Healthcare costs of patients with chronic obstructive pulmonary disease in Denmark – specialist care versus GP care only

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Abstract
Background: Many patients with chronic obstructive pulmonary disease (COPD) are treated in general practice only and have never received specialist care for COPD. They are seldom included in COPD cost studies but may account for a substantial proportion of the total costs.
Objective: To estimate and specify the total healthcare costs of patients who are treated for COPD in Denmark comparing those who have- and have not had specialist care for COPD.
Setting: Denmark, population 5.7 million citizens.
Methods: Via national registers, we specified the total healthcare costs of all +30-years-old current users of respiratory pharmaceuticals. We identified the patients with COPD and compared those with at least one episode of pulmonary specialist care to those with GP care only.
Results: Among totally 329,428 users of respiratory drugs, we identified 46,084 with specialist-care- and 68,471 with GP-care-only COPD. GP-care-only accounted for 40% of the two populations’ total healthcare costs. The age- and gender-adjusted coefficient relating the individual total costs specialist-care versus GP-care-only was 2.19. The individual costs ranged widely and overlapped considerably (p25-75: specialist-care €2,175—€12,625, GP-care-only €1,110—€4,350). Hospital treatment accounted for most of the total cost (specialist-care 78%, GP-care-only 62%; coefficient 2.81), pharmaceuticals (specialist-care 16%, GP-care-only 27%; coefficient 1.28), and primary care costs (specialist-care 6%, GP-care-only 11%; coefficient 1.13). The total costs of primary care pulmonary specialists were negligible.
Conclusion: Healthcare policy makers should consider the substantial volume of patients who are treated for COPD in general practice only and do not appear in specialist statistics.
Keywords: COPD, Cost of illness, Public health, Primary care, Epidemiology

Background
In developed countries, chronic obstructive pulmonary disease (COPD) is among the diseases that poses the highest economic burdens on the healthcare systems [1]. In Denmark, around 10% of all adults above 30 years of age have COPD [2, 3]. The COPD-specific healthcare costs include costs for hospital admissions mostly for exacerbations, outpatient follow-up visits for COPD, pharmaceuticals for COPD, and COPD-specific services by general practitioners (GPs) and primary care specialists in internal- (including pulmonary) medicine. However, COPD is associated with increased risk of developing almost all other diseases and many COPD-related healthcare costs regard treatment of comorbidities [4–6]. Therefore, estimates of COPD-related costs usually include all excess costs that COPD-patients have
compared to otherwise comparable individuals without COPD. Some COPD cost studies are based on small clinically examined or questionnaire surveyed populations [7–9], while the majority are register-based [4–6, 10–15]. A common problem for the register-based studies is that treatment for COPD in general practice is poorly recorded in the registers. As a result, studies fail to account for the costs of patients who are only treated for COPD in general practice and do not appear in specialist statistics. These patients tend to be falsely included in the non-COPD comparator group biasing cost estimates.

Knowing their volume and specified costs is important to healthcare planners and economists when allocating resources, budgeting, and organizing the health care systems.

In Denmark, virtually all subjects are listed with a general practice, being the primary caregiver for COPD. Specialist care for COPD requires a referral from the GP [16]. There are negligibly few pulmonary specialists working outside the hospitals. Family medicine is a medical specialty equal to all other most highly ranked medical specialties in terms of duration of training, level of courses and other authorization requirements.

This study aims to estimate and specify the total healthcare costs for patients who are treated for COPD in Denmark comparing those who have- and have not had pulmonary specialist care for COPD.

**Methods**

**Design**

Register-based nation-wide cohort study.

**Setting and data material**

Denmark is a north European country with 5.7 million citizens, each with a unique identification number allowing linkage between national registers. The tax-funded public healthcare system provides almost all primary- and secondary care services free of charge. Outpatients' pharmaceutical expenses are substantially reimbursed. The Danish National Prescription Registry keeps record of all fillings of prescriptions including the pharmaceutical's Anatomical Therapeutic Chemical code (ATC) and the price of the purchase [17]. The National Patient Registry (NPR) contains information on all in- and outpatient visits to the few small private- and the many large public hospitals, diagnosis coded using the International Classification of Diseases 10th revision (ICD-10) [18]. The Danish National Health Service Registry contains information on the type and cost of each service provided in primary care, except for few services paid privately or by privately held health insurances [19].

