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Predicting and preventing relapse of depression in primary care

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Predicting and preventing relapse of depression in primary care

Andrew S Moriarty¹, Joanne Castleton², Simon Gilbody¹, Dean McMillan¹, Shehzad Ali^{1,4}, Richard D. Riley³, Carolyn A Chew-Graham³

1. Department of Health Sciences and the Hull York Medical School, University of York
2. Patient representative
3. Research Institute, Primary Care and Health Sciences, Keele University
4. Department of Epidemiology and Biostatistics, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada

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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

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

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23 There are few studies looking at relapse prevention strategies specifically in a primary
24 care setting (8); the vast majority of studies looking at relapse have been undertaken
25 in secondary care. During the development of the most recent update to the
26 Depression Guideline, NICE recommends that work be done to identify individuals at
27 increased risk of relapse and provide relapse prevention strategies for these
28 individuals (9).
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35 Current relapse prevention interventions recommended by NICE are a minimum of
36 two years treatment with antidepressant medication for patients who have had two or
37 more episodes of depression; high-intensity mindfulness-based cognitive therapy
38 (MBCT) for patients who have had three episodes or more of depression; and high-
39 intensity individual cognitive behavioural therapy (CBT) for patients who have
40 relapsed despite antidepressant medication (10). In more severe cases, patients are
41 usually referred for specialist treatment where relapse prevention interventions can
42 include further high-intensity psychological treatment and lithium augmentation of
43 antidepressant medication. There is some evidence that acute treatment with
44 electroconvulsive therapy (ECT) and an antidepressant is more effective at preventing
45 relapse rather than antidepressant medication alone, although the NICE Guideline
46 Committee recognised that the evidence for this was of low quality (9).
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57 The availability and supply of psychological treatments as recommended by NICE is
58 inadequate at present and it is possible that these interventions do not constitute
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3 realistic treatment options in the real-world NHS (11). Evidence for their
4 effectiveness and cost-effectiveness in a primary care setting is also lacking (9).
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6 Lessons need to be learned from trials of primary care-based relapse prevention
7 interventions and novel feasible, scalable interventions are likely to be required to
8 ensure effective implementation and improved outcomes for patients. More research
9 is needed to better understand relapse prevention of depression in primary care to
10 guide optimal allocation of interventions in practice.
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18 **Can relapse be predicted?**

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21 If relapse and remission of depression could be reliably predicted at the individual
22 patient-level, then resources can be better targeted towards relapse prevention of
23 depression and support precision medicine, i.e., tailoring of intervention decisions
24 conditional on an individual predicted risk and response to treatment (12). This
25 process requires prognosis research; specifically, the identification of prognostic
26 factors and the development, validation and impact evaluation of prognostic models
27 for outcome risk prediction. Prognosis is “the forecast of future outcomes for people
28 with a particular disease or health condition” (12). A recent systematic review
29 identified several prognostic factors associated with increased risk of relapse and
30 recurrence in depression including: childhood adversity; recurrent depression;
31 presence of residual symptoms; comorbid anxiety; rumination; neuroticism and age of
32 onset of depression (13). In the UK, NICE currently highlights only a small number
33 of these (in particular, number of previous depressive episodes and presence of
34 residual depression symptoms) to guide prognostication in people with depression
35 (10).
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47 We are not yet at the point where we can reliably predict outcomes for a given patient
48 with depression in primary care based on their demographic, clinical and disease-level
49 characteristics. Single prognostic factors are seldom sufficient to effectively aid risk-
50 stratification at the individual level. Rather, individualised outcome prediction is
51 better shaped by using multiple prognostic factors in combination, to create a
52 multivariable prognostic model (14). Such risk prediction tools are increasingly
53 recommended by policymakers and, in general practice, can be successfully built into
54 IT systems (15). A robust clinical tool to risk-stratify patients and then target relapse
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3 prevention interventions to those at increased risk would be of significant benefit to
4 patients, healthcare professionals and the NHS as a whole.
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10 **Implications for patients and practice**

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13 Improving risk-stratification and the allocation of relapse prevention interventions in
14 primary care will involve discussion with patients about the risk of relapse and, for
15 some patients, the framing of depression as a potentially chronic, on-going illness
16 rather than something that can be “cured”. Do patients want to have these discussions
17 and is relapse something that concerns people with a lived experience of depression?
18 Are such discussions required for all patients following a first episode of depression?
19 How do clinicians decide when to adopt a chronic disease model of depression
20 management and for which people aiming towards a more definitive treatment might
21 be appropriate? Patient expectations and understanding may affect outcomes and so
22 these are important questions to consider.
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31 The majority of existing research addressing patient preferences has been in the
32 context of discussions around antidepressants, with fear of relapse recognised as a
33 barrier to patients discontinuing antidepressant medication (16) and some patients
34 confusing relapse with discontinuation symptoms (17). Research has also shown that
35 patients may not have full confidence in the GPs’ ability to discuss discontinuation of
36 antidepressants due to a perceived lack of knowledge and time (18). Interestingly,
37 GPs felt that they did have sufficient knowledge to manage continuation therapy and
38 would be more inclined to continue antidepressant medication in patients with a
39 history of relapse (18). They did agree, however, that time constraints and a lack of
40 evidence-based guidance on long-term depression management resulted in some
41 patients being sub-optimally managed (18).
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51 Another consideration is whether the results of risk predictions can be used and
52 shared in a clear and helpful manner and result in improved outcomes or lower costs
53 when applied. To be useful in practice, prognostic models must include unambiguous
54 prognostic factors, address a common and important problem and have face validity
55 (doctors must trust a model to guide their practice rather than their own experience)
56 (19). It is possible that a statistical prediction tool aligns too closely with a biomedical
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3 model of depression that does not fully describe the course of depression in many
4 patients. It may be that, for some patients, we should be aiming to “minimise relapse”
5 or “prolong remission” rather than to set the unrealistic goal of preventing relapse
6 altogether. At the same time we recognise that, due to limitations imposed by the
7 healthcare system, GPs must gather and synthesise information to aid clinical
8 decision-making in a relatively short amount of time and a prognostic model could
9 facilitate the identification and stratification of these different risk groups. The views
10 and preferences of patients, healthcare professionals and commissioners certainly
11 need to be more robustly explored.
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20 We hope that this editorial will encourage GPs to reflect on how relapse is currently
21 discussed in consultations with a patient with depression. We highlight the need for
22 further research into risk-stratification and more effective relapse prevention for
23 people with depression managed in primary care.
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