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ORIGINAL RESEARCH

Socioeconomic Status Related to Prescription of Triple Therapy and Anticholinergic Monotherapy in Patients with Chronic Obstructive Pulmonary Disease (COPD) in Sweden - A Retrospective National Registry Study

Kjell Larsson[1], Staffan Betnér[2], Barbara Fuchs[3], Lowie EGW Vanfleteren[4,5], Caroline Stridsman[6]

[1]National Institute of Environmental Medicine, Integrative Toxicology, Karolinska Institutet, Stockholm, Sweden; [2]Department of Public Health and Clinical Medicine, Northern Registry Centre, Umeå University, Umeå, Sweden; [3]Chiesi Pharma AB, Medical Affairs, Stockholm, Sweden; [4]Department of Respiratory Medicine and Allergology, COPD Center, Sahlgrenska University Hospital, Gothenburg, Sweden; [5]Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [6]Department of Public Health and Clinical Medicine, Division of Medicine/The OLIN-Unit/Sunderby hospital, Umeå University, Umeå, Sweden

Correspondence: Caroline Stridsman, Department of Public Health and Clinical Medicine, Division of Medicine/The OLIN-unit/Sunderby Sjukhus, Sjukhusvägen 10, S-971 88, Luleå, Sweden, Tel +46-920 28 44 82, Email caroline.stridsman@norrbotten.se

Purpose: There is an association between low socioeconomic status and chronic obstructive pulmonary disease (COPD), but it is not known whether this impacts on drug prescription for COPD treatment. The aim of the study was to explore whether drug prescription differs between COPD patients with low and high socioeconomic status.

Patients and methods: Data from patients with incident and prevalent COPD (age>40 years), without an asthma diagnosis, visiting primary care in 2021–2022 were extracted from The Swedish National Airway Register (SNAR) and linked to Swedish National Health registries. Socioeconomic status was assessed by educational level and annual income. Statistical analyses were conducted by means of chi square tests, together with post-hoc test.

Results: In total, 38692 patients (mean age 73.6 years, 55.5% women, FEV_1 59.5% of predicted value) were included. Subdivision into GOLD group A, B and E was possible in 29128 patients. Triple therapy (long-acting antimuscarinic antagonists, LAMA + long-acting beta-2-agonist, LABA + inhaled steroids, ICS), was more often prescribed in the low education group (observed/expected ratio 1.09; p<0.0001) and low income group (ratio 1.05; p<0.05) and less often in the high education group (ratio 0.87; p<0.0001) and high income group (ratio 0.88; p<0.0001). Monotherapy (LAMA) was more often prescribed in patients with high income (ratio 1.09; p<0.0001) and less often in patients with low income (ratio 0.93; p=0.0004). Differences between high and low education and income were driven by differences in group B.

Conclusion: Prescription patterns were associated with small, statistically significant differences, between COPD patients with low and high socioeconomic status. Triple therapy was more often prescribed to patients with low socioeconomic status, and monotherapy with LAMA more often to patients with high. The reason for this is not clear but may be caused by differences in exacerbation rate between the socioeconomic groups.

Keywords: prescription, education, income, socioeconomic status, COPD

Introduction

From a global perspective morbidity and mortality associated with chronic obstructive pulmonary disease (COPD) is increasing. The most important cause of the disease is exposure to airway irritants, mainly from tobacco smoke, but also other risk factors such as exposure to biomass fuels increase the risk of developing COPD.[1] There are data suggesting

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that low socioeconomic status, defined as lower education and income, is itself associated with increased risk of respiratory symptoms and development of COPD independent of the effect of smoking.[2,3] When assessing socioeconomic status by occupation, COPD is associated with manual occupations. This may be due to a higher prevalence of smoking in the group, as well as increased exposure to vapors, gases, dust or fumes in the industrial setting compared to non-industrial workplaces.[4] Moreover, patients with COPD who are disabled have lower health-related quality of life compared with employed individuals with the same severity of COPD.[5] In persons suffering from COPD, it seems clear that higher socioeconomic status is associated with better health outcomes and lower mortality.[6] The specific reasons for these differences are not understood. However, one possible explanation could be different prescription patterns between low and high socioeconomic status groups.

