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The role of relapse prevention for depression in collaborative care : a systematic review

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1 **Introduction**

2 Approximately half of patients will experience relapse or recurrence after their first episode
3 of depression and this risk increases to 70% and 90% after a second and third episode
4 respectively (Tylee et al., 2007). There is evidence that the severity of depression and
5 resistance to treatment increases with each successive episode of depression (Kendler et al.,
6 2000), highlighting the potential benefits of intervening early to prevent relapse and improve
7 the overall trajectory of depression.

8 Relapse and recurrence are both terms used to describe the reemergence of depression
9 symptoms following some level of improvement and to better conceptualise the distinction
10 between the two, we will first discuss the definitions of some other key terms: response,
11 remission and recovery. *Response* is a reduction in symptom severity (usually 50%) relative
12 to baseline, usually as a result of initial treatment. *Remission* can be thought of as a period of
13 time (usually 2 months or longer), following a response to treatment, during which patients
14 can be thought of as well but still “in episode”. *Recovery* follows an extended period of
15 remission (6-12 months) and at this point, patients are said to be no longer in episode
16 (Bockting et al., 2015). *Relapse* has been defined as the reemergence of depressive symptoms
17 following remission but preceding recovery and *recurrence* as the onset of a new episode of
18 depression after recovery (Frank et al., 1991). These definitions provide a useful theoretical
19 framework, although evidence for their clinical utility is lacking. They are helpful, however,
20 when considering the trajectory of depression and its treatment phases: those implemented
21 before any symptomatic improvement with a view to achieving remission (acute phase),
22 those employed after symptomatic improvement but before recovery (continuation phase) and
23 those that extend past the point of recovery (maintenance phase) (Bockting et al., 2015).

24 Given the wide variability in the way in which these terms relapse and recurrence have been
25 operationalized by researchers, Bockting et al. (2015) recommended using the terms
26 interchangeably to describe the “reemergence of symptoms following a period of relative
27 wellness”. Relapse prevention interventions, therefore, can be thought of as those aimed at
28 people with depression who have had symptomatic improvement and have entered the
29 continuation or maintenance phases or those applied during the acute phase with the intention
30 of exerting a protective effect against relapse or recurrence in the future (Bockting et al.,
31 2015). Most commonly they constitute a combination of continuation antidepressant
32 medication and psychological therapies. There have been only a small number of studies
33 exploring which relapse prevention interventions are most effective, particularly in a primary
34 care context (Gili et al., 2015; Rodgers et al., 2012).

35 Collaborative care is a framework, originally developed for chronic disease management, and
36 successfully used to optimise the provision and delivery of depression care. As such, it is best
37 thought of as a system level intervention rather than as a therapeutic intervention in and of
38 itself. Collaborative care incorporates the following four constituent parts to support the
39 delivery of depression interventions: i) multidisciplinary working with input from two or
40 more health care professionals, ii) structured evidenced-based case management, iii)
41 proactive and scheduled patient follow-up, and iv) enhanced inter-professional
42 communication systems (Gunn et al., 2006).

43 A Cochrane review of 79 RCTs showed that, compared with usual care or active control
44 groups, collaborative care is more effective for treating depression and anxiety in the short-
45 term (6 months or less) and that these effects persist into the longer term (13-24 months)
46 (Archer et al., 2012). Improvements in social functioning outcomes have also been
47 demonstrated in patients treated using a collaborative care approach compared with those

48 receiving usual care (Hudson et al., 2016). Further work has explored study-level factors,
49 and participant-level factors moderating treatment outcomes in the short term, for example
50 depression outcomes are improved where a psychological treatment was included in the
51 intervention (Coventry et al., 2014) and collaborative care has been shown to be effective
52 for patients with isolated depression as well as those with depression and chronic physical
53 conditions (Panagioti et al., 2016) As such, we have a good understanding of the
54 components driving acute phase response (up to 6 months in the case of these reviews).

55 It is important to be mindful of the risk of relapse and recurrence associated with depression
56 when developing and implementing interventions for people with depression. While the long-
57 term beneficial effects of collaborative care are well evidenced (Camacho et al., 2018), it is
58 unclear whether a focus on relapse prevention might account for this. We are now well
59 positioned, with a large number of trials of collaborative care, to identify and characterise
60 relapse prevention strategies to gain a better understanding of how these approaches might be
61 used in the context of implementing collaborative care.

