Maintaining recovery after depression: what are relapses and how might they be prevented?

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PhD thesis

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Declaration

I, Katherine Clarke, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Abstract

Depression is a prevalent and often disabling mental health condition, and relapses are of major concern for patients, health professionals and researchers. There are several interventions that, when offered after recovery from an episode of depression, can reduce the risk of relapse. The mechanisms by which these interventions operate are not well-understood. It may be that they target one part of what is a complex and interactive system, and there are several possible routes to relapse prevention. The PRotect intervention was developed to be offered after recovery from depression, and designed to provide people with self-help relapse prevention options in a brief format that would be practical for routine delivery in an NHS psychological therapies service. It focusses on increasing wellbeing and maintaining recovery, which in turn may reduce the risk that a person experiences a relapse. It was tested in a pilot randomised trial and was feasible to deliver. Participants reported changes in behaviour that they attributed to the intervention, and their clinical outcomes were better than those who were not offered the PRotect intervention, although the sample size was not large enough for effectiveness to be tested. Staff experienced the intervention as being different to their normal practice, with a focus on wellbeing and a 'level playing field' between clinicians and patients. The trial was small and was not powered to detect a significant difference in clinical outcomes, but the findings warrants consideration for testing in a full-scale trial.

Impact Statement

The work contained in this thesis has the potential for further impact as follows:

Inside academia: This thesis outlines the development and evaluation of a novel complex intervention to address a well-defined clinical need. The work begins by reviewing existing high-quality evidence, with recommendations for the design and eligibility criteria of future studies. In the design and development of the novel intervention, consideration was given to its feasibility for delivery and testing in an existing therapies service. This process is recommended for all applied health research to ensure participant time and research funding is not wasted on trials that are not feasible. In contrast to many other relapse prevention programs, this intervention focuses primarily on the promotion of health and wellbeing and potentially offers a new avenue for research in this area that may have transdiagnostic applications.

Several publications from this thesis are available to academics to build upon and critique, furthering our understanding of relapse and of depression (for details see 'Dissemination' section). Further publications that detail the experience of staff and service users could contribute to future intervention development within this health domain. The use of up-to-date guidance on good conduct of research (as detailed throughout) mean that researchers may look to this as examples of how this guidance can be used.

Outside academia: There is the potential for impact within clinical services in two ways. Firstly, the evidence base in the systematic review could be used to inform clinical guidance for the NHS (and has been used in updated NICE Guideline of the Treatment of Depression in Adults). Secondly the intervention developed in this thesis could be offered within NHS psychological therapies services. The pilot trial had positive outcomes, particularly in terms of the experience of staff and people who received the intervention. It is a brief intervention which is compatible with current approaches to the delivery of psychological interventions and given the brief training and supervision requirements is easily scalable.

The intervention was a finalist (one of three, and the only mental health intervention) in the ‘AbbVie Big Ideas for Better Health’ awards, category ‘Improving Self-management and Self-care’. The finals were held at the Houses of Parliament and opened by the Secretary of State for Health and Social Care. At the event, conversations with public policy makers and MPs focused on the shortlisted interventions’ focus on recovery and supporting wellbeing. This has the potential to have wider impacts within the health system that may be realised in the longer term.

Acknowledgements

This thesis was made possible through the support of countless people over several years. I would like to thank my colleagues (both past and present), and my supervisor Professor Stephen Pilling, for providing years of support, engaging conversations and practical help. I would also like to thank the staff of the IAPT service for their guidance and help with developing the intervention tested in this thesis, and the people who agreed to participate in the pilot trial of this intervention. I would also like to thank my friends, family and husband for their incredible patience, and my late father who would have been very proud of this work.

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List of Abbreviations

ADM:	Antidepressant Medication
CBT:	Cognitive Behavioural Therapy
CI:	Confidence Interval
CONSORT:	Consolidated Standards of Reporting Trials
DSM:	Diagnostic and Statistical Manual
GAD:	Generalised Anxiety Disorder
GP:	General Practitioner
HI:	High-Intensity
IAPT:	Improving Access to Psychological Therapies
IPT:	Interpersonal Psychotherapy
LI:	Low-Intensity
LIFE:	Longitudinal Interval Follow-up Evaluation
MBCT:	Mindfulness-Based Cognitive Therapy
MDD:	Major Depressive Disorder
MDE:	Major Depressive Episode
MRC:	Medical Research Council
NHS:	National Health Service
NICE:	National Institute for Health and Care Excellence
NNT:	Number Needed to Treat
NR:	Not Reported
OR:	Odds Ratio
PHQ:	Patient Health Questionnaire
PRISMA:	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PRotect:	Promoting Recovery, or Preventing Relapse
PSR:	Psychiatric Status Rating
PWP:	Psychological Wellbeing Practitioner
RCT:	Randomised Controlled Trial
RR:	Relative Risk
SPIRIT:	Standard Protocol Items: Recommendations for Interventional Trials
SD:	Standard Deviation
SMD:	Standard Mean Difference
TIDieR	Template for Intervention Description and Replication
TAU:	Treatment-As-Usual
UCL:	University College London
UK:	United Kingdom
USA	United States of America
WHO:	World Health Organisation
WSAS:	Work and Social Adjustment Scale

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Contributions

Katherine Clarke (KC), with the support and guidance of Professor Stephen Pilling (SP), designed and conducted the research in this thesis. KC drafted and SP reviewed all chapters.

The systematic review of relapse risk presented within Chapter 1 was conceived by Joshua Buckman (JB) and SP. KC helped to design the approach to meta-analysis, conduct the meta-analyses and review versions of the manuscript.

KC, SP and Evan Mayo-Wilson (EMW) designed the systematic review contained in Chapter 2 and wrote the publicly registered protocol. KC designed and wrote the search strategy, and KC and Jocelyne Kenny (JK) extracted data. Katie Greenfield for assisting with sifting references, data extraction and management. KC and Laura Gibbon assessed risk of bias. KC conducted the statistical analysis. KC drafted the paper and SP, EMW and JK contributed to interpretation. Rob Saunders and Ellie Bishop commented on a draft.

Staff of Camden and Islington NHS Psychological Therapies Services contributed to the design of the PRotect intervention (Chapter 4) through both formal consultation and informal conversations, and advised on trial procedures (Chapter 5). The workshop format used within those services was adapted for the PRotect intervention. Service-user groups and a focus group with members of the public advised on intervention content and delivery (including language used) during intervention development.

In terms of delivering the PRotect trial, Adam Gudalajtys and Alice Winters (AW) conducted randomisation. Shah Alam, Laura Franklin, Heather Grey, Ruhana Hussain, Pinar Marasli, Symone McEachron, Eleanor Popp, and Beth Pritty delivered the intervention and Shah Alam coordinated intervention delivery. They followed their usual risk procedures and supervision arrangements with additional supervision from KC. The recruitment process was supported by Assistant Psychologists in the IAPT services including Michelle Tse and Iona Kynaston. Lauren Becker provided their training in motivational interviewing techniques.

AW and Krupa Vakani facilitated the focus group of clinicians. KC analysed and Georgie Parker reviewed themes and illustrative quotes.

Ethical approval

The PRotect trial received Health Research Authority approval and NHS ethics approval. The trial was sponsored by the UCL Joint Research Office.

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Dissemination

Parts of chapter 1 have been published in the following review:

Buckman, J. E. J., Underwood, A., Clarke, K., Saunders, R., Hollon, S. D., Fearon, P., & Pilling, S. (2018). Risk factors for relapse and recurrence of depression in adults and how they operate: A four-phase systematic review and meta-synthesis. Clinical Psychology Review, 64, 13–38. https://doi.org/10.1016/j.cpr.2018.07.005

A version of Chapter 2 has been published in a peer-reviewed journal and presented at conferences. Details are as follows:

Clarke, K., Mayo-Wilson, E., Kenny, J., & Pilling, S. (2015). Can non-pharmacological interventions prevent relapse in adults who have recovered from depression? A systematic review and meta-analysis of randomised controlled trials. *Clinical Psychology Review*, *39*, 58–70. https://doi.org/10.1016/j.cpr.2015.04.002

Clarke, K., & Pilling, S. (2016). Staying well after depression: is there an alternative to medication? (Poster presentation). Mental Health & Dementia Research Showcase for CRN North Thames and NoCLOR. Royal College of General Practitioners. 17th February 2016

Clarke, K., & Pilling, S. (2016). Preventing relapse after depression: is MBCT the answer? (Invited Talk). Warwick Research Network Mindfulness Conference. Warwick University. 29th September 2016.

