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A Clinical Research Practice Datalink Analysis of Antidepressant Treatment Patterns and Health Care Costs in Generalized Anxiety Disorder

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ABSTRACT

Objective: To describe real-life prescription patterns, health care resource use, and costs in adults with generalized anxiety disorder (GAD) initiating antidepressant (AD) treatment in the United Kingdom. **Methods:** A retrospective longitudinal cohort study using data from Clinical Research Practice Datalink was conducted. Adults with incident prescription of an AD (index date) between January 1, 2006, and June 30, 2010, and with a diagnosis of GAD within the 2 months preceding or following the index date were included. Patients with a diagnosis of schizophrenia or bipolar disorder were excluded. **Results:** A total of 29,131 patients with GAD were included in the analysis. Their mean age was 48.5 ± 15.5 years, and two thirds were women. GAD-licensed ADs (i.e., escitalopram, paroxetine, venlafaxine XR, and duloxetine) represented only 12.5% of the index AD prescriptions. At least one anxiolytic was prescribed for 23.5% of the patients. Only 33.2% of the patients continued index AD treatment over the study period. Discontinuation occurred for 46.0% of the patients, after a mean of 3.7 months of treatment. The health care costs were £338.4 per patient in the 6 months before the index date and £984.6 in the 9 months after the index date. Psychiatric hospitalization (relative risk = 4.18; 95% CI 3.53–4.96; $P < 0.001$) and duloxetine as index treatment (relative risk = 1.85; 95% CI 1.30–2.63; $P < 0.001$) were the main determinants of increased costs for these patients. **Conclusions:** The significant rate of AD discontinuation and associated treatment duration indicate unmet needs among patients with GAD. As described in American studies, substantial health care costs were also observed in this study.

Keywords: antidepressant, generalized anxiety disorder, General Research Practice Database, health care costs, health care resource use.

Introduction

Anxiety disorders comprise a range of conditions including panic disorder (with and without agoraphobia), post-traumatic stress disorder, obsessive-compulsive disorder, social phobia, specific phobias, acute stress disorder, and generalized anxiety disorder (GAD). The lifetime and 12-month prevalence of anxiety disorders in Europe was estimated, respectively, at 13.6% and 6.4% [1]. In the United States, anxiety disorders are the most common mental health disorders with a 12-month prevalence of 18% and a lifetime prevalence reaching 29% of the population [2,3].

Among anxiety disorders, GAD has a high prevalence and a large underdiagnosis. GAD is a chronic, common anxiety disorder in which the patient has excessive worry and apprehension with regard to circumstances. This disorder is characterized by difficult-to-control feelings of threat, restlessness, irritability, sleep disturbance, and tension, and symptoms such as palpitations, dry mouth, and sweating [4]. A systematic international review showed that the prevalence of GAD is 2.6% over 1 year and 6.2% over lifetime [5]. In the United Kingdom, it was recently estimated that 4.4% of the population has GAD, and represents one third of all patients with anxiety disorders [6]. The economic burden of GAD is substantial. The overall indirect and direct costs for GAD have been estimated at $2165 to $3607 per patient per year in Europe [7,8] and direct health care costs at $6472 in the United States [9].

In the United Kingdom, the National Institute for Health and Care Excellence (NICE) edited national clinical guidelines for the management of GAD [10]. Depending on the increasing severity of the condition, GAD should be managed according to the following steps: "i) identification and assessment; education about GAD and treatment options; active monitoring; ii) low-intensity psychological interventions: individual non-facilitated self-help, individual guided self-help and psychoeducational groups; iii) choice of a high-intensity psychological intervention (CBT/applied relaxation) or a drug treatment; and iv) highly specialist treatment, such as complex drug and/or psychological treatment regimens; input from multi-agency teams, crisis services, day hospitals or inpatient care." The preference of the patient should be taken into account at any of these steps. If

Conflicts of interest: J.C., D.S., and C.F. were full-time employees of Lundbeck at the time of the study. E.C. is a full-time employee of Creativ-Ceutical, which has received honoraria from Lundbeck.

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immediate management is required, any or all of the following should be considered: support and information, problem solving, benzodiazepines, sedating antihistamines, self-help. If benzodiazepines are needed, they should not usually be used beyond 2 to 4 weeks. In addition, the longest duration of effect has been shown for the following interventions, in descending order: "i) psychological therapy (cognitive behavioural therapy – CBT); ii) pharmacological therapy (selective serotonin reuptake inhibitors, SSRIs); or iii) self-help" [10].

Multiple randomized, placebo-controlled trials support the use of SSRIs as first-line pharmacotherapy in anxiety disorders, particularly in GAD [11]. Currently, in the United Kingdom, two SSRIs (escitalopram and paroxetine) and two serotonin noradrenalin reuptake inhibitors (venlafaxine XR and duloxetine) have marketing authorizations for the treatment of GAD. Despite its lack of a UK marketing authorization for this indication, and based on economic models showing higher cost-effectiveness, NICE recommends sertraline for the treatment of GAD in its national clinical guideline. This guideline, however, also states that "it is difficult to draw conclusions on the cost effectiveness of particular pharmacological interventions for the treatment of people with GAD based on existing evidence."