62 In this review, we aim to better understand whether relapse prevention is a common and
63 key component of collaborative care. We describe the means by which relapse prevention
64 has been addressed in trials of collaborative care and how the principles of collaborative
65 care have been utilised to optimise the delivery of relapse prevention strategies.

66

67 **Methods**

68 This systematic review is reported in accordance with the Preferred Reporting Items for
69 Systematic Reviews and Meta-Analyses Statement (PRISMA) and was produced according

70 the Centre for Reviews and Dissemination guidance on systematic reviews for healthcare
71 (Centre for Reviews and Dissemination, 2009).

72

73 **Literature search**

74 The literature search was originally conducted for a Cochrane review (Archer et al., 2012)
75 and has been subsequently updated in December 2013, October 2016 and May 2017. This last
76 update added 1 study to the review.

77 The original review (Archer et al., 2012) searched the Cochrane Collaboration Depression,
78 Anxiety and Neurosis (CCDAN) group (now Common Mental Disorders group) trial register
79 on 9th February 2012. The CCDAN trial register comprehensively indexed trials registered to
80 MEDLINE, EMBASE, PsychINFO, CENTRAL, World Health Organisation's trials portal,
81 Clinicaltrials.gov, and CINAHL. The search was updated using the CENTRAL database in
82 December 2013 and to inform a subsequent meta-regression (Coventry et al., 2014). For the
83 current review, we updated the search using the CENTRAL database in October 2016 and in
84 May 2017. This method is considered a sufficient and cost-effective approach for the
85 systematic detection of RCTs of health care interventions (Royle and Waugh, 2005).

86

87 **Inclusion criteria**

88 We kept to the same inclusion criteria used in previous systematic reviews and meta-
89 regression analyses of collaborative care (Archer et al., 2012; Coventry et al., 2014). RCTs
90 were included if they met the following criteria:

91 *Participants:* Adults (aged 18 years or over) who met criteria (self-report or diagnostic
92 interview) for a diagnosis of depression or who had mixed anxiety and depression.

93 *Intervention:* Collaborative care must include all of the following four components (Gunn et
94 al., 2006):

- 95 a. A multidisciplinary approach to care delivery, defined as two or more health
96 care professionals, of which one must include a primary care provider.
- 97 b. A structured treatment plan delivered by a health care professional/case
98 manager who is not the patient's primary care provider. Treatment plans could
99 include pharmacotherapy and/or psychotherapy.
- 100 c. Scheduled and proactive patient follow-up consisting of one or more planned
101 sessions.
- 102 d. Enhanced inter-professional communication/support, for example: team
103 meetings, supervision from a senior health care professional/mental health
104 specialist.

105 *Comparator:* Usual care or enhanced usual care.

106 *Outcome:* Measured change in depression end of treatment outcomes using self-report
107 measures or diagnostic clinical interviews. Binary self-report depression outcomes may have
108 included either remission or reduction in depression symptoms according to a priori defined
109 threshold (e.g. $\geq 50\%$).

110 *Study Design:* Individual or cluster RCT, in primary or community setting. The original trial
111 report paper was in the English language.

112

113 **Study Selection**

114 For this review, eligible studies were identified for inclusion from a previous meta-regression
115 of 84 collaborative care RCTs for depression (Coventry et al., 2014). In addition, 3 authors
116 (JH, PC, RC) screened potentially eligible studies identified from CENTRAL search updates
117 against the above inclusion criteria, as described above.

118

119 **Other sources**

120 In addition to using the RCT report papers for details of intervention content, we contacted
121 the authors to request that they share any additional trial materials, particularly manuals used
122 to train the professionals implementing the intervention (provider manuals) and materials
123 given to patients to guide their self-management (patient workbooks). The aim was to
124 optimise the amount of information available for deriving a description of relapse prevention
125 strategies. We attempted to contact corresponding or other appropriate authors to request
126 materials up to a maximum of 3 times. In the absence of materials or where authors did not
127 reply, we accessed publically available protocols and companion papers that provided more
128 information on intervention content.