**Population**

In the Danish population, we identified all patients aged 30 years and above who redeemed a prescription for a drug for obstructive lung disease (ATC R03) during year 2015 or 2016. This cohort was subsequently split into four mutually exclusive populations (Table 1):

1) Specialist-care: Patients who had had at least one episode of pulmonary specialist care for COPD were identified in NPR as those who during the past five years had at least one episode of in- or outpatient care in any Danish hospital diagnosis coded with ICD-10 code DJ44 or subgroups (COPD) as primary diagnosis or secondary to J13-18 (pneumonia) or J96 (respiratory insufficiency). The Danish Register of COPD uses this validated algorithm [18, 20].

2) GP-care-only: Patients who were treated for COPD in general practice and had had no pulmonary specialist treatment for COPD were identified among the remaining patients as those who on at least two different dates during the years 2015 and 2016 had redeemed a prescription with indication code 379 or 464 (COPD) or on a pharmaceutical with ATC code R03AC18, R03AC19, R03AL02-06, R03BB84-

### Table 1  Total health care costs in Denmark year 2016 of all patients ≥ 30 years of age treated for obstructive lung disease

| Patient population: | Means of identification | No. Pts n (%) | Total costs in 1000 € (% | Costs / pt. yr. in € | Coefficient age & sex adjusted |
|---------------------|-------------------------|---------------|-------------------------|---------------------|--------------------------------|
| Specialist care COPD| COPD diagnosis code < 5 yrs | 46,084 (14)  | 506,909 (34)  | 11,605               | 2.19                           |
| GP-care-only COPD   | Prescription of LAMA or with indication code = COPD | 68,471 (21)  | 344,958 (23)  | 5,117               | 1 reference                    |
| GP care LABA (Asthma or COPD) | Prescription of LABA or ICS/LABA | 116,757 (35) | 317,589 (21)  | 2,736               | 0.70                           |
| GP care other R03 (Asthma or COPD) | Prescription of other ATC R03 drugs | 98,116 (30)  | 339,421 (22)  | 3,482               | 0.83                           |

All included patients fulfilled a prescription on a drug for obstructive lung disease (anatomical therapeutic chemical code R03) in year 2015 or 2016

LAMA Long-acting muscarinic antagonist, LABA Long-acting beta-2-agonist, ICS Inhaled corticosteroid, COPD Chronic obstructive pulmonary disease

The patient populations are hierarchically exclusive of each other. The coefficients are relative per patient costs compared to GP-care-only COPD
07, or R03DX07 (long-acting muscarinic antagonists (LAMA) in 2016 in Denmark, approved only for treatment of COPD). The Danish Register of Chronic Diseases (RUKS) uses this algorithm to identify COPD outside hospitals [21], except that to increase the specificity of the algorithm opposed to RUKS we required two separate redemptions.

3) GP care LABA (Asthma or COPD): Remaining patients who at least twice had redeemed a prescription on long-acting beta-2-agonist (LABA) alone or in combination with inhaled corticosteroids (ICS/LABA).

4) GP care other R03 (Asthma or COPD): Remaining patients who at least twice had redeemed a prescription on any respiratory drug (ATCR03) being the same or two different drugs.

We excluded patients who only redeemed a prescription on ATCR03 on one date during year 2015–2016 or had cystic fibrosis (ICD-10 code DE84 or at least two different redemption dates of prescriptions with indication code 369 or 433 or ATC code R05CB13 (Dornase alfa)).