Like other healthcare systems, the Swedish system aims for equal access to care and treatment for all patients, regardless of socioeconomic status. Recent Swedish reports indicates that differences may exist and individuals with higher socioeconomic status tend to seek healthcare more often than those with lower socioeconomic status.[7] In this regard, the differences in seeking care in groups stratified by their level of education have been of the most concern.[8,9] As the risk of developing COPD is increasing in individuals with low socioeconomic status,[10,11] it is of great importance to assure that the structure of public healthcare is adjusted accordingly and that this patient group is receiving the same quality of care as patients with a more favorable socioeconomic situation. It is unclear if access to prescription medication or choice of medication by the healthcare provider varies between socioeconomic groups. This could be a contributing factor to the difference in outcome. We hypothesized that dispensation of triple therapy, ie a combination of long-acting muscarinic antagonists (LAMA), long-acting beta$_2$-agonists (LABA) and inhaled corticosteroids (ICS), is more frequently prescribed than monotherapy with LAMA in patients with high socioeconomic status.

Methods

Patient data were extracted from national registries: The Swedish National Airway Register (SNAR),[12] The longitudinal integrated database for health insurance and labour market (LISA), Statistic Sweden (SCB),[13] The National Prescribed Drug Register and the National Patient Register (The National Board of Health and Welfare).[14] The current study was approved by the Swedish Ethics Review Authority (2019–04915; 2020–00508). Informed consent is not required in Sweden when anonymized public register data is used for research.

Study Population and Design

A retrospective observational study using Swedish national registries was undertaken. The COPD cohort was defined by data obtained from SNAR and consisted of incident and prevalent patients with COPD (J44, ICD-10) aged 40 years or older. The patients had visited primary care and registered at least once in the SNAR from January 2021 to December 2022. If multiple registrations, the last registration was used as index-date. Patients with concomitant asthma (J45, ICD-10) were excluded from the study population, Figure 1.

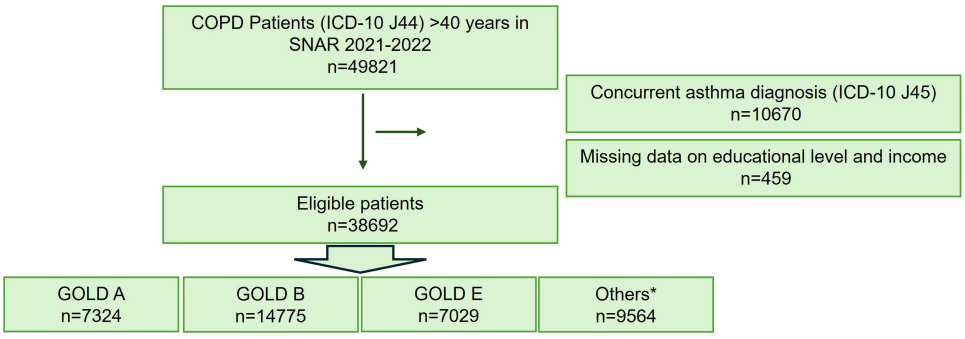

Figure 1 Flow-chart of the study population.
Notes: *Others=Patients with missing data on CAT and/or information on prescribed OCS or no hospitalization 12 months pre-index.
Abbreviations: SNAR, Swedish National Airway Register, GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Extracted data from SNAR included sex, age, Body Mass Index (BMI), smoking habits (non-smoker, ex-smoker since more than 6 months, current smoker), the COPD Assessment Test (CAT), and lung function values. Swedish reference values for lung function were used.[15,16]

Linkages of SNAR to other Swedish registers were conducted. Level of education and annual household income were extracted from The Longitudinal Integrated Database for Health Insurance and Labor Market (LISA). The level of education was divided into low (elementary school), medium (high school) and high (university education). Data on annual household annual income was divided into tertiles: low: ≤181 000 SEK (16,250 €) per year, medium:181000-≤253 000 SEK per year, and high: >253 000 SEK (22,715 €) per year.