129

130 **Data extraction and synthesis**

131 We extracted data about intervention content (i.e. the commonly used relapse prevention
132 strategies and approaches reported by trialists) and intervention delivery (i.e. the ways in
133 which collaborative care facilitated the delivery of intervention content).

134 In terms of intervention content, we defined relapse prevention components as any that are
135 introduced after acute treatment has been successfully completed (once patients had reached
136 remission and entered the continuation phase, as defined by the investigators of the individual
137 trials), or that were applied during the acute phase with the intention of exerting a protective
138 effect against relapse in the future (Bockting et al., 2015). We identified four common relapse
139 prevention components *a priori*, on pragmatic grounds:

- 140 1. Formal relapse prevention planning: taking place either during the acute or
141 continuation phase;
- 142 2. Proactive symptom monitoring and follow-up beyond the acute phase;
- 143 3. Strategies to promote continuation medication adherence: occurring during the acute
144 or continuation phase, as long as focus was on long-term medication adherence and
145 relapse prevention rather than initial symptom improvement;
- 146 4. Psychological or psycho-educational treatments: again, these could be implemented
147 during the acute phase with a focus on strategies for relapse prevention or could be
148 implemented during the continuation phase (e.g. “booster” sessions).

149 Each trial was reviewed for information about the intervention content. We reviewed the
150 materials for each RCT and identified the components used in the intervention. Where relapse
151 prevention components were present, a descriptive paragraph was written on the approach
152 taken for each trial.

153 The intervention content was mapped to the four key components of collaborative care, as
154 described by Gunn et al. (2006), to better understand how collaborative care facilitates the
155 delivery of intervention content aimed at relapse prevention. By definition, all four
156 components were present in each trial and so we have recorded specifically where these

157 components have been used to facilitate relapse prevention. Results were validated and coded
158 by two independent reviewers per paper (AM, NC and OJF) and any disagreements were
159 referred to a third reviewer (DM).

160

161 **Risk of bias**

162 Risk of bias assessment has been undertaken and reported elsewhere for all included trials
163 using the Cochrane Collaboration's tool for assessing risk of bias in randomised trials
164 (Higgins et al., 2011).

165

166 **Results**

167 **Study selection**

168 In total, 93 RCTs of collaborative care for depression were identified for inclusion in this
169 review (see Figure 1 for PRISMA flow diagram outlining search). See Appendix 1 for
170 relevant study characteristics. 79 of these were identified for the original Cochrane review
171 (Archer et al., 2012), 5 were added in updated search in 2014 (Coventry et al., 2014), 8 were
172 added in the CENTRAL search update in October 2016 and 1 study was added during the
173 updated search in May 2017.

174

175 **[Figure 1: PRISMA Flow chart of included studies]**

176

177 After collating responses from authors and accessing materials online where they were
178 available, we identified additional trial materials for 44 (47.3%) of the 93 trials identified. Of
179 these 13 had a provider manual, 2 had a patient workbook and the remainder (n=29) had both.
180 For the trials where there were no materials available, we were able to gain further
181 information regarding intervention content from email correspondence with the authors of 7
182 of the trials and from reference to the original programme grant application for 1.
183 For the remaining trials (n=49), we consulted the main trial papers and any associated
184 publications.

185

186 **Data synthesis**

187 The relapse prevention components identified were: presence of a formal relapse prevention
188 plan (31 out of 93, 33.3%), active monitoring and follow up after the acute phase (42 out of
189 93, 45.2%), focus on medication adherence beyond the acute phase (39 out of 93, 41.9%) and
190 psychological therapies beyond the acute phase (20 out of 93, 21.5%).

191 RCTs of collaborative care for depression have addressed relapse prevention to varying
192 degrees. Table 1 maps the relapse prevention components used across trials. Table 2 provides
193 a description of the relapse prevention approach taken and how the collaborative care
194 framework has facilitated the delivery of these.

