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Research report

The public health impact of antidepressants: An instrumental variable analysis

Ramin Mojtabai *

Department of Mental Health, Bloomberg School of Public Health, and Department of Psychiatry, Johns Hopkins University, Baltimore, MD, United States

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ABSTRACT

Background: There has been a marked increase in antidepressant medication prescription and use over the past three decades with unclear effects on the mental health status of the population. This study examined the impact of expansion of antidepressant use on prevalence and characteristics of depression and suicidal ideations in the community.
Method: Instrumental variable models were used to assess the impact of antidepressant treatments on the prevalence of depressive episodes, mixed anxiety and depression states and suicidal ideations in 22,845 participants of the 1993, 2000 and 2007 National surveys of psychiatric morbidity of Great Britain who were between 16 and 64 years of age.
Results: Increased prevalence of antidepressant treatment did not impact the prevalence of depressive episodes or mixed anxiety and depression states. However, antidepressant treatment was associated with decreased prevalence of severe and, to a lesser extent, mild depressive episodes and suicidal ideations and a corresponding increase in prevalence of moderate depressive episodes.
Limitations: The data were cross-sectional and based on self-report of symptoms in the past month and current medication use with no information on dose and duration of medication treatment.
Conclusions: Expansion of antidepressant treatments in recent years has not changed the community prevalence of depression overall, but it has reduced the prevalence of more severe depression and suicidal ideations. The findings call for better targeting and more judicious use of antidepressants in cases of more severe depressive episodes which are more likely to respond to such treatments.

There has been a marked increase in prescription and use of antidepressant medications in different parts of the world in the past 3 decades (Baldessarini et al., 2007; Brugha et al., 2004; Mojtabai, 2008; Olfson and Marcus, 2009). However, the health impact of the increased use of these medications remains unclear (Baldessarini et al., 2007; Brugha et al., 1992; Moncrieff and Kirsch, 2005; Patten, 2004). Studies of prevalence of mental disorders or symptoms over periods of rapid growth in antidepressant use generally failed to show any reduction in disorders or symptoms (Brugha et al., 2004; Compton et al., 2006; Kessler et al., 2005), and studies of trends in suicidal behavior have shown mixed results (Baldessarini et al., 2007; Rihmer and Akiskal, 2006). These findings are puzzling as antidepressants have been shown to be at least moderately efficacious in treatment of depression in randomized clinical trials (Arroll et al., 2009) and small scale population intervention studies (Rutz et al., 1992).

A possible reason for the discrepancy between the increase in antidepressant use and the prevalence of mental disorders, at least in the case of depression, is that the greatest increase in antidepressant use has occurred among individuals with less severe depression (Brugha et al., 2004; Mojtabai, 2008), who may not benefit from antidepressant treatments to the same extent as individuals with the more severe forms of

* Department of Mental Health, Hampton House, Rm 797 624 N. Broadway, Baltimore, MD 21205, United States.
E-mail address: rmojtaba@jhsph.edu.

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depression (Fournier et al., 2010; Ghaemi, 2008; Khan et al., 2002). As a result, the overall prevalence of depression might not have changed as much as the prevalence of more severe forms of depression.

Assessment of the public health impact of antidepressants in community settings is hampered by a number of methodological obstacles, with the problem of "confounding by indication and severity" (Patten, 2008) being a major obstacle. Individuals with more severe mental health problems are more likely to seek treatment and be treated with antidepressants. As a result, observational studies in community settings often find that individuals who use mental health treatments are more symptomatic or more likely to meet the diagnostic criteria for mental disorders. The use of econometric techniques such as instrumental variable models may allow researchers to overcome this obstacle and to obtain unbiased estimates from observational studies (Bhattacharya et al., 2006; Rassen et al., 2009). This study used instrumental variable models in data from three waves of a general population survey of mental health in Great Britain between 1993 and 2007 to assess the impact of antidepressant use on the prevalence of depression and suicidal ideations. More specifically, the study capitalized on rapid changes in antidepressant use across the survey years to assess the impact of increased antidepressant use on the prevalence of depressive episodes overall and according to levels of severity and duration of episodes. Furthermore, the study examined the effect of increased antidepressant use on the prevalence of anxiety and depression states and suicidal ideations.