Calculation of costs

We included all the secondary care, primary care, and pharmaceutical costs of the patients in 2016 not requiring any direct link to COPD. We did not include the municipalities’ costs of nursing and rehabilitation, and any indirect costs e.g., welfare expenses and income lost due to sick leave. The secondary care costs were calculated based on the patients’ individual data in the NPR using diagnosis-related-group (DRG) tariffs updated on an annual basis. All in- and outpatient hospital services were included. The primary care costs were based on the Danish National Health Service Registry, including services rendered by GPs, primary care specialist physicians, physiotherapists, chiropractors, psychologists, dentists, and foot therapists. The pharmaceutical costs were based on the retail price of each purchased drug including the dispensing costs.

Analyses

The total and age- and sex-adjusted individual costs were compared across all four groups, but in the following specified analyses, in order to secure a high specificity of the COPD diagnoses in general practice, only population 2) GP-care-only was compared to population 1) specialist-care.

The secondary care costs were divided into the major ICD-10 diagnosis groups based on the primary diagnosis of each episode of care, the primary care costs into the different provider types, and the pharmaceutical costs into the major ATC groups. For each type of cost, the costs per patient year were compared between the two COPD populations. The reported age- and sex-adjusted coefficients indicate the relative difference in annual cost per patient between specialist-care and GP-care-only patients. In the calculations of costs per patient year, each patient only contributed with their time being alive and resident in Denmark.

A sensitivity analysis was conducted expanding the GP-care-only COPD population to also include the patients in population 3) and 4).

All analyses were performed using STATA 14.0 (StataCorp, College Station, TX, USA).

Results

We identified 329,428 users of respiratory drugs, among those 46,084 with specialist-care- and 68,471 with GP-care-only COPD. The total health care costs for patients with specialist-care or GP-care-only COPD were €852 million corresponding to €7,436 per patient per year. GP-care-only comprised 60% of the COPD population and accounted for 40% of the total costs. In the GP-care-only population 81% were included due to use of LAMA and 19% used another ATCR03 pharmaceutical specifically targeted at COPD (data not shown). Many users of respiratory drugs did not fulfil our GP-care-only criteria and were thus not included in the specified comparing analyses (Table 1).

The individual annual costs varied widely (p25-50–75: primary-care-only €1,110–€2,100–€4,350 and secondary care €2,175–€5,050–€12,625) (Fig. 1). In both groups, most costs regarded a large proportion of patients with relatively low individual costs (Fig. 2). The cost distribution curves in Fig. 1 were highly skewed and peaked around €1250 per patient year for GP-care-only patients and €1750 for specialist care patients while the mean costs per patient year were €5,117 versus €11,605 (Table 1 and Fig. 1).

Adjusted for differences in sex and age, the total costs per patient year were 2.19 times higher if the patient had been treated in specialist care compared to GP-care-only; costs for hospital services were 2.81 times higher, pharmaceuticals 1.28 times higher, and primary care services 1.13 times higher. In the sensitivity analysis expanding the GP-care-only population to include also population 3) and 4), the adjusted total cost ratio between specialist-care and GP-care-only was 2.58.

The highest total costs were for hospital services, followed by pharmaceuticals, and primary care services. The costs for hospital services were primarily for respiratory diseases, cardiovascular diseases, and cancers. Except for pregnancy- and birth related conditions, the adjusted costs in all ICD-10 diagnosis groups were higher
if the patient had been treated in specialist care compared to GP-care-only (Table 2).

The distribution of pharmaceutical costs on ATC-groups varied little between specialist-care and GP-care-only. More than half of the pharmaceutical costs were for respiratory drugs (Table 3).

Most primary care costs were for services in general practice. Compared to GP-care-only patients, specialist care patients had 2.57 times higher per patient costs for general practitioner home visits in daytime and 3.3 times after hours. Also, specialist care patients had higher costs for all other types of GP services and for physiotherapists, psychologists, and foot therapists, but lower cost for all types of primary care specialist physicians, chiropractors, and dentists. The costs of primary care pulmonary specialists were negligible as they only account for a (not distinguishable) share of the very low total costs of all services provided by primary care specialists in internal medicine (Table 4).
Discussion

We found that at least 60% of all patients who are treated for COPD in Denmark have never been treated for COPD in pulmonary specialist care. The average individual total health care cost of a patient who have had specialist care treatment for COPD is between 2.19 and 2.58 times higher than that of a patient who have only been treated for COPD in general practice, and the range of individual costs is very wide and highly overlapping between the specialist care- and GP-care-only populations.