195 8 studies (Bogner and de Vries, 2008, 2010; Bogner et al., 2012; Dwight-Johnson et al.,
196 2010; Lerner et al., 2015; McCusker et al., 2008; McMahan et al., 2007; Menchetti et al.,
197 2013) focussed on acute-phase treatment and recovery, with very short-term follow-up and
198 no emphasis on relapse prevention. 2 studies (Adler et al., 2004; Finley et al., 2003) focussed

199 entirely on pharmacological interventions with medication maintenance primarily aimed at
200 short-term improvement and only indirectly targeted at relapse prevention.

201 Only 1 of the 93 trials (Katon et al., 2001) tested a collaborative care relapse prevention
202 intervention. In this trial, patients who had recovered after 8 weeks of antidepressant
203 treatment were randomised to usual care or a relapse prevention intervention, which consisted
204 of two primary care visits with a depression specialist and three telephone calls over a one-
205 year period. The intervention aimed to monitor symptoms, increase medication adherence
206 and involved the writing of a personalised relapse prevention plan. The usual care and
207 intervention groups had similar rates of relapse, although medication adherence was
208 significantly improved in the intervention group.

209 Others reported a significant focus on relapse prevention while primarily focussing on acute
210 treatment outcomes. Notably, the inclusion of relapse prevention in CADET (Clinical
211 effectiveness of collaborative care for treatment of depression in UK primary care), the
212 largest UK-based collaborative care trial, came directly from qualitative and public
213 involvement findings in the original development and feasibility trial. The original pilot trial
214 did not address relapse prevention until analysis of the acceptability data and subsequent
215 change to the protocol to account for the findings (Richards et al., 2009; 2013).

216 30 trials had no reported approach to relapse prevention, 21 had one approach only, 25
217 reported using two approaches, 5 reported three and 12 reported using all 4 relapse
218 prevention components. 9 studies (9.6%) reported outcomes beyond 12 months and only one
219 study (Katon et al., 2001) reported relapse data (Table 2).

220 **[Table 1: Summary of relapse prevention components used in each RCT]**

221

222 [Table 2: Description of relapse prevention approaches used in RCTs of collaborative
223 care]

224

225 *Intervention content: Relapse prevention components*

226 *Relapse prevention plan*

227 One third of the studies (n=31) reported that the professional administering the intervention
228 was trained to develop a formal relapse prevention plan with patients. All of the studies
229 reporting a relapse prevention plan went on to provide further details of what this entailed
230 (Bartels et al., 2004; Buszewicz et al., 2010, 2016; Ciechanowski et al., 2004, 2010; Coventry
231 et al., 2015; Datto et al., 2003; Davidson et al., 2013; Ell et al., 2008; Gilbody et al., 2017;
232 Grote et al., 2015; Huijbregts et al., 2013; Johnson et al., 2014; Katon et al., 1996, 2001,
233 2004, 2010; Ludman et al., 2007, 2016; Mavandadi et al., 2015; Oslin et al., 2003, Piette et
234 al., 2011; Richards 2008, 2012; Rollman et al., 2009; Ross et al., 2008; Salisbury et al., 2015;
235 Simon et al., 2004; Smit et al., 2005; Unutzer et al., 2002; Vlasveld et al., 2011). 5 of the
236 included studies used the Foundations for Integrated Care manuals (US Department of
237 Veterans Affairs, 2017) to guide the delivery of their intervention (Bartels et al., 2004; Datto
238 et al., 2003; Mavandadi et al., 2015; Oslin et al., 2003; Ross et al., 2008). The manuals advise
239 that patients are educated about risk of relapse and to make a plan for “relapse prevention
240 treatment”, including “reinforcing self-monitoring skills for signs of recurrence”. Patients are
241 encouraged to identify “personal” early warning signs of recurrence and individual triggers.
242 Self-care skills in the event of recurrence may include “calling friends or relatives, preparing
243 for stressful events by writing down a coping plan, pursuing interests, and continuing to take
244 medication as prescribed”. Patients are also given written instructions on when they should

245 consult a doctor (worsening PHQ-9 or GAD-7 scores, especially if scoring 14 or above,
246 unable to perform daily activities or thoughts of suicide).