The intervention presented in Chapter 4 was a finalist in the AbbVie Big Ideas for Better Health awards.

I convened a symposium on 'Maintaining Recovery After Depression: Predicting and Preventing Relapses' and presented parts of Chapter 4,5 and 6 as part of this:

Clarke, K., (2019). Preventing Relapse After Depression Using the PRotect Brief Wellbeing Intervention (Symposium Presentation). The British Association for Behavioural and Cognitive Psychotherapies Annual Conference. Bath University. 4th September 2019.

Parts of Chapters 5 and 6 were presented at an international conference:

Clarke, K., & Pilling, S. (2018). PRotect after depression: a randomised pilot study of a brief wellbeing intervention (Poster presentation), *European Association of Behavioural and Cognitive Therapists,* 6th September 2018

I have also presented parts of Chapters 1-3 in Psychological Wellbeing Practitioner Diploma training at UCL on 20th January and 27th February 2014. I have regularly presented this work and its progress to patient advisory groups and to the IAPT service throughout.

Thesis overview

In this thesis I use a combination of research methods to explore and address the question:

“Maintaining recovery after depression: what are relapses and how might they be prevented?”

Chapter 1: Background and introduction

Chapter 1 provides some background to depression, its prevalence, and its importance as a global health problem. The classification of depression described has three key elements: the symptoms, the severity level, and the time-period. I detail existing approaches to changing the course of depression and justify why a focus on relapse prevention after recovery may be a worthwhile addition to tackling the burden of depression.

Chapter 2: Systematic review of relapse prevention interventions

Chapter 2 explores the evidence-base for relapse prevention interventions in the form of a systematic review. This included trials that randomly allocated participants, after recovery from depression, to be offered a non-pharmacological intervention or to be part of a comparison group. The meta-analysis suggests that psychological therapies delivered after completion of acute treatment can reduce the risk of relapse by around 22% in the following year (95% CI=15-29%), which is similar to the risk reduction in meta-analyses in the pharmacological domain. Only one study tested a psychological therapy adapted for accessibility or ease of implementation, which may be an important area for future development given the magnitude of the problem of relapse of depression and the current lack of routine relapse prevention work.

Chapter 3: A complex systems approach to relapse prevention

Chapter 3 develops a theoretical framework as to how the interventions in Chapter 2, and any future interventions may exert their influence. Some biological, psychological and social models of depression are summarised. These approaches may all offer valid models of the interrelated processes involved in depression but at different ‘levels of explanation’. Depression could be seen as an emergent phenomenon from a complex system, and as such

there may be multiple possible therapeutic targets for interventions, and a relapse preventive one may attempt to focus on long-term change. A cognitive neuropsychological model of the onset and maintenance of depression (proposed by Roiser, Elliott, & Sahakian, 2011) is used to provide potential intervention 'targets': the person's environmental influences, their information or affective biases and cognitive control, and their negative thoughts, and overall health.

Chapter 4: Development of the PRotect intervention

This chapter begins with an instantiation of the framework for relapse prevention that was developed in Chapter 3. This chapter reviews research that looks at ways in which people can:

- Provide a positive environmental influence on themselves (such as regular phone calls with friends, or adding pleasant items such as flowers into their physical environment).
- Address negative biases or improve cognitive control (perhaps through cognitive bias modification apps, mindfulness, or everyday activities like crossword puzzles).
- Increase 'positive' thoughts or actions (positive psychology tasks like writing a letter of gratitude, or having a positive impact on others such as through volunteering).
- Improve the health of the physical body, such as actively managing physical health problems, nutrition, self-care, and exercise.
- Form new habits which then have lasting preventive effects with the minimum of continued effort by following three steps derived from habit formation research.

The development of intervention materials and delivery methods included a consultation period with staff from a psychological therapies service, service user advisory groups, and a focus group of non-experts. The intervention's delivery methods and materials are described.

Chapter 5: Trial design

This chapter includes the design of a feasibility randomised controlled trial of the PRotect intervention, and the strategies used to establish referrals, deliver the intervention with fidelity, and encourage complete outcome measure collection. Participants were eligible after experiencing depression if completing treatment with the IAPT service, and if they consented

to participate were asked clinical and demographic questions, and further questions about their mental health after 3- and 6- months. The Protect intervention was delivered by existing staff from the IAPT service and intervention delivery was monitored. There was also an embedded qualitative study about experience of the intervention from study clinicians who were invited to take part in a focus group, and intervention and control arm participants were asked questions at the end of their final follow up phone call, all. I discuss the choice of trial delivery protocols and feasibility measures.

Chapter 6: Feasibility trial results

This chapter includes the results of the randomised controlled trial in terms of the feasibility outcomes: recruitment and retention of participants and intervention delivery; the clinical outcomes; and the experience of staff and participants. I report a preliminary data analysis that could be used in a future definitive randomised controlled trial, and comment on the suitability of the clinical outcome measures used and the data analysis methods. I report key themes from the qualitative interview and focus group data, and discuss their implications for the future development of the PRotect intervention.

Chapter 7: Discussion

The final chapter contains a discussion and critical analysis of this work. I outline the main findings, and provide some context for this work within related fields and as compared with recent developments in relapse prevention interventions. I discuss the strengths and limitations as well as implications of this work, and make three suggestions for our future understanding of depression and prevention of relapse.

Chapter 1 Introduction

Depression is a common disorder, and its consequences are significant. It has been estimated that there are over 300 million people with (unipolar) depressive disorder worldwide (Vos et al., 2016). It results in reduced life expectancy, and also results in the largest non-fatal burden of disease in the world (Üstün, Ayuso-Mateos, Chatterji, Mathers, & Murray, 2004, Whiteford et al., 2013). For those who experience depression the effects can be far-reaching. Writing in a blog post (Karen, 2018) for the national anti-stigma campaign 'Time to change', Karen describes the impact depression has on her:

> *"I feel like I've lost a lot of things to depression: time, energy, motivation. But none of these compares with the feeling that I lose myself and my identity when I'm depressed."*

Given the extent of suffering it is unsurprising that there are calls for the prevention and treatment of depression to be made a global public health priority (Whiteford et al., 2013).

Treatments for depression have the potential to help people to recover from what is a distressing and debilitating disorder. Both pharmacological and psychological therapies can be effective at treating depression, and are therefore offered by NHS services (NICE, 2010). In a single year costs of over £522 million were attributed to GP appointments, antidepressant medication prescriptions, and inpatient and outpatient secondary care for depression (House of Commons, 2010). NHS psychological therapies services are now established throughout England, and offer evidence based psychological therapies for depression and other common mental health problems (Clark, 2018). Despite this, there remains a large proportion of people who experience depression and do not receive adequate treatment (Kohn, Saxena, Levav, & Saraceno, 2004; Thornicroft et al., 2017; Wang et al., 2007).

The value of offering effective interventions that lead to recovery from depression is evident. In his ground-breaking memoir 'Darkness Visible', William Styron, the multi-award-winning American novelist, describes his experience of the end of a period of depression:

> *"Whoever has been restored to health has almost always been restored to the capacity for serenity and joy, and this may be indemnity enough for having endured the despair beyond despair."*

Styron remained free of depression for years, in which time he was able to campaign for more openness about mental health problems and to provide hope to people with depression (Cox, 2011). Yet ten years after leaving his hospital treatment, Styron suffered a catastrophic relapse with sudden onset. This episode endured for longer than his first, prevented his ability to function, and put him at serious risk of death by suicide. These deteriorations in the mental health of people who have recovered from depression are common (Buckman et al., 2018), and preventing them is of fundamental importance in addressing the problem of depression (Arean & Ayalon, 2010).

This thesis focusses on the ways that people may be able to maintain their wellbeing after recovery from depression. It takes an applied health approach: focussing on psychological and behavioural interventions that are feasible to offer to the large numbers of people recovering from depression, with the aim of reducing the suffering and costs associated with experiencing depression more than once. In order to provide some context, I first describe what is commonly understood by 'depression', its estimated prevalence and burden, and the difficulties in differentiating the contribution of first episodes and relapses in these figures.

Classification of depression

Depression falls within the diagnostic category of 'mood disorders' although it has behavioural, physical and cognitive aspects as well as emotional ones. People with depression tend to experience low mood, or a loss of pleasure or interest in everyday activities, and may withdraw from normal life. Physical symptoms such as pain and fatigue are often present. At the cognitive level, memory problems and biases in attention or

information processing are characteristic of the disorder, and have been the focus of a growing body of research into potential mechanisms through which depression develops (see Chapter 3).

