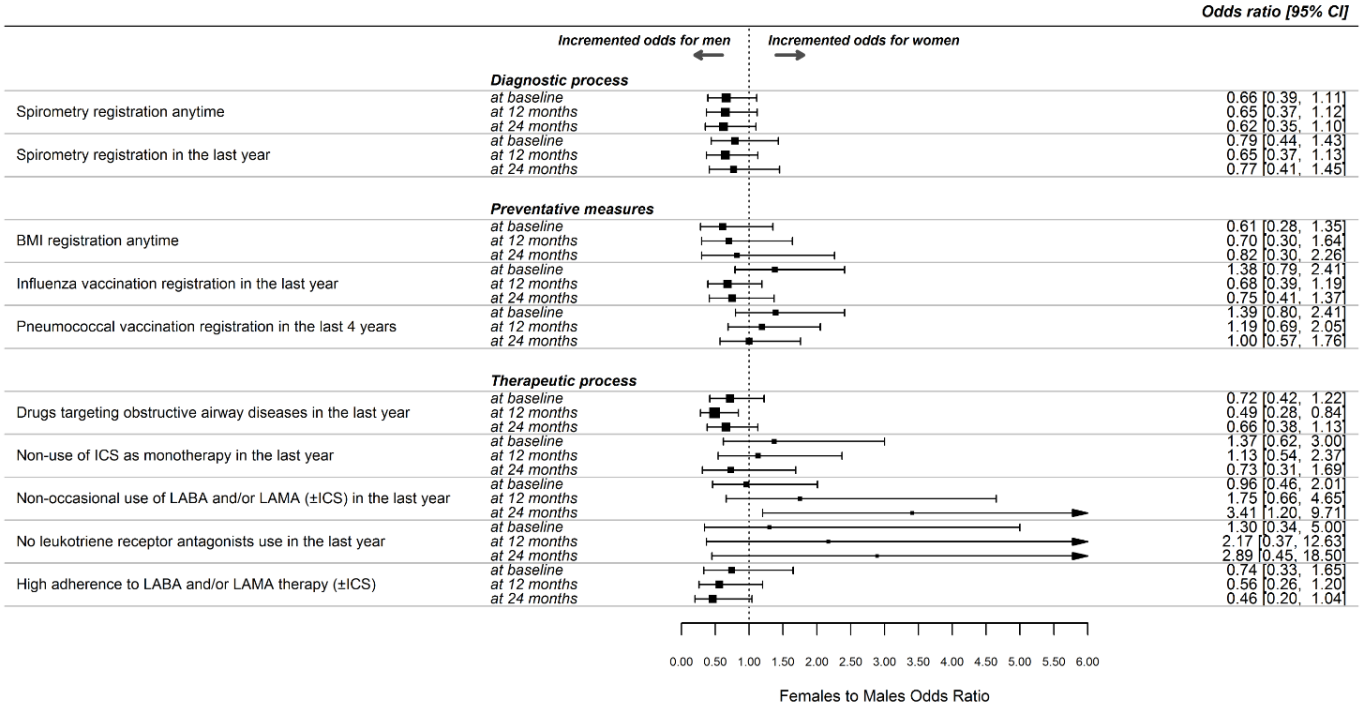
Abbreviations: BMI: body mass index; CI: confidence intervals; ICS: inhaled corticosteroid; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic agonist; OR: odds ratio

Supplementary Figure 3. Gender differences in individual quality of care indicators before and after the educational intervention, restricted to former smokers.



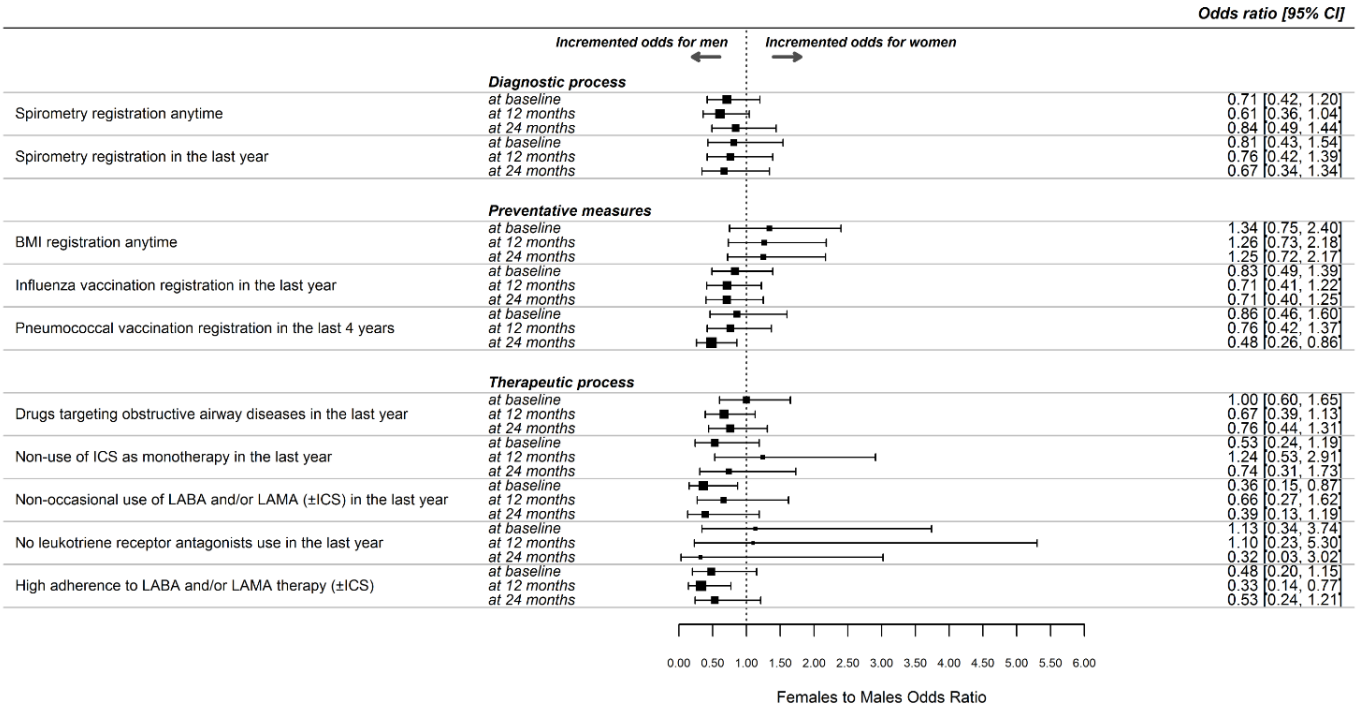
Abbreviations: BMI: body mass index; CI: confidence intervals; ICS: inhaled corticosteroid; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic agonist; OR: odds ratio. **Note**: It was not possible to estimate odds ratios for BMI registration any time and non-occasional use of LABA and/or LAMA (± ICS) in the last year due to a very low number of patients.

Supplementary Figure 4. Gender differences in individual quality of care indicators before and after the educational intervention, restricted to never smokers.



Abbreviations: BMI: body mass index; CI: confidence intervals; ICS: inhaled corticosteroid; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic agonist; OR: odds ratio

Supplementary Figure 5. Gender differences in individual quality of care indicators before and after the educational intervention, restricted to patients with no information on smoking status.



Abbreviations: BMI: body mass index; CI: confidence intervals; ICS: inhaled corticosteroid; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic agonist; OR: odds ratio