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Impact of initial medication non-adherence to SSRIs on medical visits and sick leaves

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ABSTRACT

Background: Initial medication non-adherence (IMNA) to antidepressants, which are commonly used to treat depression in primary care (PC), is around 6–12%. Although it is well known that post-initial non-adherence to antidepressants increases the cost of depression, the impact of IMNA on cost is unknown. The aim of this study is to assess the impact of IMNA to Selective Serotonin Reuptake Inhibitors (SSRI) on medical visits and sick leave in patients with depression treated in PC in Catalonia (Spain).

Methods: This was a four-year retrospective register-based study (2011–2014). All PC patients of working age who received a new SSRI prescription and had a diagnosis of depression were included (N = 79,642). Treatment initiation, number of visits and days on sick leave were gathered from the database. We assessed the impact of IMNA on costs with ordered logistic regressions.

Results: The 3-year incidence of IMNA was 15%. Initially non-adherent patients made a lesser number of GP visits (OR = 0.82; 95% CI = 0.79–0.84) but had more days on sick leave (OR = 1.25; 95% CI = 1.20–1.31). There were no differences in the number of specialist visits (OR = 1.04; 95% CI = 0.99–1.08).

Limitations: Differences between adherent and non-adherent patients could be explained by non-observed variables. GP recognition and documentation of depression might be inaccurate. Costs of unpaid work and use of hospital services were not considered.

Conclusions: Although IMNA decreases the use of medical PC services, it increases the number of days on sick leave. This could also indicate worse health status. These consequences are currently overlooked when considering post-initial medication non-adherence.

1. Introduction

Depression is mainly treated in Primary Care (PC) (Serrano-Blanco et al., 2010) where antidepressants are the first-line pharmacological treatment and one of the most commonly-used medications (Bauer et al., 2008; Rubio-Valera et al., 2012). In European countries, up to 80% of patients treated with antidepressants for a new episode of depression received selective serotonin reuptake inhibitors (SSRIs) (Bauer et al., 2008). This rate is almost 70% in the USA (Marcus et al., 2010).

Non-adherence to antidepressants is highly prevalent in PC. Up to 56% of patients discontinue antidepressants in the first 6 months (Ereshefsky et al., 2010; Serna et al., 2010) and it has recently been estimated that about 6–12% of patients never initiate the treatment (Aznar-Lou et al., 2017a; Pottegård et al., 2014). This is known as initial medication non-adherence (IMNA) or primary non-adherence (Hutchins et al., 2015).

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Adherence to antidepressants impacts direct and indirect depression costs. A recent systematic review showed that non-adherence to antidepressants is associated with worse clinical outcomes (remission or response rate, time to relapse and severity) and higher healthcare costs (drug and inpatient and outpatient medical costs) (Ho et al., 2016). Although indirect costs represent a substantial proportion of total depression costs (Ekman et al., 2013; Salvador-Carulla et al., 2011), few studies have evaluated the relationship between non-adherence and productivity losses. These studies showed that non-adherence increased productivity losses (Birnbaum et al., 2010; Burton et al., 2007; Loeppke et al., 2011).

A recently study conducted by our group shows that IMNA is associated with increased use of healthcare services and productivity losses in acute and chronic diseases (Aznar-Lou et al., 2017b). However, to our knowledge, no studies have explored the impact of IMNA to antidepressants on these outcomes. IMNA could impact differently from other forms of non-adherence –such as early discontinuation or suboptimal dosing– and its costs should be added to those of other forms of non-adherence.

To fill this gap, this study assesses the impact of IMNA to SSRI on medical visits and sick leave in patients with depression treated in PC.

2. Methods

This study was a 4-year longitudinal retrospective register-based cohort study. It included all PC patients treated in the Catalan public healthcare system (Spain) who fulfilled inclusion criteria. We followed STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) recommendations for observational studies in epidemiology. This study is part of a large study aiming to estimate IMNA prevalence and cost. The methods have been described elsewhere (Aznar-Lou et al., 2017a, 2017b). The Idiap-Jordi Gol i Gurina Ethics Committee (P14/140) and the Fundació Sant Joan de Déu Ethics Committee (PIC-111-14) approved this study.