To be diagnosed with depression a person must experience low mood, or a loss of interest or pleasure in everyday activities and experiences. Other symptoms include sleep disturbance, changes in appetite, decreased energy, thoughts of suicide, feelings of worthlessness or guilt, and difficulty thinking, concentrating or making decisions. If a person experiences five or more of these symptoms for more than two weeks, and their everyday functioning is sufficiently impaired, they may meet criteria for a major depressive episode (MDE). Diagnostic criteria and systems vary slightly, but the Diagnostic Statistical Manual (V) (which is commonly used in the clinical research studies) specifies the symptoms must continue for at least two weeks and affect nearly all activities (American Psychiatric Association, 2013). The ICD-10, a medical classification system used internationally, specifies similar criteria in terms of symptoms, impairment, and duration (World Health Organization, 1992).

Given these criteria, it would be possible for two people to report symptoms that do not overlap, and still both be diagnosed with depression. For example:

> Person A has been feeling low, tearful, and overwhelmed by the world. They are going to work but they feel worthless and like a failure. They wake up during the night every night worrying about work the next day, and wonder how they will get through it. They think about ending their life every day. No one at work thinks anything is wrong. It has been this bad for the past 3 weeks.
>
> Person B has no motivation. They cannot get out of bed in the morning, and have stopped seeing friends and family except for when one they come over unannounced. They have been eating more unhealthy food and have put on weight. This has been going on for 3 years.

As such depression is often considered a 'syndrome': *"a group of symptoms which consistently occur together, or a condition characterized by a set of associated symptoms"* (Oxford English Dictionary, 2018), rather than a unitary disorder with one probable cause and a common presentation. Diagnosis depends on clinical judgement using the criteria set out above. If a person experiences a major depressive episode (or more than one) without a history of manic, mixed, or hypomanic episodes, they may meet criteria for 'major depressive disorder' (MDD) (American Psychiatric Association, 2013). Although it is clinical practice to impose a threshold or 'cut-off' to differentiate between what is 'within the normal range', and what is 'depression', each of the dimensions described above lie on a continuum.

These systems of disease classification and diagnosis have both benefits and disadvantages, which have been discussed extensively in the literature (Harald & Gordon, 2012; Hegerl, 2014). It is practical to use self-reported symptoms to indicate disorder in clinical and research settings, particularly given the absence of any well-validated biomarkers. Of course, the specificity of the language used is limited: a person may report feeling 'fatigue' if they are having difficulty sleeping, and equally describe feeling 'fatigue' if they are constantly sleepy and have a difficulty staying awake (Hegerl, 2014). The system is therefore perhaps more practical than it is valid (Hegerl, 2014), and it probably does not reflect the aetiology of depression. The International Classification of Diseases describes its purpose as to *"provide a common language for reporting and monitoring diseases"* and to allow people *"to compare and share data in a consistent and standard way"* (Sutyak, 2013). It appears to meet this need for reporting and monitoring, such as when estimating the prevalence of depression across populations and across time, and subsequently in estimating the burden of disease.

Prevalence of depression

Depression has often been called the "common cold" of mental illness. There are various ways to describe exactly how 'common' depression is: the proportion of the population that experiences it at any single point in time (point prevalence), over a certain time-period (period prevalence), and at some point within the life course (lifetime prevalence). Inevitably with a

disorder such as depression, which can be experienced over long periods and can be experienced more than once, point prevalence estimates are lower than period and lifetime.

In terms of point prevalence, the most recent UK population survey on mental health and wellbeing found that 3.3% of the population met criteria for an episode of depression in any given week, with a further 7.8% meeting criteria for mixed anxiety and depression, and many more experiencing sub-threshold yet debilitating depressive symptoms (Stansfield et al., 2016). Population surveys, which randomly sample from the whole population (and not just people who have sought treatment), are perhaps our most accurate picture of the prevalence of depression. However, they are expensive and difficult to conduct: to minimise the effects of selection bias response rates of 80% or more are recommended (Evans, 1991), higher than the 57% response rate of the UK Psychiatric population survey (Stansfield et al., 2016).

Estimates of lifetime prevalence of depression can be varied. Reviewing epidemiological studies, Waraich et al (2004) estimated that the lifetime risk of having a major depressive episode is 6.7%, which seems low in relation to the one-week prevalence of 3.3% reported in the UK population survey. It is likely an underestimate as people were not surveyed at the end of their lives, and so episodes of depression that occurred after data collection would not have been included: I would argue they are perhaps better described as 'life-so-far' estimates. There is evidence that if the years up to death are considered, estimates of prevalence are much higher. Kruijshaar et al., (2005) modelled this and found that approximately 30% of men and 40% of women in samples from the Netherlands and Australia would experience one or more episodes of depression at some point in their lifetime. There is evidence that use of prospective rather than retrospective data collection (which relies on accurate recall of experiences of depression over long time periods) also increases prevalence estimates. One study found this almost doubled rates of 1 year prevalence, and suggested that experience of DSM-defined depression by age 32 may be as high as 41.4% (Moffitt et al., 2010).

These figures serve to highlight that depression is common, but that accurate estimates of its prevalence are difficult to collect both at a single point in time and over longer time periods. This provides a challenge to public health, particularly when attempting to provide accurate

and comparable estimates of the impact of health problems in different countries and over different time periods. The 'Global Burden of Disease' study was set up to attempt to address this challenge, and uses the most accurate point prevalence estimates that are available across health conditions (Lopez & Murray, 1998). They then use a consistent method to derive reliable and comparable estimates of burden of disease across disorders and countries (Prüss-Üstün et al., 2003).

Burden of disease

The World Health Organization has estimated that depression would be the second biggest cause of burden of disease by 2020 (Lopez & Murray, 1998) and the first by 2030 (Mathers, Fat, & Boerma, 2008). The functional impairment core to a depression diagnosis involves decreased physical, social and role functioning (Wells et al., 1989). Depression has been the biggest cause of years lived with disability in the world for a number of years (Murray & Lopez, 1997), perhaps due to its potential for prolonged and repeated impact during years commonly filled with work and family responsibilities (Vos et al., 2012). People with depression are also at increased risk of premature death from a range of physical health problems (Chesney, Goodwin, & Fazel, 2014).

Disease burden is derived from a consideration of several components: classical burden (residual symptoms, cognitive impairment, relapse and recurrence, decreased quality of life), morbidity and mortality burden (e.g. increased risk of suicide, cardio and cerebrovascular disease), disability burden (e.g. psychosocial impairment, work days lost), family burden and a wider economic burden (Lépine & Briley, 2011). The burden of depression, in contrast to a disease which has high initial costs, seems to be spread throughout episodes, and may even increase in later episodes of depression (Lépine & Briley, 2011). Most estimates of burden of disease do not take this into account. For example, the World Health Organisation disease burden estimates are a cross-sectional picture of disease burden, and therefore treat each episode of depression as a single statistically independent 'unit'. If risk of relapse increases with each episode experienced (e.g. (Mueller et al., 1999; Solomon et al., 2000), an effective relapse prevention intervention could offset a large proportion of the burden of disease. One

large Australian cohort study examined ‘remission’ rates for 5 years after an episode of major depression, and found that maintenance ADM and maintenance CBT could avert 50% and 52% respectively of disease burden (Vos et al., 2004). This serves to highlight the importance of relapse prevention: not as an optional addition to effective treatment, but as a core part of tackling depression.

Course of depression

The age of onset, and characteristics of major depressive disorder vary considerably from person to person, but the average age of onset is in the mid-20s, and average length of an episode is 4-6 months (Semple & Smyth, 2013). Depression can follow different courses: a person may recover and remain well, recover and become ill again one or multiple times, or never recover. It is sometimes estimated that around 50% of people who experience an episode of depression recover and remain well, 35% recover and become ill again in the future, and the remaining 15% have a chronic or unremitting depression (NICE, 2010). Many people who would be considered to have recovered still have some ‘residual’ symptoms (depression symptoms which remain), which are a risk factor for further episodes (Buckman et al., 2018). A further group of people have depressive symptoms that are debilitating but do not reach the threshold to be diagnosed with a major depressive episode (although they may reach the threshold for a dysthymia diagnosis). Within this thesis I focus on the approximately 85% of people who recover from their episode of depression, and consider what can be done to improve the chances that they remain in recovery.