Specialist care patients have higher individual costs than GP-care-only for most types of pharmaceuticals and services in both primary and secondary care. It follows the intentions of the Danish health care system that severe cases are referred to specialist care and though the study lacks clinical characteristics of the patients (spirometry measures, dyspnoea score, and exacerbation frequency) our results, especially the higher costs for GP home visits, indicates a higher overall severity among specialist-care patients than GP-care-only [22]. This difference in case severity between specialist-care and GP-care-only impairs any fair comparison of costs and our findings should not lead to the unsupported conclusion that the current patients with COPD in specialist care could have been treated in general practice at a lower cost. Our intentions when comparing the GP-care-only patients’ consumption of health care resources to that of specialist-care are rather to relate the burden of disease in the two populations and explore any differences in the populations’ specified use of healthcare resources.

As confirmed by our findings, in Denmark almost all COPD treatment in primary care is delivered by the GPs. Shortly after the present study period and among other reasons to save hospital resources, the Danish Regions and the GPs agreed that the GPs should take responsibility for treating a larger proportion of the COPD population and therefore receive a capitation fee (€247 per year) replacing the previous fees for daytime consultations, telephone calls, and E-mails used in this study [23]. Notably, the GP costs in Table four sum to somewhat more than €247 because the daytime consultation costs include fees for laboratory test and other services not covered by the new capitation fee. We found that already before the new agreement, the Danish GPs were responsible for treatment of most patients with COPD, and usually without any involvement of pulmonary specialists.

Prior studies, including two from Denmark, have found that patients with COPD have three to five times higher

| COPD care level five years back: | GP care only (reference) | Specialist care at least once | Comparison |
|--------------------------------|--------------------------|------------------------------|------------|
| Primary diagnosis (ICD10 codes) registered with the costs | Cost total in 1000 € Costs / pt. year in € % Cost total in 1000 € Costs / pt. year in € % CoefAdj (95%CI) | | |
| Total (any diagnosis) | 211,725 3,141 | 100 | 395,158 9,047 | 100 | 2.81(2.81–2.81) |
| Respiratory (J*) | 23,681 351 | 11.2 | 186,975 4,281 | 47.3 | 12.0(12.0–12.0) |
| Cardiovascular (I*) | 38,021 564 | 18.0 | 40,417 925 | 10.2 | 1.58(1.58–1.58) |
| Factors and contacts (Z*) | 31,209 463 | 14.7 | 32,275 739 | 8.2 | 1.59(1.59–1.59) |
| Symptoms and findings, NEC (R*) | 16,029 238 | 7.6 | 24,608 563 | 6.2 | 2.31(2.31–2.32) |
| Neoplasm (C* & D00-D48) | 27,700 411 | 13.1 | 22,247 509 | 5.6 | 2.24(2.24–1.24) |
| Gastrointestinal (K*) | 14,376 213 | 6.8 | 16,639 381 | 4.2 | 1.76(1.76–1.76) |
| Infection (A*) | 9,106 135 | 4.3 | 15,256 349 | 3.9 | 2.45(2.45–2.45) |
| Trauma, outer causes (S*) | 10,535 156 | 6.0 | 12,170 279 | 3.1 | 1.63(1.63–1.63) |
| Musculoskeletal (M*) | 13,875 206 | 6.6 | 10,764 246 | 2.7 | 1.19(1.19–1.19) |
| Urology (N00-N51) | 6,453 96 | 3.0 | 9,559 219 | 2.4 | 2.13(2.13–2.13) |
| Endocrine metabolic (E*) | 5,529 82 | 2.6 | 7,542 173 | 1.9 | 2.00(2.00–2.00) |
| Neurological (G*) | 4,291 64 | 2.0 | 5,052 116 | 1.3 | 1.87(1.86–1.87) |
| Eyes and ears (F*) | 4,914 73 | 2.3 | 4,254 97 | 1.1 | 1.23(1.23–1.23) |
| Blood and immune (D50-D99) | 2,120 31 | 1.5 | 2,176 50 | 0.6 | 2.10(2.10–2.10) |
| Dermatological (L*) | 1,603 24 | 0.8 | 2,035 47 | 0.5 | 2.45(2.45–2.46) |
| Psychiatric (F*) | 1,293 19 | 0.6 | 2,035 47 | 0.5 | 2.45(2.45–2.46) |
| Gynaecology and Mamma (N60-N99) | 664 10 | 0.3 | 469 11 | 0.1 | 1.17(1.17–1.18) |
| Inborn or genetic (Q*) | 200 3 | 0.1 | 179 4 | 0.0 | 1.61(1.60–1.62) |
| Pregnancy and birth (O* & P*) | 94 1 | 0.0 | 19 | 0 | 0 | 0.520(0.51–0.53) |