2.1. Setting

The Spanish public healthcare system provides universal coverage for citizens through a public system financed by taxes. It is free at the point of use with some exceptions, such as medicines. During the study period, two co-payment policies were implemented in Catalonia. PC is patients' first point of contact with the public health system. Each individual has an assigned General Practitioner (GP) that prescribes most pharmacological treatments and sick leave. Specialist visits require a GP referral.

In Catalonia, a Spanish region of over 7.5 million inhabitants, almost 300 of 371 publicly-funded Primary Care Centers (PCC) are managed by the Catalan Health Institute (Institut Català de la Salut, ICS), which covers 80% of the population (5.8 million).

2.2. Data source

Data were obtained from the System for the Development of Research in PC (SIDIAP) (Bolíbar et al., 2012). This database was set up in 2010 and contains information on PC patients covered by ICS (Bolíbar et al., 2012) i.e., patients' sociodemographic and clinical data; prescribed and dispensed medication; sociodemographic characteristics of the prescriber; and PCC characteristics. It also includes use of healthcare services and days on sick leave by all patients. The SIDIAP is managed by public healthcare authorities and meets all current legal requirements: it is anonymous, encoded and secure. It has information on filled prescriptions generated by the monthly registries that pharmacies make to claim reimbursement for ICS covered dispensed medications (Aznar-Lou et al., 2017b).

2.3. Study population

This study included all working age patients (16–65 years) that were newly prescribed a SSRI (Anatomical Therapeutical Classification [ATC] code: N06AB) between July 2011 and June 2014 and had a diagnosis of a depressive disorder (depressive episode, recurrent depressive disorder, persistent mood disorders (cyclothymia, dysthymia) or other mood disorders) according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10) classifications. The specific ICD-10 codes are detailed in Supplementary Material. To ensure that only newly prescribed medicines were considered, a 3-month pre-period was set so that patients who had been prescribed another SSRI in the 3 months prior to the prescription were excluded (Hutchins et al., 2015). A 3 month period without any prescription prior to the new prescription for SSRI was considered enough to be sure that we were identifying a newly prescribed medication. Patients were only considered the first time they had a new SSRI prescription in the period of study.

2.4. IMNA definition

IMNA was defined, following International Society for Pharmacoeconomics and Outcomes Research (ISPOR) recommendations, as not filling the prescription (index prescription) for a newly-prescribed medicine in the month of prescription or the following month (follow-up period)(Hutchins et al., 2015).

2.5. Medical visits and days on sick leave

Medical visits (to GP or specialist) and days on sick leave were obtained for the 6 months prior to and after the index prescription. Six months is a reasonable period for remission to occur; longer periods could increase bias by considering medical visits and sick leave unrelated to depression.

2.6. Patient, GP and PCC characteristics

Patients' characteristics included gender, age, socioeconomic status (5 categories, from lowest to highest for urban areas, and a rural category), nationality (Spaniard, European non-Spaniard, African, American and Asian-Oceanian), comorbidities (number of active diseases other than depression) at the moment of prescription and number of new prescriptions (apart from SSRI prescription) issued 6 months prior to and after the SSRI prescription. Diseases were recorded according the ICD-10 and were grouped as follows: allergy; pain, respiratory, disability, cardiovascular, mental (other mental disorders were included in this category), neurological (migraine was included), diabetes mellitus, digestive and thyroid-related diseases. We also retrieved GPs' gender and age, GP type (assigned or substitute/resident) and type of PCC (resident-training centre).

2.7. Statistical analysis

Four variables had missing values: nationality (40%), socioeconomic status (5%), GP gender (5%) and age (5%). GP age was missing only for those GPs that were substitutes and/or resident GPs who were younger than the sample of GPs registered in the database. Thus, GP age was assumed to be 32.5 years, which corresponded to the mean age of substitutes and residents. We used all the available variables to generate one imputed database using imputation with chained equations. Erroneous imputation values were less than 10% for all the imputed variables so that the imputation method was considered to produce reliable estimators.

The incidence of IMNA was estimated as the proportion of patients who were initially non-adherent in the period of study. None of the families of the generalized linear models was a good fit for the