The problem of how exactly to characterise the course of depression has been the subject of considerable debate over several decades. For the majority of this thesis I describe whether a person is ‘in episode’ or ‘out of episode’ according to the depression classification systems described earlier in this chapter, and any episode following partial or full recovery from depression is be described as a relapse (Richards & Perri, 2010). I specify wherever possible the three dimensions that make up the depression classification system: the symptoms, severity or level of impairment, and time period, with the aim of providing a replicable description of a person’s depression. The risk of using one ‘label’ is that these could be

defined and operationalised in different ways, therefore making two groups of people seem to be experiencing the same when they are not. For example, I may note in study A people were in ‘partial’ recovery (score on ‘measure A’ below threshold for 12 weeks), and in study B they were in ‘partial’ recovery (score on ‘measure B’ reduced by 30% at a single assessment).

The terms ‘relapse’ and ‘recurrence’ are often used within depression literature but I will use the term ‘relapse’ to encompass both: to describe any clinical episode of depression following recovery. Wherever possible I will include details of exactly how this episode of depression was measured. To support this decision, I will now provide some background on the origins and challenges of differentiating between relapse and recurrence (and remission and recovery) in this field.

Origins of the relapse recurrence distinction

The proposed distinction between the term relapse (for an episode of depression soon after recovery which is perhaps a reversion back into the original episode), and recurrence (for an episode that occurs a significant period of time after recovery and is perhaps an entirely new episode), was originally suggested by Frank and colleagues more than three decades ago (Frank et al., 1991). The work by Frank and colleagues was based on a review that found that there were many different terms used to describe the course of depression and that these terms were defined and operationalised in different ways (Prien, Carpenter, & Kupfer, 1991).

In their original review (Prien et al., 1991) identified an important an issue with the clarity by which people described the course of depression. They looked at research into unipolar depression in selected journals over a two-year period, and found that authors used 64 different terms to describe it’s course over time (Prien et al., 1991). The most common terms in long-term study reports were ‘relapse’ (in 10 reports), ‘response’ (or ‘responder’), ‘remission’ or ‘recovery’ (in 8). Interestingly no articles used the term ‘recurrence’. There was a further problem, in that even when authors did use common terms, their definition and operationalisation was inconsistent. For example, to indicate ‘recovery’ some used cut-offs

on depression rating scales, some used a percentage change in score on a depression scale, some used functional criteria such as a person's ability to complete everyday activities, and others would use length of time without hospital admission.

Following this review, Frank and colleagues proposed a conceptual framework by which to build consistent definitions and operationalisations of key terms in depression (Frank et al., 1991). The principles underlying their approach were: 1. to look at observable phenomena, 2. to describe the course of depression irrespective of treatment, and 3. to focus on the lifetime of the person rather than a single episode. This approach is now widely accepted and is one I largely adopt in this thesis (particularly in terms of point 1 and 3).

Frank et al., (1991) also suggest terms that might be used to describe the course of depression. They suggest differentiating between stages of recovery: using the word 'remission' to indicate reduction of symptoms to below the diagnostic threshold for depression for a brief time, and 'recovery' to indicate remission that lasted for a longer period. Similarly, a 'relapse' would denote an episode of depression occurring during remission, and 'recurrence' an episode that followed recovery.

The terms relapse and recurrence now have more widespread use than before 1991, a fact easily illustrated by the fact that the term 'recurrence' is now in common use, but was not used in any of the studies that Prien and colleagues identified. However, there remains an important issue that the key 'difference' between the terms, the length of time spent in remission/recovery, remains varied, and can sometimes overlap. For example, one study uses the term 'relapse' throughout an entire 6 month study (Ali et al., 2017) and another used the term 'recurrence' after 8 weeks (Solomon et al., 2000), episodes of depression between 8 weeks and 6 months are in the first study be labelled as relapses and in the second, recurrences. The lack of consistency in the use of the terms, and in the distinction between relapse and recurrence, means that to ensure clarity, researchers must still define how they are using the terms.

Frank and colleagues strongly recommended that studies should be conducted to test the validity and utility of the distinction between remission and recovery, and that empirical work must be conducted to decide the appropriate length of time where ‘remission’ becomes ‘recovery’ (Frank et al., 1991). Rather than specifying and defining these terms, they were suggesting a framework by which consistent, empirically supported definitions of key change points within the course of depression could be developed. Yet despite this, the distinction between relapse and recurrence still does not have clear empirical support. When Frank and colleagues met to review progress ten years after proposing their framework, they commented that it had not received the empirical testing that they had recommended (Rush et al., 2006). Indeed, some have argued that the distinction between ‘relapse’ and a ‘recurrence’ is in fact not supported by evidence from intervention trials (Richards & Perri, 2010), and there is no evidence of a dimensional shift between, say, a relapse at 5 months, and a recurrence at 7 months. There is, however, evidence to suggest a continuous change in the period following an episode of depression, and a gradual reduction in risk of a further episode (Buckman et al., 2018). Other factors such as the level of residual symptoms are perhaps as important when predicting further episodes of depression as the time spent in recovery (Buckman et al., 2018).

It appears that as well as being potentially misleading and lacking empirical support, the distinction may difficult to use in practice. Indeed, a recent review of the lifetime approach to depressive disorder initially describes and advocates for the use of distinct terms for relapse and recurrence, but then reverts to using the broader ‘relapse/recurrence’ summary term to describe the majority of research (Bockting et al., 2015). It is difficult to do otherwise, given the continued lack of consistency over the use of the terms. I take a similar approach but simply use the word ‘relapse’, which has a common English meaning, as my summary term.

> *Relapse: (of a sick or injured person) deteriorate after a period of improvement.* (Oxford English Dictionary, 2018)

Risk of relapse

People have different experiences after recovery from depression. Estimates of the exact proportion of people who go on to relapse are varied. This may be in part due to different baseline risks of relapse in the study population. There are also methodological difficulties in producing accurate estimates (similar to those detailed above in estimating lifetime risk of depression): namely that recall is not accurate, and estimates are highly dependent on when data is collected if retrospective, or the length of follow-up if prospective. In one of the first studies that attempted to quantify the risk of relapse, in a cohort from the 1950s (Angst et al., 1973), the authors commented that *"the number of episodes observed depends in the first instance on the duration of observation".* They found that the longer their follow-up, the less likely they were to find anyone had only a single episode of depression. In this group the chances of only having one episode were 'vanishingly small' when they followed their sample for 15 years. Of course, this was only one sample, and their entry to the study was when in an acute psychiatric ward, so could be a group who had particularly severe depression.

Of course, as described previously, prospective longitudinal studies with long periods of follow-up are difficult to conduct, expensive, and loss to follow-up can put the validity of an estimate of the proportion of people who will relapse in their lifetime, into question. What these studies can provide, is information about who may be more or less likely to relapse depending on certain measured characteristics, by comparing people who relapse and who don't within each cohort. I collaborated with colleagues on a systematic review and meta-analysis of prospective cohort studies which a) collected baseline data on factors which might be associated with relapse, and b) included at least 100 participants who relapsed during follow-up (Buckman et al., 2018).

Factors associated with increased risk of relapse

We sought to pool information from several prospective cohort studies in order to identify which factors were associated with an increased risk of relapse in those who have experienced an episode of depression (Buckman et al., 2018) Five large mental health cohorts were identified that continuously assessed their populations' depression symptoms throughout the (minimum one year) follow-up period. These studies measured eleven

potential factors that might be linked with relapse. I summarise those which were identified to have the strongest evidence linking them with relapse risk, although of course there may be other important factors which were not (or were less frequently) monitored.

I have grouped the factors that were identified as linked to relapse in to three categories. The first, 'current clinical factors' includes any depressive symptoms that remain following an episode of depression (residual symptoms) and any other mental or physical health conditions that the person has (comorbid disorders). The second, 'clinical history', includes the number of episodes of depression the person had previously experienced, and the length and severity of these episodes. The final category, 'life events' includes a history of childhood maltreatment.

1. Current clinical factors:

- All the studies that examined **residual symptoms,** found evidence of increased risk of relapse in those with higher levels of residual symptoms. In a meta-analysis of data from 3 studies (Judd et al., 1998; Spinhoven et al., 2016; Wang et al., 2014), the odds of experiencing a relapse in those who had residual symptoms (compared to those without them) was 2.77 (95% CI 2.08-6.68).
- **Comorbid disorders** were found to be associated with higher risk of relapse. Anxiety disorders were the most often associated (OR=1.74, 95% CI= 1.37 to 2.22), and there was some evidence for an association of multiple physical symptoms, chronic pain, comorbid physical health problems, and avoidant personality disorder.

