What evidence is there that general practitioners follow guidelines on the use of antidepressants to treat depression and how can this be improved?

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Abstract

Despite the availability of guidelines regarding the dosage and length of treatment with antidepressants for a depressive episode, it has been shown repeatedly that general practitioners do not always prescribe according to the guidelines. Several papers written between 1996 and the present demonstrate this fact. The implication is that patients in primary care in the UK do not receive treatment for an adequate time span and often at too low a dose, especially if older antidepressants are used. This can lead to a higher likelihood of recurrence of depressive symptoms and higher consequent morbidity. The solution we propose is the development of joint doctor-practice-nurse clinics for the treatment of depression, as part of the Quality and Outcomes Framework (QOF) program. The outcomes of these clinics should be auditable against the guidelines. This, when linked with easy access to advice and referral to secondary care psychiatry specialists, argues for a collaborative care, or shared care, program for the treatment of depression in primary care.

Keywords: depression, antidepressants, primary care, collaborative care

Introduction

Guidelines regarding the dosage and length of treatment with antidepressants for a depressive episode have been available for several years but despite this, several papers have shown that general practitioners do not always prescribe according to the guidelines. In this article, we review the evidence as to whether GPs follow antidepressant guidelines, covering the data between 1996 and the present, and discuss the implications of this evidence. We then propose solutions which could be used to improve adherence to the guidelines.

The evidence

The recognition and management of depression in general practice has long been influenced by the advice given in Paykel and Priest's 1992 paper (1), which was subsequently included in the National Institute for Health and Care Excellence (NICE) guidelines for the recognition and management of depression in adults . Reviewed in 2013, the current guidelines encourage medication for the treatment of a depressive episode to be prescribed for at least six months, including two months of treatment after diagnosis followed by four months of maintenance treatment after remission of an episode of depression, in order to prevent relapse. Furthermore they recommend that treatment should be continued for two years if the patient has a significant risk of relapse. A number of studies over several years have suggested that these guidelines frequently have not been strictly followed by general practitioners, and that this may be limiting the effectiveness of the treatment of depression. These papers have discussed the causes of, and potential solutions to, this issue.

The initial evidence that many GPs prescribed antidepressants at too low a dose and for too short a time was the article by Donoghue and Tylee on the use of antidepressants in the treatment of depression (2).

In the time period analysed by the authors, 88% of prescriptions for the older tricyclic antidepressants (TCAs) by GPs were at doses which were below those recommended by the current consensus guidelines. However, selective serotonin reuptake inhibitors (SSRIs) and newer antidepressants appeared to be prescribed at effective doses. Furthermore, it was demonstrated that with regard to both TCAs and SSRIs, the medication was not prescribed for the recommended six months but for a much shorter period of time. The study combined data from three different sources: PACT (prescribing analysis and cost) data, GP notes and the DIN-LINK database from Compufile. Between the three sources, nearly two million patient records were analysed. As suggested by the authors, the cross-sectional nature of the study meant that the doses calculated did not take into consideration the position of the prescription on the treatment timeline, for example whether they were starting or maintenance doses. It was therefore considered unlikely that titration could account for the high proportion of low doses. SSRIs and newer antidepressants were recommended in the conclusion to be first line treatment for depression as a short-term solution because these were being already administered at effective doses. It is worth noting that it is not too surprising that SSRI antidepressants were prescribed at adequate doses, since the tablet size of all SSRIs is exactly the recommended dose for these drugs, while tricyclics are produced in tablet sizes which are lower than the therapeutic dose. Concerns raised by the study led to the development of training in order to improve the capability of GPs to treat depression with antidepressants (3).

The consensus guidelines at that time (1996) could be open to dispute. One point of controversy was that research into the effects of antidepressants in older patients (4) has provided some evidence for the efficacy of lower than recommended doses (75mg) of tricyclics in the elderly. However, the sample size analysed was small (only 58 patients by the end) and a Cochrane review (5) concluded that no clear recommendations could be made on the basis of the available evidence. Meta-analysis of data in a 1999 paper (6) concluded that with a low dose of antidepressants clinicians "trade off" a slightly reduced chance of improvement for a higher chance of avoiding adverse reactions.