Dispensation of pharmacological maintenance treatments were collected from The National Prescribed Drug Register in 2022; inhaler treatment both as monotherapy and separate combination of drugs (R03), cardiovascular and hypertension medication (C01, C02, C07, C08, C09), antidepressive medication (N06), and diabetes medication (A10). To define moderate and severe exacerbations, the use of oral corticosteroids (OCS; H02AB) was extracted from the National Prescribed Drug Register and respiratory hospitalization (J41-J44, J96, J12-J18 or J20-J22) was extracted from the National Patient Register 12-months pre-index date. Based on CAT and exacerbation history patients were categorized into group A (CAT <10, ≤1 non-hospitalized exacerbation last year), B (CAT ≥10, ≤1 non-hospitalized exacerbation last year) and E (≥2 exacerbation or one hospitalization due to an exacerbation last year) according to GOLD criteria.[1] Patients with missing data on CAT and/or information on prescribed OCS or no hospitalization 12 months pre-index, were labeled as "others".

Statistical Methods

The association between categorical variables was assessed using Pearson's Chi-square test. In cases where any cell in the contingency table had an expected count of less than five, p-values were calculated using Monte Carlo simulations (with 10,000 replications), ensuring robustness despite sparse data. If an overall Chi-square test yielded a statistically significant result, a post-hoc analysis was conducted to identify which specific cells contributed to the association. The statistical significance for each cell was determined using the exact approach detailed by Shan and Gerstenberger.[17] Specifically, the contingency table was collapsed into a 2×2 table for each cell of interest (comparing the observed cell count against the counts of all other cells in its row and column). Fisher's exact test was then applied to each of these 2×2 tables to generate a cell-wise p-value. The resulting set of p-values was subsequently adjusted for multiple comparisons using Hommel's method[18] to control the family-wise error rate. This adjustment procedure was chosen as it is valid for the positively associated test that arise from this type of cell-wise analysis, while being more powerful than traditional corrections like Bonferroni.[19] To quantify the direction and magnitude of each contribution, the ratio of observed to expected counts was calculated for each cell.

To confirm the robustness of the primary findings, a sensitivity analysis using log-linear (Poisson) regression was conducted. A series of models were fitted to test for potential three-way interaction between type of COPD medication, socioeconomic factors, and other variables (smoking habits and exacerbations). No three-way interactions were found to be statistically significant. The overall lack of significant higher-order interactions supported the reporting of the simpler two-way Chi-square analyses. A p-value <0.05 was considered statistically significant. All statistical analyses were conducted using R version 4.4.2.[20]

Results

Study Population

In total 38,692 patients with COPD (55.5% women) were included in the study. Mean age was 73.6 (SD 9.09) years and mean FEV_1 was 59.5% (SD 18.9) of predicted value. Full information on CAT score and exacerbation history enabled classification into GOLD groups A, B and E in 29,128 patients. For the remaining 9564 patients no group was assigned, and they were analyzed as "others". Patient data are given in Table 1.

No COPD medication was prescribed for 17.5% of the patients in GOLD A, 6.6% in group B and 5.0% in group E. Among group A and B patients who had experienced one exacerbation during the last year no medication was prescribed to 9.0% and 2.6% of the patients, respectively. Dual bronchodilatation (long-acting antimuscarinic agents,

Table 1 Patient Characteristics. Number of Patients with Percent Within Brackets Are Given if Not Otherwise Indicated

