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Predicting and preventing relapse of depression in primary care

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Introduction

Depression is now the leading cause of disability worldwide (1). The majority of people with depression are managed in primary care (2). There has been a shift in the understanding of depression as a discrete or episodic illness to being considered a long-term relapsing-remitting condition with possibly incomplete recovery between episodes for some patients. The literature draws a distinction between relapse (the re-emergence of depressive symptoms following some level of remission, but preceding full recovery) and recurrence (the onset of a new episode of depression following recovery), recurrence rates being lower than relapse rates (3). This dichotomy may be more important to researchers and clinicians than it is to patients, who are likely to be less concerned with terminology and more concerned by the risk of "becoming unwell again" and what can be done to reduce this risk.

After treatment of the first episode of depression, approximately half of all patients will relapse, and this risk increases for every subsequent episode (70% and 90% after a second and third episode respectively) (4). A recent study of a cohort of patients who had received psychosocial treatment through the Improving Access to

Psychological Therapies (IAPT) service (5) showed that, of those who relapse, the majority (79%) do so within the first six months (6). There is also evidence to suggest that the severity of depression and resistance to treatment increases with each successive episode (7), so there are potential benefits of providing on-going care following remission, perhaps after the first episode, to prevent relapse and improve overall disease trajectory. This editorial examines the current evidence around relapse prevention in primary care before discussing the case for improved risk-stratification of patients and the implications that this would have for clinical practice.

Can relapse be prevented?

There are few studies looking at relapse prevention strategies specifically in a primary care setting (8); the vast majority of studies looking at relapse have been undertaken in secondary care. During the development of the most recent update to the Depression Guideline, NICE recommends that work be done to identify individuals at increased risk of relapse and provide relapse prevention strategies for these individuals (9).

Current relapse prevention interventions recommended by NICE are a minimum of two years treatment with antidepressant medication for patients who have had two or more episodes of depression; high-intensity mindfulness-based cognitive therapy (MBCT) for patients who have had three episodes or more of depression; and high-intensity individual cognitive behavioural therapy (CBT) for patients who have relapsed despite antidepressant medication (10). In more severe cases, patients are usually referred for specialist treatment where relapse prevention interventions can include further high-intensity psychological treatment and lithium augmentation of antidepressant medication. There is some evidence that acute treatment with electroconvulsive therapy (ECT) and an antidepressant is more effective at preventing relapse rather than antidepressant medication alone, although the NICE Guideline Committee recognised that the evidence for this was of low quality (9).

The availability and supply of psychological treatments as recommended by NICE is inadequate at present and it is possible that these interventions do not constitute

realistic treatment options in the real-world NHS (11). Evidence for their effectiveness and cost-effectiveness in a primary care setting is also lacking (9). Lessons need to be learned from trials of primary care-based relapse prevention interventions and novel feasible, scalable interventions are likely to be required to ensure effective implementation and improved outcomes for patients. More research is needed to better understand relapse prevention of depression in primary care to guide optimal allocation of interventions in practice.

Can relapse be predicted?

If relapse and remission of depression could be reliably predicted at the individual patient-level, then resources can be better targeted towards relapse prevention of depression and support precision medicine, i.e., tailoring of intervention decisions conditional on an individual predicted risk and response to treatment (12). This process requires prognosis research; specifically, the identification of prognostic factors and the development, validation and impact evaluation of prognostic models for outcome risk prediction. Prognosis is "the forecast of future outcomes for people with a particular disease or health condition" (12). A recent systematic review identified several prognostic factors associated with increased risk of relapse and recurrence in depression including: childhood adversity; recurrent depression; presence of residual symptoms; comorbid anxiety; rumination; neuroticism and age of onset of depression (13). In the UK, NICE currently highlights only a small number of these (in particular, number of previous depressive episodes and presence of residual depression symptoms) to guide prognostication in people with depression (10).

We are not yet at the point where we can reliably predict outcomes for a given patient with depression in primary care based on their demographic, clinical and disease-level characteristics. Single prognostic factors are seldom sufficient to effectively aid risk-stratification at the individual level. Rather, individualised outcome prediction is better shaped by using multiple prognostic factors in combination, to create a multivariable prognostic model (14). Such risk prediction tools are increasingly recommended by policymakers and, in general practice, can be successfully built into IT systems (15). A robust clinical tool to risk-stratify patients and then target relapse

prevention interventions to those at increased risk would be of significant benefit to patients, healthcare professionals and the NHS as a whole.

Implications for patients and practice

Improving risk-stratification and the allocation of relapse prevention interventions in primary care will involve discussion with patients about the risk of relapse and, for some patients, the framing of depression as a potentially chronic, on-going illness rather than something that can be "cured". Do patients want to have these discussions and is relapse something that concerns people with a lived experience of depression? Are such discussions required for all patients following a first episode of depression? How do clinicians decide when to adopt a chronic disease model of depression management and for which people aiming towards a more definitive treatment might be appropriate? Patient expectations and understanding may affect outcomes and so these are important questions to consider.

The majority of existing research addressing patient preferences has been in the context of discussions around antidepressants, with fear of relapse recognised as a barrier to patients discontinuing antidepressant medication (16) and some patients confusing relapse with discontinuation symptoms (17). Research has also shown that patients may not have full confidence in the GPs' ability to discuss discontinuation of antidepressants due to a perceived lack of knowledge and time (18). Interestingly, GPs felt that they did have sufficient knowledge to manage continuation therapy and would be more inclined to continue antidepressant medication in patients with a history of relapse (18). They did agree, however, that time constraints and a lack of evidence-based guidance on long-term depression management resulted in some patients being sub-optimally managed (18).

Another consideration is whether the results of risk predictions can be used and shared in a clear and helpful manner and result in improved outcomes or lower costs when applied. To be useful in practice, prognostic models must include unambiguous prognostic factors, address a common and important problem and have face validity (doctors must trust a model to guide their practice rather than their own experience) (19). It is possible that a statistical prediction tool aligns too closely with a biomedical

model of depression that does not fully describe the course of depression in many patients. It may be that, for some patients, we should be aiming to "minimise relapse" or "prolong remission" rather than to set the unrealistic goal of preventing relapse altogether. At the same time we recognise that, due to limitations imposed by the healthcare system, GPs must gather and synthesise information to aid clinical decision-making in a relatively short amount of time and a prognostic model could facilitate the identification and stratification of these different risk groups. The views and preferences of patients, healthcare professionals and commissioners certainly need to be more robustly explored.

We hope that this editorial will encourage GPs to reflect on how relapse is currently discussed in consultations with a patient with depression. We highlight the need for further research into risk-stratification and more effective relapse prevention for people with depression managed in primary care.

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