Abbreviations: COPD Chronic obstructive pulmonary disease, CoefAdj Sex- and age-adjusted coefficient, CI Confidence interval, NEC Not elsewhere classified, Factors and contacts Factors of significance for health state, and contacts to health care services—including for example check-ups and rehabilitation after disease, and admissions with negative findings ruling out suspicion of e.g., myocardial infarction or cancer.
## Table 3  Costs of all pharmaceuticals used by patients treated for COPD in Denmark 2016

| Drug target (ATC codes) | Cost total in 1000 € | Costs / pt. year in € | % | Cost total in 1000 € | Costs / pt. year in € | % | CoefAdj (95%CI) |
|-------------------------|----------------------|----------------------|---|----------------------|----------------------|---|-----------------|
| All pharmaceuticals, total (A00-V20) | 93,208 | 1,383 | 100 | 81,942 | 1,876 | 100 | 1.28(1.28–1.28) |
| Respiratory organs (R* & V01) | 52,768 | 783 | 56.6 | 45,009 | 1,030 | 54.9 | 1.21(1.21–1.22) |
| Coagulation or blood (B*) | 5,795 | 86 | 6.2 | 6,087 | 139 | 7.4 | 1.49(1.49–1.49) |
| Neurology or psychiatry (N03-99) | 6,515 | 97 | 7.0 | 5,824 | 133 | 7.1 | 1.47(1.47–1.47) |
| Pain, muscles, joints (N00-02 & M01-09*) | 5,358 | 79 | 5.7 | 5,142 | 118 | 6.3 | 1.47(1.47–1.48) |
| Diabetes (A10) | 4,543 | 67 | 4.9 | 3,808 | 87 | 4.6 | 1.32(1.32–1.32) |
| Hypertension or heart (C00-09*) | 4,123 | 61 | 4.4 | 3,523 | 81 | 4.3 | 1.24(1.24–1.24) |
| Other digestive system (A00-16d) | 2,602 | 39 | 2.8 | 2,946 | 67 | 3.6 | 1.64(1.63–1.64) |
| Diabetes (A10) | 2,178 | 32 | 2.3 | 2,669 | 61 | 3.3 | 1.80(1.79–1.80) |
| Coagulation or blood (B*) | 1,299 | 19 | 1.4 | 1,408 | 32 | 1.7 | 1.59(1.58–1.59) |
| Neurology or psychiatry (N03-99) | 1,531 | 23 | 1.6 | 1,048 | 24 | 1.3 | 1.00(0.99–1.00) |
| Pain, muscles, joints (N00-02 & M01-09*) | 1,749 | 26 | 1.9 | 1,028 | 24 | 1.3 | 0.91(0.91–0.91) |
| Diabetes (A10) | 1,123 | 17 | 1.2 | 785 | 18 | 1.0 | 0.97(0.97–0.97) |
| Gastric acid (A02) | 716 | 11 | 0.8 | 601 | 14 | 0.7 | 1.26(1.25–1.26) |
| Female organs or hormones (G01-03) | 923 | 14 | 1.0 | 528 | 12 | 0.6 | 0.86(0.85–0.86) |
| Dermatology (D*) | 702 | 10 | 0.8 | 525 | 12 | 0.6 | 1.11(1.11–1.12) |
| Osteoporosis (M05) | 530 | 8 | 0.6 | 514 | 12 | 0.6 | 1.37(1.36–1.38) |
| Neoplasms or immune system (L*) | 309 | 5 | 0.3 | 120 | 3 | 0.1 | 0.59(0.59–0.60) |
| Others | 444 | 7 | 0.5 | 377 | 9 | 0.5 | 1.41(1.40–1.41) |