	Education			Annual Income		
	Low (N=12,853)	**Medium (N=18,559)**	**High (N=7280)**	**Low (N=12,901)**	**Medium (N=12,901)**	**High (N=12,890)**
Sex						
Man	6209 (48.3)	7944 (42.8)	3076 (42.3)	4904 (38.0)	5959 (46.2)	6366 (49.4)
Woman	6644 (51.7)	10,615 (57.2)	4204 (57.7)	7997 (62.0)	6942 (53.8)	6524 (50.6)
Age						
Years, mean (SD)	74.8 (9.16)	72.5 (9.05)	74.2 (8.76)	73.8 (9.47)	75.7 (8.42)	71.3 (8.82)
Body Mass Index (BMI)						
BMI <22	2206 (17.2)	3090 (16.6)	1319 (18.1)	2479 (19.2)	2241 (17.4)	1895 (14.7)
22 < BMI <30	6065 (47.2)	8908 (48.0)	3615 (49.7)	5772 (44.7)	6320 (49.0)	6496 (50.4)
BMI ≥30	2885 (22.4)	4226 (22.8)	1393 (19.1)	2874 (22.3)	2782 (21.6)	2848 (22.1)
Missing	1697 (13.2)	2335 (12.6)	953 (13.1)	1776 (13.8)	1558 (12.1)	1651 (12.8)
Smoking habits						
Non-smoker	1571 (12.2)	2269 (12.2)	1271 (17.5)	1480 (11.5)	1776 (13.8)	1855 (14.4)
Ex-smoker	5401 (42.0)	7935 (42.8)	3323 (45.6)	4775 (37.0)	5854 (45.4)	6030 (46.8)
Current smoker	4454 (34.7)	6593 (35.5)	1910 (26.2)	5215 (40.4)	3952 (30.6)	3790 (29.4)
Missing	1427 (11.1)	1762 (9.5)	776 (10.7)	1431 (11.1)	1319 (10.2)	1215 (9.4)
$FEV_{1\%}$ pred value						
Mean (SD)	58.4 (19.1)	59.2 (18.5)	61.9 (19.3)	57.8 (18.8)	59.2 (18.8)	61.3 (18.9)
Missing	4363 (33.9)	5730 (30.9)	2237 (30.7)	4394 (34.1)	4030 (31.2)	3906 (30.3)
COPD Assessment Test						
Mean (SD)	13.0 (6.7)	12.6 (6.8)	12.0 (6.1)	13.6 (7.3)	12.6 (6.7)	11.7 (6.1)
Missing	4480 (34.9)	5930 (32.0)	2408 (33.1)	4711 (36.5)	4099 (31.8)	4008 (31.1)
GOLD A, B, E & others						
GOLD A	2214 (17.2)	3656 (19.7)	1454 (20.0)	2047 (15.9)	2458 (19.1)	2819 (21.8)
GOLD B	4731 (36.8)	7286 (39.3)	2758 (37.9)	4932 (38.2)	4954 (38.4)	4887 (37.9)
GOLD E	2571 (20.0)	3188 (17.2)	1270 (17.4)	2438 (18.9)	2426 (18.8)	2165 (16.8)
Others	3337 (26.0)	4429 (23.9)	1798 (24.7)	3484 (27.0)	3061 (23.7)	3019 (23.4)

Abbreviations: FEV_1% pred value, Forced Expiratory Volume in one second as percent of predicted value; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

LAMA + long-acting beta-2 agonists, LABA), fixed or open combination, as the only treatment was prescribed to 19.1% in group A, to 25.7% in group B, and to 15.5% in group E. A fixed or open combination of inhaled steroids (ICS) and LABA as the only treatment was prescribed to 8.4% of the patients in group A, 7.0% of the patients in group B and 14.4% in group E. Triple therapy (LAMA + LABA + ICS) was prescribed to 17.1% of the patients in group A, 33.9% in group B and to 51.5% of the patients in group E. Among patients in group A who had not experienced an exacerbation last year 15.7% had been prescribed triple therapy and in group B, triple therapy had been prescribed to 31.5% of the patients without a history of exacerbation last year. Cardiovascular drugs were prescribed to 30,026 patients (77.6%), antidepressive medication to 11530 patients (29.8%) and diabetes medication to 8311 patients (21.5%). Pharmacological treatment for COPD (divided by GOLD group A, B and E) and treatment for other conditions stratified by level of education and income are shown in Table 2.

