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Research paper

Testing for clinical inertia in medication treatment of bipolar disorder

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ABSTRACT

Background: Clinical inertia has been defined as lack of change in medication treatment at visits where a medication adjustment appears to be indicated. This paper seeks to identify the extent of clinical inertia in medication treatment of bipolar disorder. A second goal is to identify patient characteristics that predict this treatment pattern.

Method: Data describe 23,406 visits made by 1815 patients treated for bipolar disorder during the STEP-BD practical clinical trial. Visits were classified in terms of whether a medication adjustment appears to be indicated, and also whether or not one occurred. Multivariable regression analyses were conducted to find which patient characteristics were predictive of whether adjustment occurred.

Results: 36% of visits showed at least 1 indication for adjustment. The most common indications were non-response to medication, side effects, and start of a new illness episode. Among visits with an indication for adjustment, no adjustment occurred 19% of the time, which may be suggestive of clinical inertia. In multivariable models, presence of any indication for medication adjustment was a predictor of receiving one (OR=1.125, 95% CI =1.015, 1.246), although not as strong as clinical status measures.

Limitations: The associations observed are not necessarily causal, given the study design. The data also lack information about physician-patient communication.

Conclusions: Many patients remained on the same medication regimen despite indications of side effects or non-response to treatment. Although lack of adjustment does not necessarily reflect clinical inertia in all cases, the reasons for this treatment pattern merit further examination.

1. Introduction

Bipolar disorder (BD) is among the twenty leading causes of years lived with disability worldwide (Vos et al., 2012). It is a severe, chronic disorder that impairs functioning in multiple life domains, in particular psychosocial and occupational (Hirschfeld, Lewis and Vornik 2003; Judd et al., 2008; Keck, Kessler and Ross 2008; Kessler et al., 2006; Kessler, Merikangas and Wang 2007; Lee et al., 2010; Ruggero et al., 2007), imposing a total economic burden estimated at $151.0 billion for the US in 2009 (Dilsaver 2011). In addition, individuals with bipolar disorders have an annual risk of suicide attempts that is 30-60-fold higher than the general population (Gonda et al., 2012). Some of these poor outcomes may result from lack of treatment, with large numbers of individuals not receiving treatment, or not adhering enough to benefit. For example, in one national study, only 64% of people with bipolar I disorder who had an active major depressive, manic, or hypomanic episode in the previous 12 months reported receiving medication (Merikangas et al., 2007). However, another concern is that some bipolar patients are not receiving the right treatment to relieve their symptoms, in a context where different medications and dosages work for different patients. Pharmacological treatment for BD typically involves use of medications from multiple classes, and requires monitoring patients for side effects and nonresponse, in case medication adjustment is needed (Yatham et al., 2013).

For several other chronic medical conditions, clinical inertia is increasingly discussed as a possible explanation for poor treatment outcomes. Clinical inertia has been defined as "failure of health care providers to initiate or intensify therapy when indicated" (Phillips et al., 2001). Evidence for this phenomenon has been studied for a variety of diseases, as documented in a 2009

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review by Faria et al. (Faria et al., 2009). For example, a study of hypertensive patients found that anti-hypertensive medications were intensified in only 13% of visits where an elevated blood pressure was recorded (Okonofua et al., 2006). In the case of depression treatment, one study found that treatment adjustment was recommended in only one-third of observation periods that ended with less than a full response (Henke et al., 2009). Other diseases for which clinical inertia has been studied include diabetes, renal disease and dyslipidemia (Faria et al., 2009). However, no studies have yet evaluated the existence of clinical inertia in treatment of bipolar disorder.

This study attempts to measure the potential prevalence of clinical inertia in bipolar disorder treatment, based on rates of non-adjustment of medications where adjustment might appear to be indicated. We do not include psychosocial therapies in our definition of adjustment, as arranging psychotherapy typically takes considerably longer than changing the medication regimen, in the settings studied. We identify some demographic and clinical correlates of this treatment pattern. However, since non-adjustment may result from factors other than clinical inertia (reviewed in the Discussion), our findings should be considered to be a 'high end' estimate which could be used as a reference for future research on this topic. Given the exploratory character of the study, formal hypotheses are not tested.