Over time, many sets of guidelines for the diagnosis and treatment of common mental health problems have been published. These include local guidelines such as the Bedfordshire Guidelines for Primary Care Mental Health (7) and the international guidelines: the World Health Organization (WHO) guide to Mental Health in Primary Care (8). These guidelines are helpful and generally well received, but Thompson et al. (9) have shown that the delivery of sets of guidelines to GPs without any accompanying formal education package did not improve diagnosis or management of depression. Croudace has made the same observation with a study of the impact of the WHO International Classification of Diseases 10th Revision (ICD-10) guide (10). A series of standards have been proposed by Agius et al. (11) addressing responses to common mental health problems and providing clarification for what is considered to be adequate primary care in mental health.

The effect of following guidelines was examined in a more recent study (12) and it was concluded that the factor that had the most impact on reducing early antidepressant treatment discontinuation and encouraging a more successful outcome was diagnostic coding. To study this a large NHS database was used ensuring analysis performed was fairly reliable, but as suggested by the authors, it is possible that coding and prolonged treatment are both indicators of severity. However, the differences in severity of depression in patients at the practices were not considered to be significant in terms of the influence of coding rates. Similarly, in a study by Upton et al. (13), it was observed that although guidelines had no impact on the overall detection of mental disorders or prescription of antidepressants, there was a significant increase in the number of patients diagnosed with depression. GPs also made a greater use of psychological interventions and so it was concluded that, despite there being no certainty of guidelines successfully bringing about change, there were some areas that were more responsive than others. These mixed messages on the effectiveness of guidelines throw a certain amount of doubt on the absolute necessity of their usage but, from the studies mentioned, it seems that following guidelines is more likely to secure positive patient outcomes. However, it is clear that the distribution of guidelines cannot be seen as a substitute for the continued developmental training of primary care doctors and staff.

There have been some studies that compare the different treatment received by patients from primary care centres and from psychiatrists. The study conducted by Simon et al. (14) concluded that, although patients of psychiatrists made more frequent follow-up visits, the proportion of patients receiving antidepressant medication at an adequate dose was very similar in the two groups. This similarity suggests that

there is widespread deviation from guidelines throughout the whole of the healthcare provider system. Therefore any conclusions made from this investigation could be used as a foundation to investigate improvement options for the treatment of depression throughout the healthcare system.

The reasons behind the reluctance of GPs to follow guidelines are wide-ranging as indicated in a number of articles over the years. A major reason behind the prescription of lower doses for tricyclics is the fear of cardiac adverse effects. Burton et al. (12) suggested that a reason for the small percentage of coding for depression stems from aspects of performance-related pay in the QOF. There is also a large degree of overlap between depression and anxiety disorders, which further complicates diagnosis within primary care and consequently which treatment guidelines to follow. Indeed, in many patients anxiety disorders are co-morbid with both unipolar and bipolar depression. Because of this, anxiety with depression is a diagnosis with a specific code in ICD-10. Whether GPs have the necessary skills, both regarding diagnosis and treatment, to treat patients with several co-morbid mental health disorders requires further consideration.

Another major reason for the prescription of lower than optimal doses for tricyclics is likely to be the risk of toxicity. Cheeta et al. (15) investigated antidepressant-related deaths with reference to the main classes of antidepressants. Their results showed that most deaths were due to suicide; SSRIs were associated with a significantly lower risk than other types but deaths could occur, particularly when SSRIs are combined with other drugs such as TCAs. It was suggested that when combination therapy is used, patients should be screened by taking a history of drug use/misuse. Such a screening programme could assuage some of the fear regarding adverse effects. However, if combinations of antidepressant classes are required, for example, in the case of 'resistant depression', patients should be referred to secondary care. There are further NICE guidelines providing advice about doses for treatment when used in combination.

Another study into the prevalence of self harm (16) compared the frequency of deliberate self harm (DSH) in patients prescribed TCAs and SSRIs prior to the DSH event. Results showed that significantly more events followed SSRI prescription compared to TCAs and so it was concluded that merely prescribing overdose-safe antidepressants was unlikely to reduce overall morbidity. Over-caution in only one aspect of the possible risk factors resulted in inadequate prescribing with increased morbidity and mortality.