Gender Distribution

Based on the expected distribution of patients within the different GOLD groups there was a significant over-representation of women (ratio 1.04) and under-representation of men (ratio 0.95) in group E (p=0.001) whereas no such differences were found in group A and B. More men (ratio 1.14) and less women (ratio 0.89) than expected had no pharmacological treatment (p<0.0001). Fixed combinations of bronchodilators (LAMA + LABA) were more often prescribed than expected among men (ratio 1.05) and more seldom among women (ratio 0.96; p=0.002) and there was

Table 2 The Most Frequently Used Pharmacological Treatment for COPD (Divided by GOLD Group A, B and E) and Treatment for Other Conditions in Patients with Low, Medium and High Education and with Low, Medium and High Income. Drug Combinations Are Presented as Total Use (Drugs Given in Separate Inhalers or as Fixed Combination in One Inhaler) and Use of Fixed Combination in One Inhaler

	GOLD A					
	Education			**Income**		
	Low	**Medium**	**High**	**Low**	**Medium**	**High**
COPD medication						
No medication	357 (16.1)	648 (17.7)	274 (18.8)	349 (17.0)	431 (17.5)	499 (17.7)
LAMA monotherapy	497 (22.4)	829 (22.7)	337 (23.2)	432 (21.1)	539 (21.9)	692 (24.5)
LABA/LAMA	466 (21.1)	688 (18.8)	246 (16.9)	378 (18.5)	558 (22.6)	518 (18.4)
LABA/LAMA fixed	442 (20.0)	639 (17.5)	227 (15.6)	350 (17.1)	473 (19.2)	485 (17.2)
ICS/LABA	178 (8.0)	313 (8.5)	124 (8.5)	176 (8.6)	194 (7.9)	245 (8.7)
ICS/LABA fixed	164 (7.4)	294 (8.0)	115 (7.9)	163 (8.0)	178 (7.2)	232 (8.2)
ICS/LABA/LAMA	384 (17.4)	618 (16.9)	251 (17.3)	387 (18.9)	438 (17.9)	428 (15.2)
ICS/LABA/LAMA fixed	132 (6.0)	231 (6.3)	80 (5.5)	142 (6.9)	149 (6.1)	152 (5.4)
	GOLD B					
	Education			**Income**		
	Low	**Medium**	**High**	**Low**	**Medium**	**High**
COPD medication						
No medication	328 (6.9)	460 (6.3)	191 (6.9)	338 (6.9)	319 (6.4)	322 (6.6)
LAMA monotherapy	811 (17.1)	1258 (17.3)	528 (19.1)	797 (16.2)	847 (17.1)	953 (19.5)
LABA/LAMA	1209 (25.5)	1883 (25.9)	702 (25.5)	1254 (25.4)	1273 (25.7)	1267 (25.9)
LABA/LAMA fixed	1136 (24.0)	1767 (24.3)	659 (23.9)	1174 (23.8)	1209 (24.4)	1179 (24.1)
ICS/LABA	325 (6.9)	507 (7.0)	209 (7.6)	365 (7.4)	349 (7.1)	327 (6.7)
ICS/LABA fixed	306 (6.5)	486 (6.7)	198 (7.2)	347 (7.0)	330 (6.7)	313 (6.4)
ICS/LABA/LAMA	1658 (35.1)	2486 (34.1)	866 (31.4)	1703 (34.5)	1763 (35.5)	1544 (31.6)
ICS/LABA/LAMA fixed	892 (18.9)	1271 (17.4)	421 (15.3)	902 (18.3)	919 (18.5)	763 (15.6)
	GOLD E					
	Education			**Income**		
	Low	**Medium**	**High**	**Low**	**Medium**	**High**
COPD medication						
No medication	126 (4.9)	153 (4.8)	72 (5.7)	127 (5.2)	118 (4.9)	106 (4.9)
LAMA monotherapy	244 (9.5)	316 (9.9)	144 (11.3)	229 (9.4)	239 (9.9)	236 (10.9)
LABA/LAMA	379 (14.7)	514 (16.1)	194 (15.4)	332 (13.6)	492 (16.1)	363 (16.8)
LABA/LAMA fixed	358 (13.9)	472 (14.8)	174 (13.7)	308 (12.6)	369 (15.2)	327 (15.1)
ICS/LABA	228 (8.9)	295 (9.2)	108 (8.5)	229 (9.4)	200 (8.2)	202 (9.3)
ICS/LABA fixed	219 (8.5)	281 (8.8)	102 (8.0)	217 (8.9)	194 (8.0)	191 (8.8)
ICA/LABA/LAMA	1361 (53.0)	1629 (51.1)	626 (49.3)	1278 (52.4)	1272 (52.4)	1066 (49.3)
ICS/LABA/LAMA fixed	840 (32.7)	960 (30.1)	348 (27.4)	781 (32.0)	757 (31.2)	610 (28.2)
	All patients					
	Low	**Medium**	**High**	**Low**	**Medium**	**High**
Cardiovascular medication	10,329 (80.4)	14,242 (76.7)	5455 (74.9)	10,115 (78.4)	10,409 (80.7)	9502 (73.7)
Antidepressive medication	3827 (29.8)	5660 (30.5)	2043 (28.1)	4583 (35.5)	3739 (29.0)	3208 (24.9)
Diabetes medication	2956 (23.0)	3983 (21.5)	1372 (18.8)	2960 (22.9)	2801 (21.7)	2550 (19.8)