Abbreviations: COPD chronic obstructive pulmonary disease defined; R03 is the anatomical therapeutical chemical code for drugs targeting obstructive lung diseases; a excluding C05A; b excluding M05; c including C05A and excluding A02 and A10; CoefAdj Sex- and age-adjusted coefficient, CI Confidence interval

## Table 4  All-cause primary care costs of patients treated for COPD in Denmark 2016

| Primary care service | Cost total in 1000 € | Costs / pt. year in € | % | Cost total in 1000 € | Costs / pt. year in € | % | CoefAdj (95%CI) |
|----------------------|----------------------|----------------------|---|----------------------|----------------------|---|-----------------|
| Primary care total | 40,025 | 594 | 100 | 29,808 | 682 | 100 | 1.13(1.13–1.13) |
| GP total | 22,199 | 329 | 55.5 | 18,635 | 427 | 62.5 | 1.26(1.26–1.26) |
| GP daytime consultations | 17,637 | 262 | 44.1 | 12,033 | 275 | 40.4 | 1.041(1.03–1.04) |
| GP daytime home visits | 924 | 14 | 2.3 | 1,822 | 42 | 6.1 | 2.57(2.56–2.58) |
| GP daytime Emails | 879 | 13 | 2.2 | 949 | 22 | 3.2 | 1.57(1.56–1.57) |
| GP out of hours consultations | 321 | 5 | 0.8 | 291 | 7 | 1.0 | 1.48(1.48–1.49) |
| GP out of hours home visits | 383 | 6 | 1.0 | 568 | 13 | 1.9 | 2.27(2.26–2.28) |
| Internal medicine specialist | 719 | 11 | 1.8 | 1,647 | 38 | 5.5 | 3.30(3.29–3.31) |
| Ophthalmologist* | 895 | 13 | 2.2 | 364 | 8 | 1.2 | 0.66(0.66–0.66) |
| Otorhinolaryngologist* | 3,144 | 47 | 7.9 | 2,021 | 46 | 6.8 | 0.94(0.93–0.94) |
| Other specialist physicians* | 1,637 | 24 | 4.1 | 981 | 22 | 3.3 | 0.90(0.90–0.91) |
| Physiotherapist* | 1,717 | 26 | 4.4 | 949 | 22 | 3.2 | 1.57(1.56–1.57) |
| Chiropactor* | 185 | 3 | 0.5 | 77 | 2 | 0.3 | 0.68(0.67–0.68) |
| Psychologist* | 214 | 3 | 0.5 | 137 | 3 | 0.5 | 1.15(1.14–1.16) |
| Dentist* | 3,694 | 55 | 9.2 | 1,880 | 43 | 6.3 | 0.81(0.81–0.81) |
| Foot therapist* | 653 | 10 | 1.6 | 548 | 13 | 1.8 | 1.25(1.24–1.25) |

Abbreviations: COPD Chronic obstructive pulmonary disease, GP General practitioner, NA Non-applicable; the * costs are exclusive of substantial patient co-payment; CoefAdj Sex- and age-adjusted coefficient, CI Confidence interval
health care costs compared to age- and gender matched control persons without COPD [4, 5, 7, 8, 10, 15]. These studies primarily sampled COPD patients from secondary care and tended to include the GP-care-only patients in the non-COPD control group. Since GP-care-only patients cost more than non-COPD patients but less than specialist care patients, moving them from the COPD to the non-COPD group will increase the per patient costs in both groups. Thus, the potential bias in cost difference can go either way. However, the estimates of total costs become substantially lower when not including the GP-care-only patients.