Discussion

The fact that there continue to be important disparities between dosages of antidepressants prescribed, and time for which they are prescribed, as well as outcomes of treatment for depression between practices is a matter for concern. Such disparities were reported by Tylee and Donaghue (2,17,18), and have since continued to be reported in more recent papers (12,19). This raises the question as to what strategy needs to be adopted in order to deal with this problem. That GPs do not tend to follow guidelines has been demonstrated by the Hampshire Depression Project, which demonstrated that there was no improvement in depression treatment outcomes despite a training program for GPs with written guidelines (9). It has also been shown that the WHO ICD-10 GP treatment guidelines have not influenced GP management (10,13).

Suggested solutions

Tylee has suggested and implemented a project whereby GP leaders are trained to offer help to GP practices in order to enable them to deal with problems in treating mental health patients, and improve the treatment of depression (20). We have, in the past, recommended that structured clinics be run by both GPs and practice nurses. The practice nurses would act as case managers to improve concordance with treatment (1, 21) and to ensure that patients are followed up regularly (at least once a month) for the six months of treatment for a depressive episode recommended by Paykel and Priest (1).

The possibility that practice nurses could act as case managers in treatment of patients with depression was first investigated by Anthony Mann (22). While it appeared possible for nurses to be used in this way, no improvement in outcomes was shown in Mann's study. However, more recent papers have shown that nurses are able to help to improve outcomes in the treatment of depression and that practice nurse care management is acceptable to patients (23). Such structured clinics could be involved in the QOF system, and also could be auditable to demonstrate improvement in depression outcomes. These structured clin-

ics could be combined with the easy accessibility of a psychiatric consultant in order to help the GP deal with difficult cases. This combination would amount to a shared or collaborative care system to optimise treatment of patients with depressive episodes in primary care (24), which would be a very different treatment model from the simple application of guidelines to treatment of depression in primary care (25).

Conclusion

On the above basis, we strongly recommend the development of such structured clinics, managed jointly by GPs and practice nurses, for depression management in primary care. We would expect that the implementation of such clinics, which could be designed on the lines of the present hypertension, diabetes and asthma clinics in primary care, could contribute substantially to the improvement in the treatment of depression in primary care in the UK.

References

1. Paykel ES, Priest RG. Recognition and management of depression in general practice: consensus statement. BMJ. 1992 Nov 14;305(6863):1198.

2. Donoghue JM, Tylee A. The treatment of depression: prescribing patterns of antidepressants in primary care in the UK. The British Journal of Psychiatry. 1996 Feb;168(2):164-8.

3. Tylee A, Gastpar M, Lepine JP, Mendlewicz J. Identification of depressed patient types in the community and their treatment needs: findings from the DEPRES II (Depression Research in European Society II) survey. DEPRES Steering Committee. International Clinical Psychopharmacology. 1999 May;14(3):153-65.

4. Jacoby R, Lunn AD, Ardern M, Bergmann K, Conway J, Cooling N, Davies G, Fisk J, Gehlhaar E, Harrison-Read P, Hawley R. How long should the elderly take antidepressants?: A double-blind placebo-controlled study of continuation/prophylaxis therapy with dothiepin. The British Journal of Psychiatry. 1993 Feb;162(2):175-82.

5. Wilkinson P, Izmeth Z. Continuation and maintenance treatments for depression in older people. Cochrane Database of Systematic Reviews. 2012(11).

6. Bollini P, Pampaliona S, Tibaldi G, Kupelnick B, Munizza C. Effectiveness of antidepressants: meta-analysis of dose-effect relationships in randomised clinical trials. The British Journal of Psychiatry. 1999 Apr;174(4):297-303.

7. Agius M. Bedfordshire Primary Care Mental Health Guidelines. PRIMHE Resource Pack 2003. 2003.

8. World Health Organization. WHO guide to mental health in primary care: a guide to mental ill health in adults. Royal Society of Medicine Press; 2000.