2. Method

2.1. Data

This paper used data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study. STEP-BD was a multisite study funded by the National Institute of Mental Health (NIMH) that was designed to evaluate the longitudinal outcome of patients with bipolar disorder. The overall design involved a large prospective naturalistic study, combined with specific randomized controlled trials, at 22 sites in the United States between November 1999 and July 2005. The sites were specialty clinics in academic medical settings (Sachs et al., 2003). The present study involved no new data collection from the STEP-BD subjects, and was approved by the institutional review board of our institution.

To enroll in STEP-BD, patients were required to be at least 15 years of age and to meet DSM-IV criteria for bipolar I disorder, bipolar II disorder, cyclothymia, bipolar disorder not otherwise specified, or schizoaffective manic or bipolar disorder subtypes. Exclusion criteria were limited to the unwillingness or inability to comply with study assessments or the inability to give informed consent. Although the study included a few small, randomized trials, most patients were seen only in the naturalistic arm, in which clinicians were trained on expert consensus guidelines and other published treatment guidelines, and encouraged but not required to follow those guidelines (Sachs et al., 2003). However, treatment decisions were based entirely on the preferences of the treating physicians in collaboration with their patients, and were not constrained in any way. This paper uses data from the naturalistic arm only. Details on subject recruitment and diagnostic methods are available in other papers from the study (Sachs et al., 2003) (Ghaemi et al., 2006).

Over the course of the STEP-BD study, psychiatrists recorded data at each study visit on patients' medication treatment; adverse side effects; self-reported adherence to prescribed medications; clinical mood state (e.g. depressed, manic, mixed or hypomanic); social and role functioning; and self-reported comorbidities (e.g. substance use, eating disorders, medical conditions). These data were recorded on a Clinical Monitoring Form (CMF), a one-page assessment tool that consists of nine parts. Its subscales were constructed as a standardized assessment substitute for the narrative process note routinely used in clinical practice. The CMF also recorded information on laboratory data, stressors, selected mental status items, and the percent time and severity of depressive, anxious and/or elevated mood symptoms experienced in the prior 10 days (Sachs, Guille and McMurrich 2002).

2.2. Analytic sample

There were 3271 patients in the study for whom at least one CMF was available. For this paper, patients were excluded if they: (1) did not have a lifetime diagnosis of bipolar disorder (n=1213), (2) had visits on the randomized pathways (n=252), (3) used a medication whose name could not be determined from the study data (n=37), or (4) lacked demographic information (n=250). In addition, 136 patients who only had one visit during the study were excluded, as any adjustment they received would not be observable. Since the CMF reported on adjustments prior to the current visit, each patient's final visit was excluded, as we would not be able to observe any adjustments that occurred at that visit. This resulted in a sample of 23,406 study visits made by 1815 patients, whose care was managed by 193 physicians.

2.3. Measures

This section describes how key measures used for this paper were constructed.

2.3.1. Clinical status

Current clinical assessments of depressed, manic, mixed, or hypomanic states and of euthymic or subsyndromal states were based on standard STEP-BD procedures that used the CMF and application of DSM-IV criteria to all depressive and manic mood symptoms. Patients who did not meet criteria for a current episode but had not recovered from their last episode were classified as either 'continued symptomatic' (if they had 3 or more moderate symptoms) or 'recovering' otherwise. Patients who did not meet criteria for a current episode and had recovered from their last episode were classified as either 'roughening' (if they had 3 or more moderate symptoms) or 'recovered' otherwise. All raters were trained during STEP-BD sessions in application of the CMF clinical mood status assessment, and adequate interrater reliability was ascertained.(Ghaemi et al., 2006) In addition, the Clinical Global Impression (CGI) Severity scale was collected at each visit, recording the patient's severity of psychopathology on a scale from 1 (not at all ill) to 7 (extremely ill).

2.3.2. Indications for adjustment

A set of indications was developed by the study team, based on the clinical and research experience of the clinician co-investigators. The definition of the indications was also informed by influential treatment guidelines (Malhi et al., 2009; Suppes et al., 2005; Yatham et al., 2013). These guidelines advise physicians to modify the medication regimen over time in response to changes in the patient's mood (e.g. mania, depression) and treatment phase (e.g. acute, maintenance), and also if the patient is not responding or is experiencing side-effects. A visit was classified as having an indication for treatment adjustment if the patient met any of the following criteria:

- Presence of any severe side effects (rated 4 on a scale of 0-4) or at least 2 moderate side effects (rated 2 or 3) at both the current and previous visits.
- Non-response to treatment. This was judged to be present if: a) the patient's current episode had lasted more than 8 weeks, or