1. Methods

1.1. Sample

The sample for this study was drawn from the psychiatric morbidity surveys of the general population of Great Britain conducted in 1993, 2000 and 2007. Overall 26,091 individuals selected from private households participated in these three surveys (McManus et al., 2009b). Delivery points for households were drawn randomly from postal sectors of the Small Area Postcode Address File, stratifying for socio-economic grouping within the English regions, Wales and Scotland. The response rate was 80% in 1993, 69% in 2000 and 57% in 2007 (Jenkins et al., 1997a; Jenkins et al., 1997b; Jenkins et al., 1998; Jenkins et al., 2003a; Jenkins et al., 2003b; Jenkins et al., 2009; McManus et al., 2009a). The 1993 survey included individuals aged 16–74 years, whereas the 2000 and 2007 surveys had a narrower age range (16–64 years). To make samples for the three surveys comparable the sample for this study was limited to 22,845 participants in the 16–64 years age range in the three surveys. All data were obtained by structured interviews with participants.

1.2. Assessments

Use of prescription antidepressants was ascertained by asking participants to choose specific medications currently taken from a list. The medications were coded according to the British National Formulary categories (British Medical Association & Royal Pharmaceutical Society of Great Britain, 2000). This study focused on tricyclic and heterocyclic antidepressants, monoaminoxidase inhibitors (MAOI), selective serotonin reuptake blockers and other antidepressants. In the 2007 survey, the interviewer also asked to see the packaging to assess whether or not the participant's report matched the packaging information. Based on these ratings, the participants were quite accurate in identifying their medications with a median of 95.5% correspondence between the individual reports and packaging information across 13 individual antidepressants (data not shown).

Psychotherapy/counseling was assessed by presenting participants with a list of different psychosocial interventions and asking if they were currently receiving that form of therapy "for mental, nervous or emotional problems." The list included psychotherapy, behavioral or cognitive therapy, art, music or drama therapy, social skills training, marital or family therapy, sex therapy and counseling. A positive response to either form of therapy was rated as receipt of psychotherapy/counseling.

Mental health contacts with general practitioners were assessed by asking if the participant had spoken to a general practitioner or family doctor in the past 12 months "about being anxious or depressed or a mental, nervous or emotional problem."

Psychiatric disorders were assessed by a structured interview—the Clinical Interview Schedule—Revised (CIS—R) (Lewis et al., 1992). Symptom data obtained in CIS—R were subjected to a computer algorithm providing diagnostic categories according to the 10th edition of the International Classification of Diseases (ICD-10) (World Health Organization., 1992). Psychometric properties of CIS—R have been previously assessed (Jordanova et al., 2004). This study focused on three ICD-10 categories of depressive episodes based on severity (mild, moderate and severe), and the CIS—R mixed anxiety and depression category. Depressive episodes in ICD-10 are defined by episodes lasting at least two weeks during which the individual experienced a number of more common or "typical" symptoms and a number of other depressive symptoms (World Health Organization., 1992). Typical symptoms included depressed mood, loss of interest and enjoyment, and increased fatiguability. Other symptoms included reduced concentration and attention, reduced self esteem and self confidence, ideas of guilt and unworthiness, bleak and pessimistic views of the future, ideas or acts of self-harm or suicide, disturbed sleep, and diminished appetite (World Health Organization., 1992). Mild depressive episodes were defined in ICD-10 by the presence of two of the three typical symptoms and at least two other symptoms; whereas, moderate depressive episodes were defined by two of the typical symptoms and at least three of the other symptoms and severe depressive episodes were defined by the presence of all three typical symptoms and at least four of the other symptoms (World Health Organization., 1992). Validity of the ICD-10 classification of depressive episodes based on severity has been previously assessed (Kessing, 2004, 2008). Mixed anxiety and depression category was defined by having a CIS—R score of ≥ 12 but not meeting the criteria for any of the specific ICD-10 mood or anxiety disorders (McManus et al., 2009a). In addition, four ICD-10 anxiety disorders (generalized anxiety disorder, panic disorder, obsessive–compulsive disorder, and phobias) were assessed and included in the analyses as comorbidity of depressive episodes and anxiety may have implications for treatment response.

Duration of depressive episode was assessed based on one question about the length of time the person has been "feeling