9. Thompson C, Kinmonth AL, Stevens L, Pevele RC, Stevens A, Ostler KJ, Pickering RM, Baker NG, Henson A, Preece J, Cooper D. Effects of a clinical-practice guideline and practice-based education on detection and outcome of depression in primary care: Hampshire Depression Project randomised controlled trial. The Lancet. 2000 Jan 15;355(9199):185-91.

10. Croudace T, Evans J, Harrison G, Sharp DJ, Wilkinson E, McCann G, Spence M, Crilly C, Brindle L. Impact of the ICD-10 Primary Health Care (PHC) diagnostic and management guidelines for mental disorders on detection and outcome in primary care: cluster randomised controlled trial. The British Journal of Psychiatry. 2003 Jan;182(1):20-30.

11. Agius M, Biocina SM, Alptekin K, Rotstein V, Morselli P, Persaud A. Basic standards for management of patients with common mental illnesses in primary care. Psychiatria Danubina. 2005 Dec;17(3-4):205-20.

12. Burton C, Cameron I, Anderson N. Explaining the variation between practices in the duration of new antidepressant treatment: a database cohort study in primary care. British Journal of General Practice. 2015 Feb 1;65(631):e114-20.

13. Upton MW, Evans M, Goldberg DP, Sharp DJ. Evaluation of ICD-10 PHC mental health guidelines in detecting and managing depression within primary care. The British Journal of Psychiatry. 1999 Nov;175(5):476-82.

14. Simon GE, Von Korff M, Rutter CM, Peterson DA. Treatment process and outcomes for managed care patients receiving new antidepressant prescriptions from psychiatrists and primary care physicians. Archives of General Psychiatry. 2001 Apr 1;58(4):395-401.

15. Cheeta S, Schifano F, Oyefeso A, Webb L, Ghodse AH. Antidepressant-related deaths and antidepressant prescriptions in England and Wales, 1998–2000. The British Journal of Psychiatry. 2004 Jan;184(1):41-7.

16. Donovan S, Clayton A, Beeharry M, Jones S, Kirk C, Waters K, Gardner D, Faulding J, Madeley R. Deliberate self-harm and antidepressant drugs: Investigation of a possible link. The British Journal of Psychiatry. 2000 Dec;177(6):551-6.

17. Donahue J. Antidepressant use in primary care. In: Depression:Social and Economic Timebomb. ed. by Dawson A, Tylee A. BMJ Books; 2001. p. 151-156.

18. Donoghue J, Tylee A, Wildgust H. Cross sectional database analysis of antidepressant prescribing in general practice in the United Kingdom, 1993–5. BMJ. 1996 Oct 5;313(7061):861-2.

19. Burton C, Anderson N, Wilde K, Simpson CR. Factors associated with duration of new antidepressant treatment: analysis of a large primary care database. British Journal of General Practice. 2012 Feb 1;62(595):e104-12.

20. Tylee A. RCGP mental health management course. Journal of Primary Care Mental Health. 1999;1:13-4.

21. Agius M, Murphy CL, Win A, Zaman R, Tavormina G. Developing primary care treatment of depression. British Journal of General Practice. 2007;57(539):501-2.

22. Mann AH, Blizard R, Murray J, Smith JA, Botega N, MacDonald E, Wilkinson G. An evaluation of practice nurses working with general practitioners to treat people with depression. British Journal of General Practice. 1998 Jan 1;48(426):875-9.

23. Buszewicz M, Griffin M, McMahon EM, Walters K, King M. Practice nurse-led proactive care for chronic depression in primary care: a randomised controlled trial. The British Journal of Psychiatry. 2016 Apr;208(4):374-80.

24. Agius M, Murphy CL, Zaman R. Does shared care help in the treatment of depression. Psychiatria Danubina. 2010 Nov 1;22(Suppl 1):S18-22.

25. Agius M, Vyas V. Differences between training GPs to manage depression in primary care and issuing them with guidelines, and a system of collaborative care in the treatment of depression between primary and secondary care. Psychiatria Danubina. 2011 Sep 1;23(Suppl 1):S79-82.