Note: Number of patients with percent within brackets are given.
Abbreviations: LAMA, long-acting muscarinic antagonist; LABA, long-acting beta-2-agonist; ICS, inhaled corticosteroid.

an over-representation of treatment with open triple therapy in women (ratio 1.06) and the opposite in men (ratio 0.92; p<0.0001, Table 3).

Education

The proportion of patients in group E was slightly higher in patients with low education (20.0%) than in patients with medium (17.2%) and high education (17.4%, Table 1). Fixed triple combination (LAMA/LABA/ICS) was more frequently prescribed than expected for patients with low education (ratio 1.09) and the opposite for patients with high

Table 3 Observed and Expected Proportion of Female and Male Patients with COPD Who Did Not Receive Any Pharmacological Treatment and Who Received Dual Bronchodilatation (LAMA + LABA) and Triple Therapy (LAMA + LABA + ICS). For All Other Drug or Drug Combination Treatment No Statistically Significant Differences Were Found

COPD Medication	Gender	Observed Value	Expected Value	Ratio	Adjusted p-value
No medication	Man	2249	1975	1.14	<0.0001
No medication	Woman	2187	2461	0.89	<0.0001
LAMA + LABA, fixed	Man	3245	3097	1.05	0.0016
LAMA + LABA, separate	Woman	3711	3856	0.96	0.0016
LAMA + ICS + LABA, fixed	Man	2431	2635	0.92	<0.0001
LAMA + ICS + LABA, separate	Woman	3487	3283	1.06	<0.0001

Notes: The ratio is the observed count divided by the expected count. Adjusted p-values are from cell-wise Fisher's Exact Tests, corrected for multiple comparisons using Hommel's method.
Abbreviations: LAMA, long-acting muscarinic antagonist; LABA, long-acting beta-2-agonist; ICS, inhaled corticosteroid.

Table 4 In the Table Prescription of COPD Medication Related to Educational Level and Income Is Presented Among All Patients and in GOLD Group B Patients Where Statistically Significant Differences Were Found. Among Patients in Group A and E Prescription Did Not Differ Statistically Significant Between Different Education or Income Levels (Data Not Presented)

	COPD Medication	Education	Observed Value	Expected Value	Ratio	P-value
Education, all patients	Triple therapy, fixed	Low	2193	2010	1.09	<0.0001
		High	986	1138	0.87	<0.0001
Education, group B	Triple therapy, fixed	High	421	482	0.87	0.0250
	COPD medication	**Income**	**Observed value**	**Expected value**	**Ratio**	**P-value**
Income, all patients	LAMA only	High	2398	2203	1.09	<0.0001
		Low	2053	2205	0.93	0.0004
	Triple therapy, fixed	High	1782	2016	0.88	<0.0001
		Medium	2141	2017	1.06	0.0081
		Low	2127	2017	1.05	0.0365
Income, group B	LAMA only	High	953	859	1.11	<0.0006
		Low	797	867	0.92	0.0476
	Triple therapy, fixed	High	763	855	0.89	<0.0009