2. Clinical history:

- There was evidence that the **experiencing previous episodes of depression** was related to increased risk of relapse. The odds of experiencing an episode of depression during the follow-up period was higher if you had experienced any previous depression (OR=1.69, 95% CI 1.28 to 2.24, Hardeveld 2014 and Mueller 1999), and higher if you had had experienced more than 3 previous episodes

compared with less than 3 (OR=1.99, 95% CI=1.33-2.97, Gopinath 2007 and Mueller 1999).

- In most cohorts there was an association between **more severe and lengthy acute episodes of depression,** and higher risk of relapse. More severe symptomatology was associated with higher risk of relapse in 3 of 4 cohorts, as well as longer duration of a prior episode in the 2 that examined this.
- There were some other aspects of clinical history, such as the age of initial onset of depression, which may impact risk of relapse, although evidence here was mixed.

3. Life events

- A **history of childhood maltreatment** was associated with greater risk of recurrence in all of the cohorts where it was assessed (Gopinath et al., 2007; Hardeveld et al., 2013a; Hardeveld et al., 2014; Hardeveld et al., 2015; Wang et al., 2014). The odds ratio for this was 1.50 (95% CI 1.27 to 1.77).

Given that these factors influence risk of relapse and therefore may moderate the efficacy of relapse prevention interventions, they are included in a conceptual framework for the review of the efficacy of relapse prevention interventions in Chapter 2. Of course, further factors may influence risk of relapse but were not measured in the trials in the review detailed here. For example: stressful life events may be strongly associated with first episodes of depression, but this link decreases with each subsequent episode (Kendler et al., 2000).

This review addressed some of the concerns about methodological confounders that I have discussed in this chapter and used a consistent method to combine data. Data were collected from studies of similar design: ones that recruited participants who had an episode of depression, used prospective data collection over the course of at least one year, used continuous measurement of outcomes, and that had at least 100 relapses within the follow-up period. Of course, the potential to pick up repeated episodes of depression is contingent on follow-up duration. One of the studies reviewed here followed people for 15 years (Mueller et al., 1999) but the rest were between one and five years (Gopinath et al., 2007; Hardeveld

et al., 2014) . As I have explored previously, recall of prior episodes over longer time periods is not particularly accurate.

Although the associations described above may indicate who is more likely to relapse, they are limited in their power to explain *why* this is. There are some associations that seem logical. It makes sense that people who nearly meet the threshold for depression (those with high levels of residual symptoms), are more likely to cross that threshold into depression than those who have fewer symptoms. The mechanisms by which people with comorbid disorders may be at increased likelihood of relapse are probably complex and bi-directional.

The fact that more previous episodes of depression that are longer or greater severity increases risk of relapse suggests the possibility that the experience of depression itself may increase the likelihood of future episodes. The 'scar' hypothesis, suggests relapses may be due to the long-term psychological and cognitive effects of depression (Zeiss & Lewinsohn, 1988), and the 'kindling' hypothesis suggests that they may be a function of neurocognitive changes arising during the course of depression (Monroe & Harkness, 2005). These hypotheses are consistent with the finding that life events are less likely to precipitate episodes of depression as more episodes are experienced (Kendler, Thornton, & Gardner, 2000). It is possible that the neural pathways associated with depression become stronger during a depressive episode (Vidailhet, 2010), although attempts to demonstrate a 'scar' at a psychological level have not always been successful (Beevers, Rohde, Stice, & Nolen-Hoeksema, 2007). Other life experiences, such as childhood trauma may result in a long-term vulnerability (e.g. Vythilingam et al., 2002).

It is probable that there are many factors at play rather than there being a unitary cause of relapse. I explore these issues in detail in Chapter 3. It is likely that biological factors (including genetics), psychological factors and cognitive biases, and social factors all play a role (Fava & Sonino, 2008). If the experience of depression can indeed increase risk of relapse, it follows that an extended period of recovery may itself have a protective impact.

Are all depressive episodes the same?

Models of depression often treat all depressive episodes as ‘equal’ or comparable and do not comment on whether the person has been depressed before. In clinical practice there are no routine differences in how first and subsequent episodes are treated (NICE, 2010). But there is evidence of differences between first and subsequent episodes of depression which may be of importance when considering the focus of this thesis on relapse (and not primary) prevention of depression. Above I have summarised the risk factors associated with increased risk of relapse in those who have experienced an episode of depression (from Buckman et al., 2018). Now I will do something slightly different, and detail some research studies which have decoupled first and subsequent episodes. Of course, a significant proportion of the ‘first-episode’ depressive patients in these studies then go on to become recurrent, so any differences identified may be underestimates.

This evidence is not possible to derive from prospective cohort studies that began before any episode of depression. Eaton et al., (2008) conducted such a study, but of their sample of 2085 people from the general population, they identified only 92 with an episode of depression at some point during the 23- year study period. Of these people, 50% remained well following their episode, and the other 50% had one or more further episodes. So in the absence of large, population based, lengthy cohort studies I consider three areas of evidence that suggest that index and subsequent episodes of depression may have important differences. The first: risk factors, is any variable associated with risk of the depressive episode in question. The second is the clinical characteristics, or features of the depressive episode. The third is in their response to treatment or intervention.

Socioeconomic factors may predict first episodes, whereas clinical characteristics may be more important for relapses. In a systematic review of the prevalence and predictors of recurrence of major depressive disorder, Hardeveld et al. (2010) found that the most important predictors of relapse were number of previous depressive episodes and subclinical residual symptoms: clinical factors, whereas socioeconomic ones were more important to predict first episodes. "*Demographic factors such as gender, SES, and civil status, which are risk factors for the onset of the first depressive episode …do not appear to predict recurrence*

after recovery." pp. 189. Similarly it seems that, although women have a greater risk of experiencing depression than men, risk of chronicity and relapse is perhaps equal among men and women (Kessler et al. 1993).

Major life events predict first episodes but may be less so for relapses. Monroe and Harkness (2005) review evidence about precipitants of (risk factors that occur before) depressive episodes. They found that a major life event (*major upheavals in life, such as primary relationship losses, deaths of significant others, serious illnesses, major problems with children, loss of permanent employment, and so on, pp418*) is a key precipitant of first episodes of depression, but this relationship decreases as the number of episodes of depression you have experienced increases. A dose response relationship is a key criteria for assessing the likelihood of causality within an epidemiological or public health approach (Bradford-Hill, 1965), and so this provides evidence for life stress to be a causal factor related to depression.

There are differences in the clinical characteristics of first and subsequent depressive episodes. Roca et al examined clinical differences between first and recurrent episodes in depressive patients (Roca et al., 2011) They found that rates and severity of somatic symptoms increase with more episodes. This could be linked to the higher prevalence of physical disorders in recurrently depressed patients. A limitation of the study they describe is that with such a large sample it is possible for small differences that may have no clinical importance to be identified as significant. There also may be more cognitive deficits in recurrent depression compared to first episode. Karabekiroğlu, Topçuoğlu, & Gönentür (2010) gave executive function tests to first episode sufferers of depression, recurrent sufferers and healthy controls. Patients with depression exhibited worse performance in all tests than controls. Recurrent depressed patients had significantly more perseveration tendency in Wisconsin Card Sorting Task, and significantly worse performance in word production (Lee et al., 2012).

Treatment response may be different in first and subsequent episodes. Some interventions seem to *work* differently depending on the number of previous episodes a person has experienced. For example, a review found that Mindfulness-Based Cognitive Therapy (MBCT) significantly reduced the risk of relapse/recurrence among those with three or more previous episodes of major depressive disorder (MDD) compared to treatment as usual (TAU) or placebo + clinical management (Piet & Hougaard, 2011). Bockting et al. (2006) found that number of previous episodes was a predictor of response to preventive cognitive therapy in recurrent depression. If they show different responses to the same treatment, this is evidence that episodes may 'behave' differently, adding to the correlational observations detailed in the previous two sections. This is an important area of evidence for the distinction between first and subsequent episodes- if they ‘act’ different rather than just ‘looking’ different.

I have highlighted some key areas where first episodes of depression may be predicted by different factors, precipitated by different events, and may look and act different to subsequent episodes. The experience of having depression may cause changes which means that the person is more susceptible to subsequent episodes (Vidailhet, 2010). Models that consider any episode of depression to be equal or comparable may miss some important considerations for the field of relapse prevention. Complex systems theory may provide an additional framework by which to incorporate these qualities into a relapse prevention intervention, which I explore further in Chapter 3.

