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Placebo treatment in mild to moderate depression

Most patients with depression seen in primary care have mild to moderate depression. In trials these patients respond equally well to placebo as to pharmacologically active treatment. We discuss the role of placebo treatment in this situation.

An estimated 3 million people in the UK are currently depressed, with winter and the economic situation likely to increase this number. Even without screening for depression in primary care it is likely that more patients with sub-threshold to moderate depressive symptoms will require care.

A recent paper by Fournier and colleagues showed that the pharmacological management of mild and moderate depression is based on poor evidence. They, and others, found that for mild to moderate depression placebo is as effective as antidepressant treatment. Fournier and colleagues concluded that ‘there is little evidence to suggest that they produce specific pharmacological benefit for the majority of patients with fewer severe acute depressions.’1

Furthermore, in clinical care, patients with mild to moderate depression can be expected to have a better placebo than in clinical trials2 and the placebo response has been shown to persist over time.3

Current NICE guidance4 recommends sleep hygiene, active monitoring, and low-intensity psychosocial interventions are first-line treatment but access to psychological therapies remains a problem.

We believe that it should be possible to augment (not replace) these options with a drug that does not carry the risks of antidepressants, is significantly cheaper, and is equally effective for mild to moderate depression — a placebo.

Folic acid is essential for the synthesis of monoamines and may well be the most suitable placebo. It may even have intrinsic activity and is currently the subject of a randomised controlled trial as an augmenting treatment in moderate to severe depression.5

We recently recommended an approach to the safe use of placebo treatment6 and believe that for patients with mild to moderate depression who cannot access psychological therapies immediately, such an approach would be more honest, ethical, evidence-based, safer, and cheaper than the use of selective-serotonin reuptake inhibitors. The period when a patient is receiving sleep hygiene, active monitoring, and low-intensity psychosocial interventions should also be used for placebo treatment.

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Depression management

We feel the need to raise two key issues regarding the management of depression at a primary care level. First, the importance of recognising occult bipolar II disorder (depression with episodes of hypomania) in a primary care setting. Such patients often present with episodes of major depression and thus screening for symptoms of hypomania may be overlooked. Moreover, there may be a lack of recognition by the patient of their, often quite brief, hypomanic episodes particularly in their depressed state. The treatment for bipolar II disorder, however, differs significantly from that of patients with major depression: mood stabilisers versus antidepressants. Besides, treating bipolar II patients with the standard cocktail of antidepressants runs the risk of driving such individuals into rapid cycling and mixed affective states. Notably, these states are associated with a high risk of suicidality and hence the importance of not missing bipolar II disorder.

Second, there is a growing body of evidence suggesting the adoption of a collaborative (shared care) model in depression management. This involves the introduction of case managers (mental health workers who are responsible for regularly following up patients, offering psychotherapy, and medication management) working with GPs. From our own experience in Luton, we found the deployment of community mental health nurses in both the primary and secondary care settings acting as both case managers and as a liaison between both teams produced high levels of patient satisfaction, and GPs felt a reduced need for referral to specialist services.7 Such an approach to care would help to better manage potential occult bipolar II patients as well as the risk of patients running into mixed affective or rapid cycling states. Furthermore, there is strong evidence indicating the clinical effectiveness of collaborative care, with regard to short and long-term depression outcomes8 as well as cost savings9 for major episodes of depression. However, further randomised controlled trials in a UK setting would be

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needed to ratify the utility of adopting a collaborative care approach to depression and bipolar II disorder in the NHS.

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**Working with non-medical prescribers**

Your editorial on non-medical prescribers’ does not mention the huge problems the grass root GPs face on a daily basis, picking up the pieces after supplementary prescribers and some independent prescribers have decided to prescribe drugs to their patients. GPs are regularly requested to write out and print FP10s for community nursing teams, leg ulcer clinics, continence clinics, and the list goes on.1 They appear in large volumes throughout our day and many times GPs just generate prescriptions and sign them because there is no time to liaise with the relevant health professionals and verify their validity. There is pressure from patients and relatives who have been asked to collect their drugs from the GP and are often waiting in surgery. This is very frustrating and raises doubts about the safety of such prescribing. As the person signing the prescription is ultimately responsible, it is not fair to ask GPs to do this. If we are going to give this duty to other professionals, they should take full responsibility for their actions. GPs could be consulted but should not be left with a pile to process with no other information. This is sadly a routine practice in our area. I wonder what the experience of GPs elsewhere is?

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**Nudging**

We would like to challenge some of the points raised in Dr Fitzpatrick’s sceptical take on the ‘latest cult’ of ‘nudging’ the behaviour of the British public.1 In particular, we were surprised at his claim that behaviour contributes only marginally to most health problems. This is not the typical experience of many doctors in the NHS, who spend significant portions of their day dealing with the consequences of behaviours such as smoking, alcohol misuse, and poor diet. Neither is it reflected in morbidity and mortality figures that show the increasing impact of such behaviours on measures of health.2

We as doctors — whether we like it or not — are in the business of influencing behaviour. This may be in encouraging some behaviours (vaccination, cancer screening) and discouraging others (smoking, excess alcohol). While we may have developed a nuanced approach to influencing the behaviour of individuals that we have known for some time, it can be more challenging for policy makers seeking to influence the health behaviour of whole populations.

Unfortunately, despite five decades of research on how to influence behaviour, we are still faced with a short supply of effective interventions that can be used to tackle these problems.2 Insights from behavioural economics and the wider behavioural sciences now provide us with a powerful set of new and refined policy tools to use. Rather than being ‘pop psychology’ such insights are built on many years of robust and cross disciplinary work — more fully explored in the MINDSPACE report.3

We need to recognise that we face an increasing burden of disease related to the decisions we make. Introducing policies that better align behaviour with underlying intentions — while ultimately respecting an individuals autonomy4 — is, in our view, something worthy of fuller consideration.

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**Competing interests**
DK is a co-author of the MINDSPACE report.

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**Author’s response**

The world of general practice looks very different from the perspective of my surgery in Hackney than it does from the lofty heights of Imperial College. As it happens, I do not spend ‘significant portions’ of my day dealing with the consequences of smoking, alcohol, and poor diet. Most of my patients are children, older people, and