Notes: Low income ≤181 000 SEK per year, medium income 181000 to ≤253 000 SEK per year, high income >253 000 SEK per year. LAMA: long-acting muscarinic antagonist. Triple therapy: LAMA + LABA: long-acting beta-2-agonist + ICS: inhaled corticosteroid. The ratio is the observed count divided by the expected count. Adjusted p-values are from cell-wise Fisher's Exact Tests, corrected for multiple comparisons using Hommel's method.
Abbreviations: Low education, elementary school; high education, university education.

education (ratio 0.87; p<0.0001 for both, Table 4). In group A and group E and in "Others" prescription of drugs and combination of drugs did not differ from what was expected, neither in patients with low, medium nor high education. In group B triple therapy was less often than expected prescribed in patients with high education (ratio 0.87; p=0.0250, Table 4).

Income

The proportion of patients in group E was slightly lower in patients with high income (16.8%) than in patients with medium (18.8%) and low (18.9%) income (Table 1). LAMA as monotherapy was more frequently prescribed among patients with high income (ratio 1.09; p<0.0001) and less frequently prescribed among patients with low income (ratio 0.93; p=0.0004, Table 4). Triple therapy was less often prescribed than expected in patients with high income (ratio 0.88; p<0.0001) and more often in patients with medium (ratio 1.06; p=0.0081) and low (ratio 1.05; p=0.0365) income (Table 4). In group A and group E and in "Others" prescription of drugs and combination of drugs did not differ from what was expected in patients with low, medium and high income. In group B monotherapy with LAMA was more often prescribed than expected among high income (ratio 1.11, p<0.0006) and less often than expected among patients with low income (ratio 0.92, p=0.0476, Table 4). In group B fixed combinations of triple therapy were less frequently prescribed than expected in patients with high income (ratio 0.89, p=0.0009, Table 4).

Discussion

In the present study small, but statistically significant, differences in prescription pattern related to socioeconomic factors were demonstrated. Thus, fixed triple therapy was more often prescribed than expected to patients with low socioeconomic status whereas monotherapy with LAMA was more often prescribed to patients with high socioeconomic status as reflected by education and income. Due to the reimbursement system in Sweden, there is a ceiling for the patients costs of drugs which imply that most patients can afford to collect prescribed drugs from the pharmacy. In addition, the cost does not differ much between different drugs and drug combinations used for treatment of COPD. In conclusion, this implies that economic and other socioeconomic factors such as education and annual income do not seem to influence much on how prescribed inhaled therapy in COPD is chosen in Sweden. Interestingly, it was found that prescription of fixed triple therapy was more often observed than expected in patients with low education and medium and low income whereas the opposite was found in patients with high education and high income. In addition, monotherapy with LAMA was more often prescribed than expected in patients with high income and less often in patients with low income. The reason for this is not clear but severity of the disease may have been of importance. It could not be excluded that a higher exacerbation rate in patients with low socioeconomic status may contribute to the higher prescription of triple therapy in that group. A slightly lower prevalence of exacerbations in patients with a higher socioeconomic status implies treatment with bronchodilators, e g monotherapy with LAMA, rather than inhaled steroids. The slightly higher prevalence of exacerbations in patients with low income and low education may be a contributing factor to these differences in prescription pattern.

Our results did not confirm the findings of Töttenborg et al[21] who showed that COPD outpatients with high educational level were more likely to receive high standard care. In another Danish study it was demonstrated that low income and low education, among other factors, were associated with poor or non- adherence to prescribed pharmacologic treatment and to increased exacerbation rate and mortality in patients with COPD.[22] This may indicate a difference from the results of the present study in which triple therapy was more often observed in patients with low socioeconomic status and that monotherapy with LAMA more often is observed in patients with high socioeconomic status. However, in the present observational study clinical outcomes and adherence to treatment were not assessed, indicating that firm clinical conclusions could not be drawn from the differences in prescription pattern.

An intriguing observation was that prescription of pharmacological treatment, both monotherapy and drug combinations, at the different educational levels and annual income did not differ from the expected prescription in group A and E whereas there were prescription differences in group B in that regard. In patients with minor symptoms and few exacerbations (group A) and in patients with frequent exacerbations (group E) the choice for drug treatment is often more

obvious. In patients with a more complex clinical picture with frequent symptoms which are not always easy to classify as exacerbations, ie patients in group B, the choice of prescription may not be as clear as it is in group A and E.