Changing the course of depression

This chapter has so far described work classifying what is meant by depression, how we describe parts of the course of depression, and how relapses may present a different problem to first episodes of depression. I will now discuss the primary aim of clinical psychology and mental health research, which is to effect change in the course of depression through interventions. The Institute of Medicine has suggested three ‘levels of interventions’: prevention (including universal, selected and indicated prevention), treatment, and maintenance (40, see Figure 1, Haggerty & Mrazek, 1994).

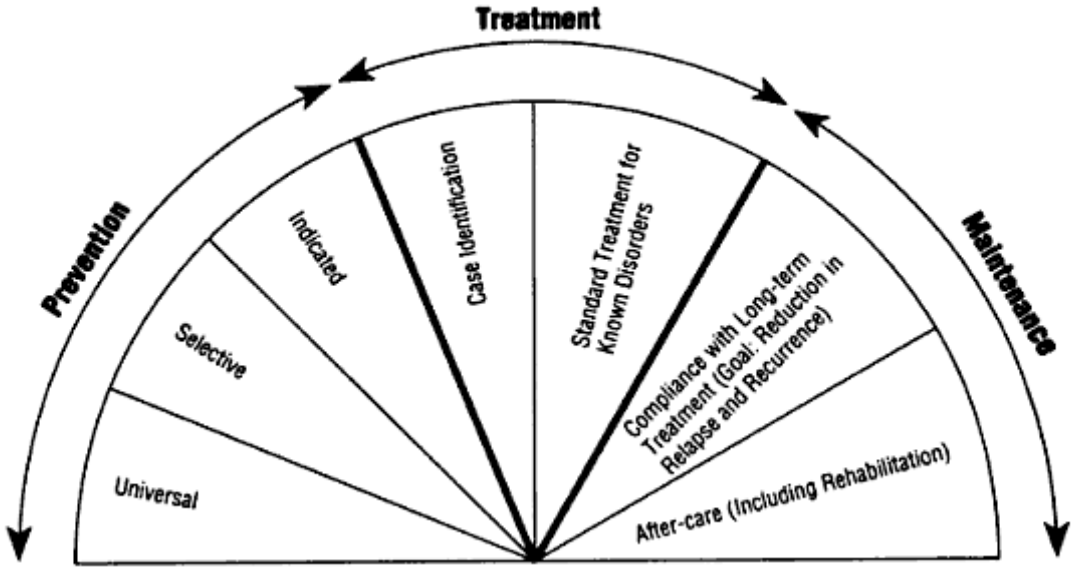


Figure 1: Three 'levels of interventions' for mental disorders, Institute of Medicine (Haggerty & Mrazek, 1994)

The majority of work towards helping people with depression has been in developing interventions that are effective in the 'treatment' phase, including pharmacological (Gartlehner et al., 2017), psychological (Hollon & Ponniah, 2010), and combination therapies (Oestergaard & Møldrup, 2011). Ensuring long-term maintenance of benefits has received less attention, a point simply demonstrated by a consideration of the respective numbers of studies in each of these areas. A series of reviews undertaken for a major national clinical guideline for depression (NICE, 2009) found over 1500 trials of antidepressant medication and over 200 trials of psychological intervention were identified in the acute treatment of depression. In contrast, a meta-analysis of maintenance medication following recovery included only 31 trials (Geddes et al., 2003), a review of second generation antidepressant medication following recovery only 27 trials (Hansen et al., 2008), and a review of non-pharmacological interventions (Clarke, Mayo-Wilson, Kenny, & Pilling, 2015 and Chapter 2) found only 29 studies. This serves to highlight the importance of further work in the area, particularly research that complements the existing evidence for acute treatments, and that extends our focus beyond 'recovery', towards prevention of relapse.

Acute treatments

The most common interventions for depression are acute treatments: those that are delivered when a person is symptomatic, with the primary aim of resolving those symptoms. They come in a range of pharmacological and psychological forms. Pharmacological treatments can be effective, bringing about a clinically meaningful improvement in around 50% of people in clinical trials (Papakostas & Fava, 2010; Trivedi et al., 2006). There are several types of pharmacological treatment that impact on different neurotransmitter systems including the serotonergic system (SSRIs), the noradrenergic system (e.g. reboxetine), serotonergic and noradrenergic systems (SNRIs), serotonergic noradrenergic and dopamine systems (MAOIs) and the melatonergic system (e.g. agomelatine). Psychological treatments derived from various theoretical approaches and delivered in different modalities also appear to be effective in treating depression (NICE, 2009).

This thesis focusses on interventions that are offered after recovery, but any enduring effects of acute treatment are of relevance to consider. Medication seems to lose efficacy when discontinued (Anderson & Tomenson, 1995), and risk of relapse returns to the level it would have been previously. In contrast to this, acute-phase psychological interventions may prevent relapse even when they are terminated at the point where a person has recovered (Gortner, Gollan, Dobson, & Jacobson, 1998). This is apparent with CBT (Hollon, Stewart, & Strunk, 2006), and potentially other psychological therapies (Nezu & Nezu, 2010). Perhaps these enduring effects are achieved through the amelioration of the causes of risk of relapse, or through the development of knowledge and skills that equip people to offset their risk (Hollon et al., 2006). There are elements of CBT that aim to address risk of relapse. Around 1-2 sessions cover triggers, relapse warning signs, and a plan to take preventive action although a dismantling trial which compared CBT without these sessions, to CBT with them, would be needed to identify whether they were having the relapse preventive effect that is their explicit aim. It seems that combining antidepressant medication with cognitive therapy at the acute stage may remove this enduring effect (DeRubeis et al., in preparation, presented by Steve Hollon at the EABCT Conference 2018), although further work in the area is needed to establish this.

Intervention after recovery

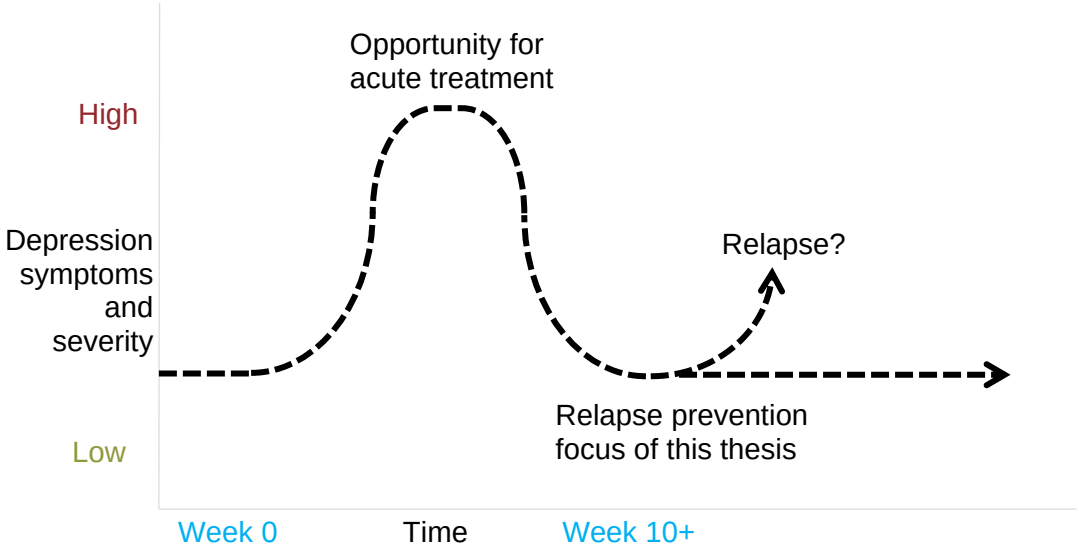
Although acute treatments may have 'enduring effects', it is additional intervention delivered after the acute phase, when patients are no longer depressed, that are the focus of this thesis (see

Figure 2). Continuation pharmacotherapy is a common form of post-recovery intervention: in practice, patients identified at an elevated risk of relapse typically stay on medication for at least a two year period (Geddes et al., 2003; Thase, 2012) and many continue indefinitely due to barriers to discontinuing mediation (Kendrick et al., 2019). However, as noted earlier in this chapter, it can be difficult to identify who is at elevated risk of relapse with confidence. Medication itself is limited in preventing relapses, as not all patients benefit, side-effects may increase over time, and people who are unwilling to stay on medication forever may relapse when they discontinue it (Anderson & Tomenson, 1995), even if discontinuation is gradual (Viguera, Baldessarini, & Friedberg, 1998). Continuation pharmacotherapy is likely only an option for people who have already received medication in the acute treatment of depression.

