Respiratory Medicine 119 (2016) 160–167

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Socioeconomic inequalities in adherence to inhaled maintenance medications and clinical prognosis of COPD

Sandra Søgaard Tøttenborg [a, *], Peter Lange [a, b], Søren Paaske Johnsen [c], Henrik Nielsen [c], Truls Sylvan Ingebrigtsen [d], Reimar Wernich Thomsen [c]

[a] Section of Social Medicine, Department of Public Health, University of Copenhagen, Øster Farimagsgade 5, Postboks 2099, 1014 Copenhagen K, Denmark
[b] Respiratory Section, Hvidovre Hospital, Kettegård Allé 30, 2650 Hvidovre, Denmark
[c] Department of Clinical Epidemiology, Aarhus University Hospital, Olof Palmes Allé 43-45, 8200 Aarhus N, Denmark
[d] Department of Internal Medicine, Respiratory Section, Roskilde Hospital, Sygehusvej 10, 4000 Roskilde, Denmark

ARTICLE INFO

Article history:
Received 14 June 2016
Received in revised form
29 August 2016
Accepted 5 September 2016
Available online 8 September 2016

Keywords:
SES
Compliance
Proportion of days covered (PDC)
Exacerbations
Admissions
Medicine
LAMA
LABA
ICS
Registries

ABSTRACT

Background: Low socioeconomic status has been associated with adverse outcomes in chronic obstructive pulmonary disease (COPD), but population-based data are sparse. We examined the impact of education, employment, income, ethnicity, and cohabitation on the risk of suboptimal adherence to inhaled medication, exacerbations, acute admissions, and mortality among COPD patients.

Methods: Using nationwide healthcare registry data we identified 13,369 incident hospital clinic outpatients with COPD during 2008–2012. We estimated medication adherence as proportion of days covered (PDC) one year from first contact. With Poisson regression we computed adjusted relative risks (aRR) of poor adherence and non-use. With Cox regression we calculated adjusted hazard ratios (aHR) of clinical outcomes.

Results: 32% were poor adherers (PDC<0.8) and 5% non-users (PDC = 0). Analyses showed a higher risk of poor adherence among unemployed (aRR1.36, 95% CI 1.20–1.54), low income patients (aRR = 1.07, 95% CI 1.00–1.16), immigrants (aRR = 1.29, 95% CI 1.17–1.44), and patients living alone (aRR = 1.17, 95% CI 1.11–1.24). Similarly, non-use was associated with unemployment (aRR = 2.75, 95% CI 2.09–3.62), low income (aRR = 1.37, 95% CI 1.10–1.70), immigrant status (aRR = 1.56, 95% CI 1.17–2.08), and living alone (aRR = 1.53, 95% CI 1.30–1.81). Low education was associated with exacerbations (aHR = 1.21, 95% CI 1.10–1.35) and admissions (aHR = 1.22, 95% CI 1.07–1.38). Low income was associated with admissions (aHR = 1.20, 95% CI 1.09–1.32), and death (aHR = 1.11, 95% CI 0.99–1.25). The unemployed and those living alone had lower exacerbation-risk but higher mortality-risk.

Conclusions: In Denmark, health equity is a stated priority in a public health care system. Nevertheless, there are substantial socioeconomic inequalities in COPD treatment and outcomes.

1. Introduction

Low socioeconomic status (SES) is associated with a high risk of developing chronic obstructive pulmonary disease (COPD) [1]. The influence of SES on treatment success and clinical outcomes, including adherence to therapeutic management, exacerbations, admissions and mortality once the COPD has developed, is poorly understood.

Randomized trials have shown that regular treatment with inhaled maintenance medications including long-acting anti-cholinergics (LAMA), long-acting beta2-agonists (LABA), inhaled corticosteroids (ICS), and fixed-dose combinations of ICS and LABA

Abbreviations: aHR, adjusted hazard ratio; aRR, adjusted relative risk; ATC, Anatomic Therapeutic Chemical; BMI, Body Mass Index; COPD, chronic obstructive pulmonary disease; DDD, daily defined doses; DNPR, Danish National Patient Register; DPR, Danish National Prescription Registry; DrCOPD, Danish Register of COPD; FEV1%pred, forced expiratory volume in first second of expiration as percentage of predicted normal value; ICS, inhaled corticosteroids; ICS/LABA, fixed-dose combinations of ICS and LABA; LABA, long-acting beta2-agonists; LAMA, long-acting anti-cholinergics; MRC, Medical Research Council scale; PDC, proportion of days covered; SES, socioeconomic status.

* Corresponding author.
E-mail address: sato@sund.ku.dk (S.S. Tøttenborg).

http://dx.doi.org/10.1016/j.rmed.2016.09.007
0954-6111/

(ICS/LABA) reduces symptoms, decreases exacerbations, and improves quality of life [2]. Concurrently, suboptimal medication adherence has been associated with increased hospitalizations and health-care expenses [3]. Suboptimal adherence in COPD has been reported consistently, with as few as 16–39% adhering to their prescribed regiments [4–7]. Studies have shown that adherence to long term treatment in chronic illness is unequally distributed across SES with more poor adherers among patients of lower SES [8]. Few studies, however, have examined this relationship in COPD patients and with varying results: A cross-sectional study of 376 US veterans found that higher education was associated with good adherence [2], while a Danish study comprising 6590 individuals with COPD found no relationship with education [9]. Another Danish study showed an inverse association between education length and adherence [4]. The three studies used education as the only SES-indicator [2,4,9], which may not sufficiently capture SES in active professional life and retirement [10,11]. Further, the US study provided no measure of COPD severity [2], while the Danish studies predominantly included less severe patients more reliant on "rescue" medication [4,9].

