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Non-persistence and non-adherence to long-acting COPD medication therapy: A retrospective cohort study based on a large German claims dataset

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ABSTRACT

Objectives: The main objectives of this study, based on a large cohort of German COPD patients, were to assess the level of non-persistence (NP) and non-adherence (NA) with long-acting COPD inhaler treatment and to describe factors that may be associated with NP and NA.

Methods: This was a retrospective cohort analysis based on claims data provided by a German statutory health insurance fund (years 2010–2012). NP was analyzed for treatment-naïve patients only; it was defined as a gap of >90 days in medication availability.

With regard to NA, first the overall yearly medication possession ratio (MPR) was analyzed, NA was defined as MPR<80%. Secondly, adherence was explored only for the period in which a patient continued therapy with a long-acting COPD agent (no gap>90 days).

Results: 45,937 COPD patients who received at least one prescription of any long-acting COPD agent were identified (mean age 71.4 years; 45.2% female). Among these, 22,276 (42.4%) were classified as newly treated. The percentage of NP patients after 12 months was 65.3% on an overall patient level. Agent-specific NP rates were: 58.5% for LABA, 47.9% for LAMA, 78.0% for ICS, and 69.4% for single-device LABA/ICS combination treatment. The overall 12-month MPR across all agent classes on a patient level was 57.9% (70.0% of patients classified as non-adherent). During periods of general treatment continuation, the mean MPR/NA rates were 85.0%/30.1% (patient level across all agents), 89.3%/28.2% (LABA), 92.1%/16.2% (LAMA), 84.2%/43.8% (ICS) and 84.1%/42.8% (LABA/ICS combination). In the Cox regression analyses, several factors like female gender, higher CCI or lower number of specialist' visits were associated with earlier discontinuation of therapy. In comparison to LABA therapy, LAMA therapy was less likely to be associated with early NP, whereas patients who initiated ICS therapy or a single-device LABA/ICS combination therapy faced a higher NP risk.

Conclusions: In German COPD patients, persistence and adherence with respect to long-acting bronchodilator therapy is poor. Approximately two thirds of patients fail to continue treatment after 12 months. In addition, about one third implement their treatment poorly during periods of general therapy continuation.

Abbreviations: ATC, Anatomical Therapeutic Chemical; CCI, Charlson Comorbidity Index; COPD, Chronic obstructive pulmonary disease; DDD, Defined daily dosage; HR, Hazard ratio; ICS, inhaled corticosteroids; ICD, International Statistical Classification of Diseases; KM, Kaplan-Meier; LABA, Long-acting beta agonists; LAMA, Long-acting muscarinic antagonist; OR, Odds ratio; PDD, Prescribed daily dosage; MPR, Medication possession ratio; NA, Non-adherence; NP, Non-persistence.

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1. Background

Chronic obstructive pulmonary disease (COPD) is one of the most significant causes of morbidity and mortality worldwide [1]. It is the third most common cause of death (8%) in the member states of the European Union (EU) [2]. In industrialized countries, the prevalence of COPD is estimated to be 10% [3].

Both international GOLD guidelines and German treatment guidelines recommend continuous medication therapy with long-acting agents for most COPD patients (German guidelines: COPD severity classes 2–4; GOLD guideline: severity classes B-D) as the initial pharmacological treatment of COPD or, as a second choice, for all COPD patients. For the real-world effectiveness of such a treatment, two factors are of key importance: a general continuation of therapy (persistence), defined as no critical treatment gap during a treatment, and a good quality of therapy implementation (adherence), defined as the regular intake of a medicine as recommended by a physician [4]. However, non-persistence (NP) and non-adherence (NA) have been found to be widespread phenomena, both in well-controlled clinical studies and in the real-world treatment of COPD [4]; [5]. This makes COPD a specifically challenging disease with respect to adherence and persistence, and this might be partially due to the additional challenges associated with inhalation therapy compared to the use of oral tablets as the principal mode of drug administration [6]; [7]. Both NA and NP contribute to rising rates of hospitalization, death and healthcare costs [4].

However, the interpretation of results reported in prior adherence/persistence studies on COPD is difficult because both the definition of NA and NP varied across studies and a substantial number of these studies did not report NP and NA rates separately. Furthermore, with respect to the real-world treatment of COPD patients in Germany, no representative data have been published so far about the degree of NP and NA across all available long-acting therapy regimens and the potential causes of NA and NP.