Perhaps 75% of patients report preferring psychological interventions to pharmacological treatments for psychiatric disorders, in particular younger adults and those who have not previously sought treatment (McHugh, Whitton, Peckham, Welge, & Otto, 2013).There have been a number of randomised controlled trials of psychological therapies delivered to participants after recovery, which I review in Chapter 2. It appears that they may be effective at reducing relapse risk (Pim Cuijpers et al., 2013; Piet & Hougaard, 2011; Vittengl, Clark, Dunn, & Jarrett, 2007). Psychological therapies delivered after recovery may be an important avenue for relapse prevention.

The Institute of Medicine's characterisation of Mental Health Interventions in Figure 1 (above) might categorise this approach as 'maintenance' however they also describe this as 'compliance with long-term treatment' or 'after-care'. In this thesis I aim to seek a potentially different approach to relapse prevention itself that does not necessarily follow from or 'continue' acute treatment. In some ways this might be defined as 'indicated' prevention (Haggerty & Mrazek, 1994) within their categorisation.

Figure 2 is provided below in order to illustrate the approach to mental health intervention taken within this thesis.



Note: The X axis on this figure represents depression symptoms and severity which can be operationalized and measured in multiple different ways. Similarly for the Y axis, 'time', a person may experience a depressive episode for 4 weeks to multiple years. This thesis will focus on interventions at any point in time a person has experienced and recovered from an episode of depression, likely 10+ weeks post-baseline.

Figure 2: Illustrative figure of a common trajectory of depression and how this thesis will approach relapse prevention

Availability of interventions in the NHS

In terms of acute treatments: both pharmacological and psychological treatments are offered within the NHS. Antidepressant medication is usually prescribed by General Practitioners within primary care, and a range of antidepressants are currently recommended for depression by NICE (NICE, 2010). Psychological therapies are also now much more widely available, particularly since the advent of Improving Access to Psychological Therapies (IAPT) Services (Clark, 2018). They offer traditional forms of face to face therapy such as cognitive behavioural therapy (CBT) or interpersonal therapy (IPT), but also 'low-intensity therapy', which are self-help interventions undertaken with the guidance of a therapist. There may be some enduring effects following high-intensity therapy, as it closely follows the model of CBT and IPT tested in randomised controlled trials, but data on this are yet to be published. The outcomes following low-intensity therapy are not clear. A recent single-centre study found that in the year following low-intensity treatment completion about 54% of people experienced a clinically significant deterioration in symptoms (Ali et al., 2017), and they suggest that

additional relapse prevention work following completion of low-intensity treatment may be important.

Interventions following recovery are less available. Continuation with medication is recommended by NICE guidelines (NICE, 2009) for up to 2 years for people at risk of relapse due to experiencing several episodes in the past. Mindfulness-based cognitive therapy (MBCT) is currently the only evidence-based psychosocial intervention that is specifically developed for relapse is recommended for use within the NHS by NICE (2009). NICE (2009) also recommend CBT for relapse prevention. Both are available in the NHS but the provision of MBCT patchy (*Psychological Therapies, Annual Report on the Use of IAPT Services 2019-20*, n.d.). Other relapse prevention interventions such as 'staying well' plans or review phone calls are offered by some services, although efficacy of these interventions is relatively unexamined. In routine clinical practice, planning for relapse prevention typically includes identifying warning signs and symptoms that would cause a patient to seek help or take action, as well as coordination of care (particularly for patients with severe or recurrent depression). Other routes to staying well include physical exercise, building networks of social support, psychologically informed self-help and engaging in meaningful activities (NICE, 2009).

Problem statement

Experiencing depression is distressing and debilitating. It affects a large proportion of the population at some point in the life course, and can affect people repeatedly. Most people recover from an episode, but following this the risk of a relapse is significant (Kruijshaar et al., 2005; Moffitt et al., 2010; Waraich et al., 2004). It has been estimated that optimal episodic treatment for depression would offset less than half of the total burden of disease, which highlights the importance of relapse prevention: not as an optional addition to effective treatment, but as a core part of addressing the problems associated with depression. After recovery from depression, the options for relapse prevention within the NHS are, for the most part, limited to continuing with medication. Psychosocial interventions may be an important option for relapse prevention but are under-developed or unavailable compared to their acute

treatment counterparts. In this thesis I use a combination of research methods to explore and address the question:

"Maintaining recovery after depression: what are relapses and how might they be prevented?"

Approach to the problem

I am seeking to develop a brief intervention to reduce relapse following recovery from depression. The Medical Research Council has provided guidance as to ways in which complex interventions should developed and evaluated in order to construct interventions that are possible to evaluate, more likely to be implemented, and more likely to be worth implementing (Craig et al., 2008; Moore et al., 2015; O'Cathain et al., 2019). They recommend that interventions are based on the best available evidence, have a pre-specified theoretical basis that the intervention is derived from, are feasible, and have the potential to improve health outcomes. During the development phase these are the main questions they suggest that researchers consider

- *Clarity about the aim: what the outcome or aim is, and how change will be brought-about*
- *Whether the intervention has a coherent theoretical basis*
- *Whether this theory has been used systematically to develop the intervention*
- *Whether the intervention can be described fully so that it can be implemented properly within the evaluation and also replicated outside of this*
- *Whether the existing evidence suggests that it is likely to be effective and cost effective*
- *Whether it can be implemented within the research and is likely to be widely implementable if results are favourable*

  (Box 1 in Craig et al., 2008)

The majority of this thesis forms intervention development work related to these questions. It finishes with piloting and feasibility work, including considerations of implementation.

I first try to build up a picture of existing interventions and their efficacy. I then draw together evidence about relapse of depression in order to develop a pragmatic theoretical approach that could guide the development of a relapse prevention intervention that could be delivered within the NHS.

It follows these steps:

- Systematically review existing evidence for the efficacy of non-pharmacological relapse prevention interventions.
- Build a theoretical framework around how to characterise relapse, and how interventions may (or may not) have an impact.
- Identify targets for a relapse prevention program, and design an intervention around these that would be feasible to deliver within the NHS.
- Design and conduct a pilot trial to explore the feasibility of recruitment, collecting outcomes, delivering the intervention, and its potential for clinical effectiveness.
- Evaluate the pilot, particularly with regard to clinician and service user experience.
- Describe and discuss the implications of these findings, and future research.

Chapter 2 Systematic review and meta-analysis of randomized controlled trials of relapse prevention interventions for adults after depression recovery

Abstract

Background: A large part of the burden of depression is due to relapses following recovery. This chapter will review and evaluate interventions that could reduce risk of relapse.

Objective: To identify randomised controlled trials of non-pharmacological interventions provided following recovery from depression, and to evaluate their efficacy in preventing further episodes.

Method: Relevant randomized controlled trials were identified from searching MEDLINE, Embase, PsycINFO, CENTRAL, and ProQuest, searching reference and citation lists, and contacting study authors. Relapse outcomes were combined in a meta-analysis.

Results: There were 29 eligible trials identified. From these, 27 two-way comparisons including 2742 participants were included in the primary meta-analysis. At 12 months cognitive-behavioral therapy (CBT), mindfulness-based cognitive therapy (MBCT), and interpersonal psychotherapy (IPT) were associated with a 22% reduction in relapse compared with controls (95% CI 15% to 29%). The effect was maintained at 24 months for CBT, but not for IPT despite ongoing sessions. There were no 24-month MBCT data. A key area of heterogeneity differentiating these groups was prior acute treatment. Other psychological therapies and service-level programs varied in efficacy.

Conclusion and implications: Psychological interventions may prolong recovery following depression. Although there was evidence MBCT is effective, it was largely tested following medication, so its efficacy following psychological interventions is less clear. IPT was only tested following acute IPT. Most interventions were intensive, which may be a barrier to

implementation, although one trial was of CBT that had been adapted to increase accessibility.

This review was prospectively registered with the PROSPERO database, registration ID: PROSPERO 2011: CRD42011001646

The majority of this chapter was published in December 2015 (Clarke, Mayo-Wilson, Kenny, & Pilling, 2015).