247 The Collaborative Interventions for Circulation and Depression (COINCIDE) trial instructed
248 professionals and patients on following a “staying well” (Coventry et al., 2015) plan that
249 encouraged patients to identify protective factors and behaviours to implement these on a
250 long-term basis. Buszewicz et al. (2012, 2016) similarly advised professionals on the
251 importance of discussing relapse prevention with patients and identifying triggers, which
252 would put patients in “a better position to avoid relapse in the future or to seek help at an
253 early stage”. Ciechanowski et al. (2004, 2010) and Richards et al. (2009, 2013) gave patients
254 a written relapse prevention plan template with headings including “personal warning signs”
255 and “things that make me feel better”.

256

257 *Proactive monitoring and follow-up*

258 A number of the trials used proactive symptom monitoring and proactive follow-up, ranging
259 from informal follow-up to regular use of psychometric tools for tracking deterioration. The
260 Foundations for Integrated Care manuals (US Department of Veterans Affairs, 2017) strategy
261 was to follow up with the patient once a month, until they had gone for 3 months without
262 depressive symptoms, to obtain a PHQ-9 or GAD-7 score. There are specific instructions
263 within the healthcare professional manual that if a patient becomes symptomatic (defined as a
264 score above 10), they should then be reassessed in one week to determine if relapsing. If the
265 score remains elevated at that point, the treatment plan will be reassessed, including
266 discussion regarding adding pharmacological treatment if the patient is not already on this.

267 Ciechanowski et al., (2004, 2010) also had provision for monthly phone calls after the acute
268 phase with administration of the PHQ-9.

269 Coventry et al. (2015) made use of a RAG (Red, Amber, Green) system wherein patients
270 were encouraged to self-administer psychometric tools (in this case, the PHQ-9 or GAD-7)
271 and the score would correspond to traffic lights system. This would prompt the patient to take
272 no action, use the “action plan” and monitor their mood more closely or consider contacting a
273 health worker if above a specified threshold (“red”). The action plan recapped signs and
274 triggers of depression and reminded patients of details of their support network. Pyne et al.
275 (2011) used regular telephone monitoring once remission had been reached, although the
276 details of these were not reported. Others such as Ell et al. (2008) provided a robust
277 monitoring system with proactive telephone follow-up to monitor symptoms and in-person
278 visits if needed.

279 In the True Blue trial, conducted in Australian general practices, patients were monitored and
280 completed a PHQ-9 at 13-week intervals for 12 months. The authors of this trial explained
281 that the intervention was designed to be feasible in the Australian Medicare system and so the
282 follow-up periods were not “unrealistically regular” (Morgan et al., 2009).

283

284 *Medication maintenance*

285 Notable methods of ensuring medication maintenance were asking patients and reassuring
286 about side effects (Landis et al., 2007), ensuring longer term medication in those at higher
287 risk of relapse (Davidson et al., 2013) and offering an alternative antidepressant in the case of
288 relapse or where the medication is poorly tolerated (Kroenke et al., 2010). Capoccia et al.
289 (2014) and Finley et al. (2003) both trialled pharmacist-led collaborative care-based

290 interventions to promote medication adherence and address medication-related issues arising
291 throughout the maintenance and continuation phases.

292 Again, the Foundations for Integrated Care manuals (US Department of Veterans Affairs,
293 2017) had detailed information about the specific medication maintenance strategies used in
294 their trial. The manuals advise that if patients are assessed to be at low risk of relapse (fewer
295 than two prior episodes of depression and no history of dysthymia), they should complete 6 to
296 9 months and if at high risk (more than 2 episodes or history of dysthymia), they should
297 complete at least two years of antidepressant therapy. Katon et al. (1995, 1999) used active
298 monitoring of automated pharmacy data to monitor medication adherence during the
299 continuation phase (3-7 months) without monitoring for depressive symptoms.

300

301 *Psychological or psycho-educational treatments*

302 The final intervention component noted was the provision of psychotherapeutic or psycho-
303 educational approaches. Araya et al. (2003) provided a psycho-educational group as part of a
304 multi-component programme of treatment and these included “booster” sessions occurring
305 during the continuation phase at weeks 9 and 12 with a focus on relapse prevention
306 techniques. It was unclear from the trial paper what these techniques were. Oladeji et al.
307 (2015) similarly provided a programme consisting of psycho-education, problem-solving
308 therapy and activity scheduling and patients who improved (as measured by PHQ-9 scores)
309 were offered four fortnightly “top up talking therapies” for a period of 8 weeks.