Therefore, the main objectives of this study, based on a large cohort of German COPD patients, were to assess the level of NP and NA with respect to therapy with long-acting COPD inhaler treatment, to describe factors that may be associated with NP and NA, and to assess whether the need for any short-acting acute medication in patients receiving long-acting COPD therapy (as a proxy for exacerbations and disease control) would be associated with NP or NA to long-acting therapy.

2. Methods

This was a retrospective, non-interventional cohort analysis based on anonymised claims data provided by a German statutory health insurance fund (AOK Nordost; 1.8 million insured in the German states of Berlin, Brandenburg and Mecklenburg-Vorpommern) for the calendar years 2010–2012.

The analysis included all continuously insured patients with a diagnosis of COPD [at least two outpatient or one inpatient COPD ICD-10 diagnoses (ICD-10: J44.-)] in the years 2010–2011. Patients who deceased after inclusion in the study remained in the database. Additionally, to ensure that only patients with COPD were observed, all patients who met one of the following criteria were excluded: age<40 years and at least one concomitant outpatient or inpatient asthma diagnosis (ICD-10 J45.- or J46.-) in 2010–2012.

We analyzed persistence/adherence to long-acting COPD medication therapy in common use. Specifically, we addressed the following agents: LABA (Bambuterol, Formoterol, Salmeterol),[1] LAMA (Tiotropium),[2] ICS (Beclometasone, Budesonide, Fluticasone)[3] or single-device combinations of LABA/ICS (Formoterol/Budesonide, Formoterol/Beclometasone, Salmeterol/Fluticasone).[4] We excluded the long-acting agents Indacaterol (ATC code R03AC18), Ciclesonide (ATC Code R03BA08) and the combination Formoterol/Fluticasone (ATC code R03AK07) because these were not available in the German market in the inclusion period.

Our analysis concerned all patients who received at least one prescription of the above-mentioned agent classes from 01/01/2010 until 31/12/2011 with a potential follow-up period of at least 12 months. Additionally, a subgroup of treatment-naïve patients defined as those without any prescriptions of the respective agents 6 months prior to the first long-acting COPD-related prescription between 01/07/2010 and 31/12/2011 was observed. The reference period, the inclusion period, the index date, and the observational period are explained in Fig. 1.

2.1. Assessment of treatment persistence

Persistence to treatment with long-acting agents was recorded in treatment-naïve patients only and was reported on an agent level separately for the following classes: LABA, LAMA, ICS and single-device combinations of LABA/ICS. NP was defined as a treatment gap of >90 days. Instead of a gap>90 days, in additional sensitivity analyses, we also used 180 days, the DDD of the last observed prescription, and 200% of the DDD of the last observed prescription as gap thresholds definitions. Drug switches within agent classes (including switch of inhalers) were interpreted as continuation of therapy, switches to another agent class were considered as NP.

Furthermore, we reported persistence to any long-acting COPD treatment on an overall patient level. Here, NP was assumed only if there was a 90-day gap in drug availability of any COPD-related long-acting medication. This means that in the patient-level analysis, drug switches from one long-acting agent class to another were not interpreted as NP as long as there was no therapy gap>90 days across all long-acting COPD agent classes.

Our analysis was based on the days' supply of the observed prescriptions. As common in German claims data analyses, we used the defined daily dosage (DDD) as formulated by the WHO and the German WIdO [8] as a proxy for the prescribed daily dosage (PDD).

In all calculations, stockpiling was included by assuming that, in case there were overlapping medications, the previous supply was taken fully before the new supply was initiated. Stockpiling was assumed to take place only within a specific agent class. Additionally, we excluded hospitalization periods from our persistence calculations because we assumed that drug supply was provided by the hospitals during these days.

2.2. Assessment of treatment adherence

Treatment adherence was analyzed in two ways. First, we analyzed the overall yearly medication possession ratio (MPR):

[1] ATC codes: R03CC12/R03AC13/R03AC12.

[2] ATC code: R03BB04.

[3] ATC codes: R03BA01/R03BA02/R03BA05.

[4] ATC codes: R03AK28/R03AK72, R03AK07/R03AK27/R03AK71, R03AK06/R03AK61.