Lack of spirometry data lowers the validity of the COPD diagnoses in our study. We used the RUKS’ COPD algorithm that was developed by Sundhedssdatstyrelsen [The Danish Board of Health Data] to identify patients with COPD in the national registries. The algorithm intentionally favours specificity over sensitivity. For specialist care it means that the diagnoses used to define COPD are highly specific, but some hospital treatments of COPD are falsely coded as pneumonia or other not COPD diagnoses leading the patient to be misclassified as GP-care-only or not even included in the study [18]. Also, the specificity of the COPD diagnoses in GP-care-only is high since most of the patients purchased LAMA at least twice in the inclusion period, which is a rather expensive drug specifically indicated for moderate to severe COPD. On the other hand, the sensitivity is low. More than twice the included number of patients redeemed prescriptions on pharmaceuticals for obstructive lung disease but did not fulfil the algorithm. Some of these patients probably have asthma and not COPD but, considering that we only include +30-year-olds, many of the patients most likely have COPD. A known error in the recording of indication codes probably caused some GP-care-only patients not to be included. Prescription of many respiratory pharmaceuticals are by default coded with the indication codes for asthma or bronchospasm and these default codes have been recorded in the registry even if the prescriber corrected the indication on the prescription. That is probably why the GP-care-only cohort consisted of far more LAMA- than LABA- or shortacting-beta-2-agonist users. Consequently, our comparison analyses include only 114,555 patients while the Danish COPD prevalence studies report around 320,000 Danes to have COPD, some of these though estimated to have undiagnosed COPD or be diagnosed with COPD but not pharmaceutically treated for COPD [2, 3].

Despite its known limitations, we used the RUKS’ algorithm partly to concur with the approach of Danish authorities but mostly to optimise the specificity of the COPD diagnoses, acknowledging that in general practice the COPD diagnoses may be less accurate than in specialist care. Even with this very restrictive approach we identified a large cohort of patients with GP-care-only COPD accounting for much of the total costs. RUKS provides sufficient case severity and accuracy of the COPD diagnoses to rely on the shown differences in resource allocation. For example, that patients with specialist care COPD are more likely than GP-care-only patients to use GPs and psychologists, but less likely to use primary care specialists and dentists. Intuitively, one could mistakenly assume that specialist-care patients would use the GP less often, but this is not the case. The specialist-care patients were identified via episodes of hospital care during the past five years, some of these episodes only lasting few days. However, COPD is a chronic progressive disease and therefore it is reasonable and customary to classify patients based on knowledge of prior rather than only current need for treatment. Inclusion of patients in the specialist-care COPD group based on only brief historic need for hospital treatment may explain why a substantial proportion of the specialist-care patients had lower costs of healthcare than the median of the GP-care-only patients. Also noteworthy, most likely some of the specialist-care classified patients were not directly treated by a fully trained pulmonary specialist. Our assumption that hospital-based treatment for COPD equals pulmonary specialist level is however the usual approach and our specialist care cost estimates are generally consistent with previous findings. A study based on the same Danish registries as this study estimated the total costs of healthcare for patients with COPD in specialist care during the period from 1998 to 2010. Compared to that study (and adjusted to 2016-prices) the present study found somewhat lower individual costs for pharmaceuticals (1794 € versus 1950 €) but considerably higher costs for primary- (729 € versus 564 €) and secondary health care (8717 € versus 6954 €) [10]. Another Danish study estimated the primary- and secondary care costs in 2002 and reported similarly lower costs than our estimates [5]. The differences in individual costs compared to the present study probably reflect the ongoing development of better but more complex and expensive health care services and that the prices of inhalator pharmaceuticals in Denmark have decreased. A Swedish study from 2013 found somewhat higher primary and secondary care COPD health care costs but lower costs of pharmaceuticals [4]. A Spanish study reported lower total annual costs per patient than us (€4,238 versus €7,436) maybe because of more sensitive inclusion criteria, other included type of costs or lower salaries to healthcare professionals in Spain than in Denmark [23]. Generally, comparisons to other COPD cost studies are impaired by differences in populations, health care
systems, methods et cetera. However, all studies agree that most health care costs relate to hospitalisations, often with comorbidities. Our findings are probably generalisable to other health care systems with a strong general practice sector e.g., the UK, the Netherlands, and Scandinavia.