310 Simon et al. (2004) offered an 8-session manualized cognitive behavioural therapy (CBT)-
311 based programme followed by three to four telephone relapse prevention sessions. Ludman et
312 al. (2007) similarly offered acute and “booster” psychotherapy sessions, focussing on

313 behavioural activation and identification and interruption of automatic negative thoughts.
314 Piette et al. (2011) offered counselling sessions monthly for nine months following the acute
315 phase to “minimize relapse”. Ell et al. (2008) provided on-going psychotherapeutic
316 approaches (behavioural activation and problem solving therapy) extending beyond the acute
317 phase.

318

319 ***Intervention delivery: Collaborative care components***

320 Gunn et al. (2006) outlined the four key characteristics of a collaborative care intervention: a
321 multidisciplinary approach to care delivery; structured treatment plan delivered by a health
322 care professional/case manager who is not the patient’s primary care provider; scheduled and
323 proactive patient follow-up consisting of one or more planned sessions; and enhanced inter-
324 professional communication/support.

325 Where collaborative care appears to be particularly well placed to address relapse prevention
326 is through its use of structured management plans, including an organised approach to
327 providing evidence-based treatments. Whether these are pharmacological or psychological or
328 a combination of both, they can be tailored to address relapse prevention in a standardised
329 and consistent manner and implemented either during the continuation phase or during the
330 acute phase with a view to maintaining longer-term health. The other key and recurring area
331 in which collaborative care seems to confer a particular benefit is its focus on scheduled
332 patient follow-up, particularly in the form of symptom monitoring and facilitating treatment
333 adherence.

334 Multi-professional approach and enhanced inter-professional communication have been less
335 explicitly employed as a means of facilitating the delivery of relapse prevention intervention

336 content. A multi-professional approach is key feature of collaborative care interventions, but
337 the way in which this has been used to optimise relapse prevention is not well documented.
338 Enhanced inter-professional communication includes strategies such as team meetings and
339 shared medical notes. The only trial to report using it in a way that facilitated relapse
340 prevention was Katon et al. (1999) which used the collaborative care framework to
341 implement a system wherein the psychiatrist reviewed monthly automated pharmacy data on
342 antidepressant refills to monitor the patient's adherence to the acute and continuation phases
343 of treatment and was able to alert the primary care physician if premature discontinuation of
344 medication occurred. It is possible and perhaps likely, however, that systems to facilitate
345 multi-professional working and enhanced communication have been a feature of relapse
346 prevention provision in collaborative care trials but have not been reported.

347

348 **Discussion**

349 This is the first systematic review to map the relapse prevention content of trials of
350 collaborative care for depression and to provide a description of the different strategies
351 employed. Overall, researchers have been inconsistent in their approaches and in the way that
352 interventions are reported and described in the literature. We identified 4 recurring relapse
353 prevention strategies or components across two thirds of the trials identified. The established
354 key features of collaborative care, particularly structured management plans and scheduled
355 patient follow-up, facilitated the delivery of these relapse prevention strategies.

356

357 *Implications for research and policy*

358 With its focus on multi-professional approach, proactive and structured follow-up and
359 enhanced inter-professional communication, collaborative care has potential advantages over
360 other methods for providing relapse prevention in depression. There are now a significant
361 number of collaborative care trials and the evidence base is such that new trials may not be an
362 efficient use of resources. The effectiveness of collaborative care on depression outcomes is
363 well established. However, relapse is an important issue and we need innovative research to
364 explore the impact of relapse prevention content. This might involve embedding studies of
365 relapse prevention in ongoing implementation of collaborative care.