While low SES has been shown to predict adverse health outcomes in the general population [12], few studies have examined this relationship in COPD. Two studies found inverse associations between income and rate of hospitalization for COPD [13,14], but used aggregate-level measures of income rather than individual income and included no information on COPD severity nor exacerbations. Lange et al. found an increased risk of exacerbations and all-cause mortality among patients with lowest education [9], but also this study relied only on education to describe SES.

Using nationwide healthcare registry data comprising detailed socioeconomic and clinical information on all COPD patients followed in Danish hospital-based outpatient clinics, we examined the associations between a range of SES indicators (education, employment, income, ethnicity, and cohabitation) with suboptimal medication adherence, exacerbation, COPD admissions, and all-cause mortality.

2. Methods

2.1. Study population

We used data from the ongoing Danish Register of COPD (DrCOPD) which has collected a set of clinical variables for all COPD patients managed in any Danish pulmonary outpatient clinic since 2008. Reporting to the DrCOPD is mandatory by law. In the registry, patients are defined as having COPD if they are ≥30 years old with primary diagnoses according to the Danish version of ICD-10: COPD (J44.X), or respiratory failure (J96.X) with COPD as a secondary diagnosis. Details of the DrCOPD have been described elsewhere [15]. For this purpose we studied the 23,741 COPD patients who had their first-ever contact with an outpatient clinic during 2008–2012 (see flow chart, Fig. 1). As medication adherence and clinical prognosis are dependent on COPD severity, we excluded patients with missing information on lung function, dyspnea, and smoking. The remaining 16,875 subjects were stratified into GOLD A-D risk group using pulmonary function (assessed as percentage of predicted FEV1 [FEV1% pred]), shortness of breath (assessed with the Medical Research Council [MRC] scale), and history of exacerbations and hospitalizations [16,17]. A total of 3506 patients with GOLD A, for whom short-acting medication is recommended were excluded, ultimately retaining 13,369 individuals who, according to GOLD recommendations, should be treated with maintenance medications. The Danish Data Protection Agency (record 2012-41-0438), the Danish National Indicator Project, Danish Regions, and the Danish Ministry of Health approved the study.

2.2. Socioeconomic exposures and demographics

Statistics' Denmark provided information on age, sex, educational attainment, ethnicity, and cohabitation status. Family equalized disposable income two years up to baseline were divided into tertiles. Patients were categorized according to labor market affiliation the year before baseline.

2.3. Outcomes

To determine adherence we searched the Danish National Prescription Registry (DPR) for dispensed claims of LAMA, LABA, ICS, and ICS/LABA. The DPR holds complete information on all out-of-hospital dispensed prescriptions at pharmacies and nursing homes [18]. Adherence was measured as proportion of days covered (PDC) by at least one respiratory maintenance medication during 365 days from baseline till end of study (December 31st, 2012), date of death, or emigration, whichever came first. PDC was calculated by dividing the volume dispensed with the Anatomic Therapeutic Chemical (ATC) classification code specific daily defined doses (DDD) [19]. In cases where DDDs deviated from recommended use in Denmark [20] DDDs were modified accordingly. An overview of ATC codes and daily doses is available in supplement Table S1. Using the specific fill dates and days' supply we created time arrays reflecting the specific dates encompassed by each fill, adjusting the start date forward if the patient had overlapping arrays of equivalent medication (e.g. LABA and LABA) to credit "early refillers" with finishing their current fill before starting a new. To account for baseline medication stock, we also created arrays in the year before baseline. In cases where arrays spanned into the follow-up period the start date of the first fill during follow-up were adjusted accordingly. A PDC ≥80% was considered as high adherence in accordance with previous literature (17, 18, 56–58). Non-use was defined as having a PDC of zero, meaning that patients were credited with using potential build-up stock from the year before baseline during follow-up. Hence, non-users were limited to those without available stock and with no claims during follow-up.

Exacerbations were identified in the DPR by claims of prednisolone (ATC: H02AB06) the year before baseline and during follow-up. To be considered an independent exacerbation, claims had to be ≥28 days apart. This method has previously been used to identify COPD exacerbations [21].

Acute COPD admissions within the previous year and during follow-up were identified searching the Danish National Patient Register (DNPR) [22] for admissions lasting ≥1 day with ICD-10 codes: COPD (DJ44) as primary diagnosis, or respiratory failure (DJ96) or pneumonia (DJ13-DJ18) as primary diagnosis and COPD (DJ44) as secondary diagnosis.

All-cause mortality was obtained from the Danish Register of Causes of Death (21).

2.4. Covariates

The DrCOPD provided information on forced expiratory volume in first second of expiration registered as a percentage of the predicted normal value (FEV1%pred), Body Mass Index (kg/m2 [BMI]), dyspnea (assessed using the Medical Research Council [MRC] scale), and smoking. We computed the Charlson comorbidity score [23] by searching the DNPR for related diagnoses excluding chronic bronchitis, emphysema and COPD ten years up to baseline. Separately, mental disorders one year prior to baseline were identified by claims for antidepressants (ATC group N06A excl. N06AX12 used for smoking cessation), and antipsychotics (ATC group N05A excl. N05AA04, N05AB04 and N05AD08 primarily used for nausea).