Strengths and limitations
The cost data from Danish registries used in this study are highly complete and valid [17]. All ATCR03 and with few exceptions all other drugs are on prescription. Based on the individual patient’s purchases in the past 365 days, the national electronic prescription system calculates a partial remuneration when buying a prescribed drug. False records of purchases are unlikely since all parts of the healthcare system use the same synchronised medication platform meaning that all purchases are immediately exposed to the patient and all involved healthcare personnel. Primary and secondary care costs in the study are equal to the actual payments to the GPs and hospitals. However, the study neither covers the healthcare costs of services provided by the Danish municipalities, including nursing, prevention, and rehabilitation, nor the societal costs related to production losses and absence from work.

Implications
Our findings imply that health care planners and researchers doing population- and cost studies of COPD in countries with a strong general practice should be aware that most patients who are treated for COPD are solely treated for the disease in general practice. These patients appear frequently in the secondary healthcare system but not directly with COPD. They account for a large share of the total health care costs of patients with COPD and should not be overlooked when comparing and/or prioritizing disease-related health care resources.

Future studies should aim to further characterize and differentiate patients with COPD in different parts of the health care systems exploring the wide and overlapping range of individual costs. Healthcare professionals, politicians, and patients think, plan, agree on, and draw pyramids where the few most resource demanding COPD patients are supposed to be treated in specialist care and only milder cases in general practice [23, 24]. However, the substantial overlap of the individual costs of specialist-care and GP-care-only patients in Denmark may reflect the weaknesses of the pyramid mindset rather than the Danish healthcare systems’ inability to fit all COPD patients in the pyramid. As our specification of the costs show, multimorbidity is common among patients with COPD and most likely the main reason for the considerable overlap between the individual cost of patients in specialist- and GP care. It may be that for many patients with COPD even among the overall most resource demanding the generalist expertise and continuity of care provided in general practice is more important than specialist care.

Abbreviations
ATC: Anatomical Therapeutic Chemical; COPD: Chronic obstructive pulmonary disease; DRG: Diagnosis-related-group; GP: General Practitioner; GP-care-only: Patients who are treated for COPD in general practice and had had no specialist care for COPD; ICD-10: International Classification of Diseases 10th revision; ICS: Inhaled corticosteroid; LABA: Long-acting beta-2-agonist; LAMA: Long-acting muscarinic antagonist; NPR: National Patients Registry; RUKS: The Danish registry of chronic diseases; Specialist-care: Patients who have had treatment for COPD in specialist care.

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Authors’ contributions
JL designed the study and drafted the manuscript, MMS conducted the analyses, JBN and JS obtained the funding and the register data, all authors revised the manuscript for important intellectual content and read and approved the final manuscript.

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Availability of data and materials
All data are available from the Danish national registers. https://sundhedsdatastyrelsen.dk/da/english/health_data_and_registers.

Declarations
Ethics approval and consent to participate
All data accessed complied with relevant data protection and privacy regulations and was approved according to Danish legislation by the University of Southern Denmark’s legal services (SDU RIO ID 10.645).

Consent for publication
Not applicable.

Competing interests
JL have unpaid made research supported by AstraZeneca. The authors declare to have no further competing interests.

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