Although some studies describe treatment patterns and health care costs of patients with GAD in the United States, we were unable to identify studies describing the real-life prescription patterns of antidepressant (AD) treatment in GAD using a large European longitudinal medical records database [9,12]. The Clinical Practice Research Datalink (CPRD, formerly known as the General Practice Research Database [GPRD]) is an important source of information for investigating the "real-life" patterns of use of prescription drugs and health care resource use in primary care patients in the United Kingdom. Analysis of its data on patients with GAD could help to choose the appropriate hypotheses to use in models to determine the most cost-effective ADs in the treatment of GAD. The present exploratory study aimed at describing the real-life prescription patterns of ADs and associated health care resource use and costs in adult patients with GAD recorded in the CPRD.

Patients and Methods

Study Design

This study was a retrospective longitudinal cohort study using data from the GPRD (now known as the CPRD).

Objective

The primary objective of the study was to explore the prescription pattern, health care resource use, and costs in adult patients diagnosed with GAD and initiating an AD treatment in the United Kingdom.

Study Population

The UK GPRD is the world's largest computerized database of anonymous longitudinal clinical records from primary care, comprising more than 62 million patient-years' worth of data collected from approximately 10 million patients since its creation in 1987 [13]. The data from the GPRD are generated by general practitioner (GP) practices throughout the United Kingdom, and participating GPs are equipped with specific software to record patient data into the database.

Participating clinicians agreed to provide data for research purposes to the GPRD. Currently, data are being collected from about 4.8 million patients in 590 primary care practices. These data cover 8% of the UK population. The patient population captured in the database is broadly representative of the overall UK population. Prescriptions are directly generated by computer, thus ensuring a complete recording of prescriptions written by the GP [14]. Diagnoses were coded by using Read or Oxford Medical Information System codes and are entered by the GP at the time of consultation on his own account. The principal information recorded, and available for analysis, consists of physician practice characteristics, patient demographics, prescriptions of medicine, clinical diagnoses, referrals to hospitals or specialists, and results of laboratory tests [13,14]. The external validity of the GPRD was demonstrated in several studies [15,16].

GAD is frequently comorbid with depression. Because this study aimed at describing the prescription pattern and resource use in AD-treated patients with GAD, and not in AD-treated patients with depression, inclusion and exclusion criteria were designed to exclude patients with comorbid depression. Patients in the CPRD corresponding to the following inclusion criteria were selected: 1) incident prescription of an AD (=index date); 2) index date between January 1, 2006, and June 30, 2010; 3) age 18 years or more at the index date; 4) a diagnosis of GAD within the 2 months preceding or following the index date; 5) a minimum of 6 months of history before the index date; 6) a minimum of 9 months of follow-up after the index date; and 7) a second prescription of AD within the 2 months following the index date.

Exclusion criteria were: 1) any prescription of AD within the 6 months preceding the index date; 2) any diagnosis of depression within the 3 months preceding or following the index date; 3) initiation of a combination of AD treatments at the index date; and 4) diagnosis of schizophrenia or bipolar disorder at any time.

Diagnoses were assessed through a search in Read codes corresponding to GAD or other psychiatric conditions.

Patient Characteristics

Patient characteristics were described according to the following sociodemographic and clinical variables extracted from the CPRD database: age, sex, psychiatric comorbidities during the pre- and postindex period (GAD, depression, panic disorder, "other anxiety disorders"—that is, "agoraphobia, specific phobia and post-traumatic stress disorders," obsessive-compulsive disorder, eating disorders, substance-related disorders) [17]. The Charlson comorbidity index (CCI) was further calculated according to adaptation made by Khan et al. [18].

AD Prescription Pattern

Within this study, all marketed antidepressant compounds in the United Kingdom have been identified and included, according to the GPRD Product Dictionary.

AD prescription pattern was described according to 1) type and duration of index AD treatments; 2) continuation, discontinuation, switch, or combination of the index AD treatment; 3) index AD dose (i.e., proportion of the defined daily dose [DDD]); 4) medication possession ratio (MPR), defined below; and 5) anxiolytic treatment before and after the index date (i.e., benzodiazepines and other anxiolytic drugs according to the GPRD Product Dictionary).

Duration of the index AD treatment was defined as the period during which a patient received one or more prescriptions for the index AD covering a continuous period of time. All AD treatment changes (e.g., addition of another AD, discontinuation of or change in AD treatment) were considered as a treatment sequence change. When two consecutive prescriptions (with overlaps or not) of the same drug were made within a period of 30 days or less following the theoretical end of the previous prescription, it was assumed that the patient was treated continuously. The duration of the index treatment was the difference