In Sweden the mortality due to COPD has steadily decreased among men during the last 25 years while, during that time, an increased mortality has been observed in women. The mortality due to COPD is thus higher among women than among men in Sweden since the last 15 years.[23] It has been shown that the mortality and readmission to hospital after a severe exacerbation is higher in patients with low socioeconomic status[24] and that mortality decreases slower over time in patients with low socioeconomic status.[6] Recent data support that not only individual but also neighborhood socioeconomic status is of importance for the mortality in COPD.[25,26] A close relationship between exacerbations and mortality in COPD is well established. In the present study 11.6% of patients in group A and 16.3% of patients in group B experienced one exacerbation throughout the last year while the remaining patients in group A and B were free from exacerbations. We found a clear over-representation of women in group E indicating that frequent exacerbations are more common in women than in men in Sweden. The findings may indicate that COPD would more severely affect women than men. These findings are in accordance with the finding that women were more often than expected treated with triple therapy which includes inhaled steroids and that men more often than expected did not receive any pharmacological treatment for their disease. Also, the over-representation of men being prescribed dual bronchodilation indicates that treatment of COPD in men may be more guided by symptoms, mainly dyspnea, while treatment in women is more focused on preventing exacerbations.

Prescription of COPD medication was twice as common in group A patients who had experienced an exacerbation last year compared with those who were free from exacerbations, and prescription of bronchodilators was similar in group A and B patients with and without a history of exacerbations. Furthermore, triple therapy was more often prescribed to group B patients with a history of exacerbation than group B patients without exacerbations. These results indicate that symptoms seem important for prescription of bronchodilators and that exacerbations are important for the decision to add ICS to the treatment.

More than one patient out of four were treated with drugs for cardiovascular diseases and/or hypertension. The prescription of cardiovascular drugs was similar in group A and B and slightly higher in group E. Lung function was similar in group A, B, E and "Others" (FEV_1 55.6–62.7% of predicted value) implicating that most patients were in stage 2 according to GOLD. This confirms earlier findings that cardiovascular comorbidities and events are common in mild and moderate COPD.[27–30]

The strength of the study is the large national sample based on extensive registry data including all patients visiting the included primary healthcare centers during the years 2021 and 2022. The data does not allow conclusions about clinical implications or adherence to prescribed treatment which are limitations of the study. Thus, future research on adherence to COPD medication in relation to socioeconomic status is needed. Although not crucial for the interpretation of the results, other limitations are missing data on FEV_1% of predicted value (32%) and CAT-scores (35%).

In conclusion, from previous Swedish studies it is known that patients with COPD have a lower socioeconomic status than matched patients with other diagnoses.[31] In the present study we found small, but statistically significant, differences in prescription pattern associated with socioeconomic status. There was a difference in prescription pattern with fixed triple treatment, which was more often prescribed to patients with low socioeconomic status and monotherapy with LAMA more often prescribed to patients with high socioeconomic status. To reach maximal health equity it is of importance that current guidelines for treatment of COPD are followed and that treatment is prescribed irrespective of socioeconomic status.

Abbreviations

COPD, chronic obstructive pulmonary disease; CAT, COPD assessment test; BMI, body mass index; FEV_1, forced expiratory volume in one second; LAMA, long-acting antimuscarinic agents; LABA, long-acting beta-2 agonists; ICS, inhaled steroids; SNAR, the Swedish national airway register; LISA, the longitudinal integrated database for health insurance and labour market.

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Disclosure

KL has, during the last five years, on one or more occasion served in an advisory board and/or served as speaker and/or participated in education arranged by AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis and Sanofi. BF is current employee at Chiesi Pharma AB. LEGWV reports grants from AstraZeneca and personal fees for lectures and/or advisory board work from AstraZeneca, GSK, Novartis, Boehringer, Pulmonx, Grifols, Sanofi, and Chiesi. CS reports personal fees from AstraZeneca and GSK, and institutional fees from Chiesi and TEVA, outside the submitted work. The authors report no other conflicts of interest in this work.

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