366 Novel trial methods offer opportunities to trial the effectiveness of relapse prevention
367 components without the need for a conventional RCT. The Cohort Multiple Randomised
368 Controlled Trial (cmRCT) allows pragmatic trials of interventions on large numbers of
369 patients at a lower cost with more detail on longer-term outcomes derived from patients
370 within routine practice. The relapse prevention components of the interventions reported in
371 this review are of low intensity and are likely to be desirable to patients and well accepted,
372 overcoming the risk of patient non-compliance or refusal to accept interventions, which is
373 one of the key limitations of cmRCTs (Relton et al., 2010). The cmRCT model itself has been
374 shown to be acceptable to patients with depression (Richards et al., 2014). We recommend
375 that this approach be considered to enable to researchers to better assess the effectiveness of
376 the components described here in practice. For example, if patients with depression consented
377 to being in an “observational cohort”, they could then be randomised, once they have reached
378 remission, to receive a relapse prevention intervention (for example, a self-monitoring system
379 such as the Red, Amber, Green (RAG) system or maintenance phase booster
380 psychotherapeutic sessions) or indeed combinations of interventions. Routine outcome data

381 could be used to assess the effectiveness of different interventions over the long-term and this
382 evidence could be used to guide implementation in practice.

383 We have described the difficulty in extracting a description of the intervention content
384 pertaining to relapse prevention from the trial publications alone. The Template for
385 Intervention Description and Replication (TIDieR) checklist provides a framework for
386 reliably reporting intervention content (Hoffman et al., 2014). We recommend that
387 researchers use the TIDieR checklist when reporting intervention content, which would better
388 enable researchers to understand what was done. In the case of this review, more consistent
389 reporting and describing of interventions would enable researchers to adopt and incorporate
390 common intervention components when developing novel relapse prevention interventions
391 for implementation in practice.

392

393 *Implications and challenges for clinical practice*

394 If effectiveness of particular relapse prevention strategies can be demonstrated, then these
395 should be incorporated into collaborative care models in practice. Implementing these in, for
396 example a primary care setting, would require several key challenges to be addressed.

397 Whitebird et al. (2015) reported several key factors as being essential for successful
398 implementation of primary care models in practice. Several of these, such as the need for
399 strong leadership, a strong primary care physician champion and working with specialist
400 mental health teams, could involve the training and engagement of professionals already in
401 post, but others would involve increased upfront financial costs, such as the employment of
402 an on-site and accessible care manager. These costs could be commissioned at an individual
403 provider level or the costs of additional staff could be shared between providers. Cost-

404 effectiveness evaluation during trials could be used support and reinforce the longer-term
405 financial benefits of taking this approach. This is particularly important as “not seeing
406 operating costs as a barrier to participation” was another of Whitebird’s key factors driving
407 successful implementation of collaborative care and was associated with improved remission
408 rates at 6 months (Whitebird et al., 2015).

409 There is a growing role for digital health interventions in the treatment of depression, which
410 could provide an opportunity to support self-monitoring. Mobile apps exist which allow
411 patients to record and monitor their scores on validated tools such as the PHQ-9 and then
412 share the results with clinicians. However, there is as yet little evidence for the effectiveness
413 of these approaches (Hollis et al., 2017) and, while one can envisage versions of these apps
414 that would flag patients and allow them to re-enter the acute phase treatment early, they
415 would require formal assessment of clinical and cost-effectiveness in practice and would need
416 to be standardised and integrated into existing systems in order to be successfully
417 implemented.

418 Cross-sectorial working is also likely to be key, given that patients will leave therapy services
419 to be monitored in primary care and one of the challenges will be setting up lines of
420 communication between providers to track patient recovery (Winters et al., 2016).

421 Collaborative care is well placed to support enhanced modes of communication across
422 disciplines and sectors to facilitate more coordinated follow-up and it is important that we
423 evaluate how best to maintain such communication models after the acute phase of treatment.

424 We recommend that work be done around understanding how monitoring and recall can be
425 built into collaborative care protocols to ensure that interventions are more responsive to
426 patients at risk of relapse.

427

428 *Limitations*

429 A limitation of this work is that we did not receive manuals for the majority of trials and, as
430 such, were limited to describing the intervention components as published and supplemented
431 by accessory materials which were freely available online. Furthermore, of the trials
432 reviewed, most had at best medium term (12 month) follow-up and only a small number
433 reported longer-term (n=9; 9.6%) or relapse data (n=1). We have therefore been unable to
434 perform a quantitative analysis to explore the effectiveness of the relapse prevention
435 intervention components described in this review.

436

437 **Declaration of interest**

438 None

439

440

441

442 **References**

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