Introduction

Given that depression is one of the largest causes of burden of disease in the world (Mathers et al., 2008), and that more than half of this burden may be due to relapses (Vos et al., 2004), improving relapse prevention is of the utmost importance. Research priorities for increasing the impact we can have on the burden of mental health problems include ‘active innovation’; particularly in terms of interventions that are accessible and would be feasible to offer to the people that would benefit from them, and in terms of progressing evidence using vigorous and high-quality research (Holmes et al., 2018). The aim of this chapter is to systematically review the best available evidence (from randomised controlled trials), of any non-pharmacological relapse prevention interventions (not limited to psychological therapies) following recovery from depression.

Recovery and relapse of depression

People who have recovered from an episode of depression (whether spontaneously or following the provision of treatment) are at an increased risk of becoming depressed in the future in comparison to people who have not experienced depression. In this review I use the term ‘recovery’ to denote any period where a person no longer meets diagnostic criteria for depression, and the term ‘relapse’ to denote “any kind of significant deterioration in depression, which was preceded by clear improvement” (Richards & Perri, 2010). This will allow the inclusion of a broad range of studies that may use varying terminology. As explored in Chapter 1: It has been argued that we should differentiate between ‘remission’ to indicate reduction of symptoms to below the diagnostic threshold for depression, and 'recovery' to indicate a longer remission (Frank et al., 1991). As well as this, ‘relapse’, a diagnosable episode of depression occurring during remission, should be differentiated from a 'recurrence' an episode that followed recovery. However inconsistent use of this terminology presents a challenge when attempting to combine data from multiple research studies. Instead, I report the specific criteria used by each study in their definitions of recovery and relapse in the Study Characteristics Table.

Intervention after recovery

This review focusses on interventions delivered after the acute phase of illness, when patients no longer meet criteria for depression. The focus is on non-pharmacological interventions, which at the time of protocol registration had not been reviewed as pharmacological interventions had been (Geddes et al., 2003). Here I will define non-pharmacological as being any intervention which does not administer a drug as the primary therapeutic activity. Most work in this area has focused on formal psychological therapies, either designed specifically for use after the acute phase, or adapted versions of acute phase psychological therapies.

There have been some systematic reviews in the area of relapse prevention for depression, and they suggest that a variety of interventions delivered after recovery can improve a person's chances of staying well. Most reviews have focussed on one particular psychological intervention, for example mindfulness-based cognitive therapy (Piet & Hougaard, 2011), continuation cognitive behavioural therapy (Vittengl, Clark, & Jarrett, 2009) or guided self-help interventions (Rodgers et al., 2012). These reviews found evidence that cCBT and MBCT can reduce risk, but found there is little evidence on the impact of guided self-help (see Section 1.2). A systematic review which included trials comparing psychological therapies to medication, found they were as effective as each other (Biesheuvel-Leliefeld et al., 2015).

Cognitive behavioural therapy (CBT) may equip people with specific skills to reduce their likelihood of relapse. As an acute treatment it aims to modify thoughts and behaviours in a way that alleviates key features of depression, such as identifying and challenging negative automatic thoughts and overcoming avoidance and reduced activity (Beck, 2011). Adaptations of CBT have focussed on relapse prevention, either as a continuation of prior acute treatment, or as a standalone intervention. In contrast to MBCT where the delivery of the intervention follows a common format, the duration, mode of delivery (individual, group, self-help), and frequency of CBT has varied. Vittengl et al (2007) reviewed the effectiveness of CBT to prevent relapse, both from studies which terminate treatment at recovery, and studies which continued CBT after this point. They estimate that continuing with CBT reduces risk of relapse by 29% compared with discontinuing treatment over '1 or 2' years.

Mindfulness-based cognitive therapy (MBCT) (Segal, Williams, & Teasdale, 2012) is the most widely known psychological intervention developed specifically to prevent relapse. It was designed to be delivered after a person has recovered from depression, and can be used following spontaneous recovery or acute treatment. It is typically delivered in groups of 12 to 15 participants with two professionals in fortnightly sessions over three months. MBCT encourages people to process experience without judgement through mindfulness and meditation techniques, thereby helping to change their relationship with troubling thoughts and feelings (Segal et al., 2012). A meta-analysis of MBCT trials (Piet & Hougaard, 2011) suggests that it is effective (with a 34% reduction in risk of relapse compared to controls), particularly for patients who have had three of more previous episodes of depression (where the reported reduction in relapse was 43%). Here the timeframe was 14-18 months and the control groups were TAU or placebo.

Interpersonal psychotherapy (IPT) (Klerman & Weissman, 1994) has also be used after recovery with reduced frequency of sessions. The model of delivery and objectives of IPT remain essentially the same as in the acute phase, focussing on strategies to deal with interpersonal and social role problems which are held to be casual in the development and maintenance of depression (Klerman & Weissman, 1994). IPT booster sessions may reduce relapse by providing continued support after the period where contact with a psychologist would typically end. As part of a wider review, (Cuijpers et al., 2011) identified four studies which compared combination of maintenance IPT and pill placebo with pill placebo alone. Maintenance IPT was more protective against relapse than pill placebo (odds ratio= 0.37, 95% CI=0.19 to 0.73, $p<0.01$; $I^2=0\%$; number needed to treat=7.63).

Other non-pharmacological approaches have sought to prevent relapse by continuing to provide enhanced monitoring and care-planning regardless of whether patients continue to be symptomatic (Gilbody, Bower, Fletcher, Richards, & Sutton, 2006; Smit, Tiemens, & Ormel, 2007). Similarly there has been some research into the impact of continued monitoring of symptoms and coordination of care post-recovery (Unützer et al., 2002) . Sequencing of interventions and support, as well as long-term management of care from different providers

may have important effects (Wells et al., 2000) as well as interventions that are used in routine clinical practice such as exercise, symptom monitoring, and building social support. Guided self-help interventions could be an important innovation in relapse prevention as they could be more accessible to those in need (which is a current priority, Holmes et al., 2018), but there is almost no research into their effectiveness when used for this purpose (Rodgers et al., 2012).

Conceptual framework for the review

A conceptual framework was developed to *"aid in the conceptualization of the review focus"*, (Anderson et al., 2011) to illustrate potential causal links, specify our outcomes of interest, and to justify a priori subgroup analyses. It has been recommended that conceptual frameworks (or 'logic models') would improve the conduct and interpretation of systematic reviews, because they make explicit the assumptions underlying the conduct and the scope of the review (Anderson et al., 2011). This would also prevent problems such as post-hoc subgroup analyses without adjustments multiple testing (Bender et al., 2008).

The framework was developed following the Kellogg foundation guide (Kellogg Foundation, 2004). I first specified the context for the review (as detailed above and in Chapter 1) in the form of short statements that summarise the clinical problem that the review seeks to inform, and the assumptions that underlie the review process. The framework links the population of interest [those who have been depressed and had some recovery], to our desired outcomes [long-term prevention of further episodes of depression], through the focus of this review [relapse prevention interventions]. It posits potential elements of the interventions that could affect outcomes, as well as other influential factors.

An assumption of the review approach is that the efficacy of interventions depends somewhat on the content of the intervention, and how it is delivered. By specifying this in the model it is acknowledged that this is an assumption and must be tested. I propose that the intervention content, such as the focus or the skills taught may relate to the efficacy in preventing relapses, and whether or not a person has previous experience of an intervention (such as if it were

delivered in the acute phase) may modify this effect. Efficacy may also be influenced by the mode of delivery of the intervention materials: one-to-one or group based, delivered by a professional or through guided self-help, length of contact time, frequency, and clarity of intervention materials such as booklets or online resources.

The influential factors are those that the evidence reviewed suggests could have an impact on a person's baseline risk of relapse, and therefore the efficacy of a relapse prevention intervention (see Chapter 1). Although this thesis will focus on interventions that are offered after recovery, the potential for certain acute treatments to have enduring effects mean that prior treatment experience may be an important factor to consider in a relapse prevention intervention. Treatment history, including prior experience of psychological therapies and antidepressant medication, is included as an influential factor in the conceptual framework for this reason. The list of influential factors does not attempt to be exhaustive, but rather propose factors that are to be considered in the assessment of efficacy in reviewed studies (if and where available). For example, social and interpersonal factors may be important in the baseline risk of relapse and in moderating the impact of relapse prevention interventions, but I do not expect these to be consistently reported in studies within the review. Similarly, I do not expect childhood maltreatment to be consistently reported.

It is important to consider the most well-established risk factors a priori so that sub-group analyses can be conducted that might identify moderators or mediators of effectiveness of interventions in the trial, or confounders to results. Analysis was planned and conducted in line with this a priori conceptual framework (Figure 3).

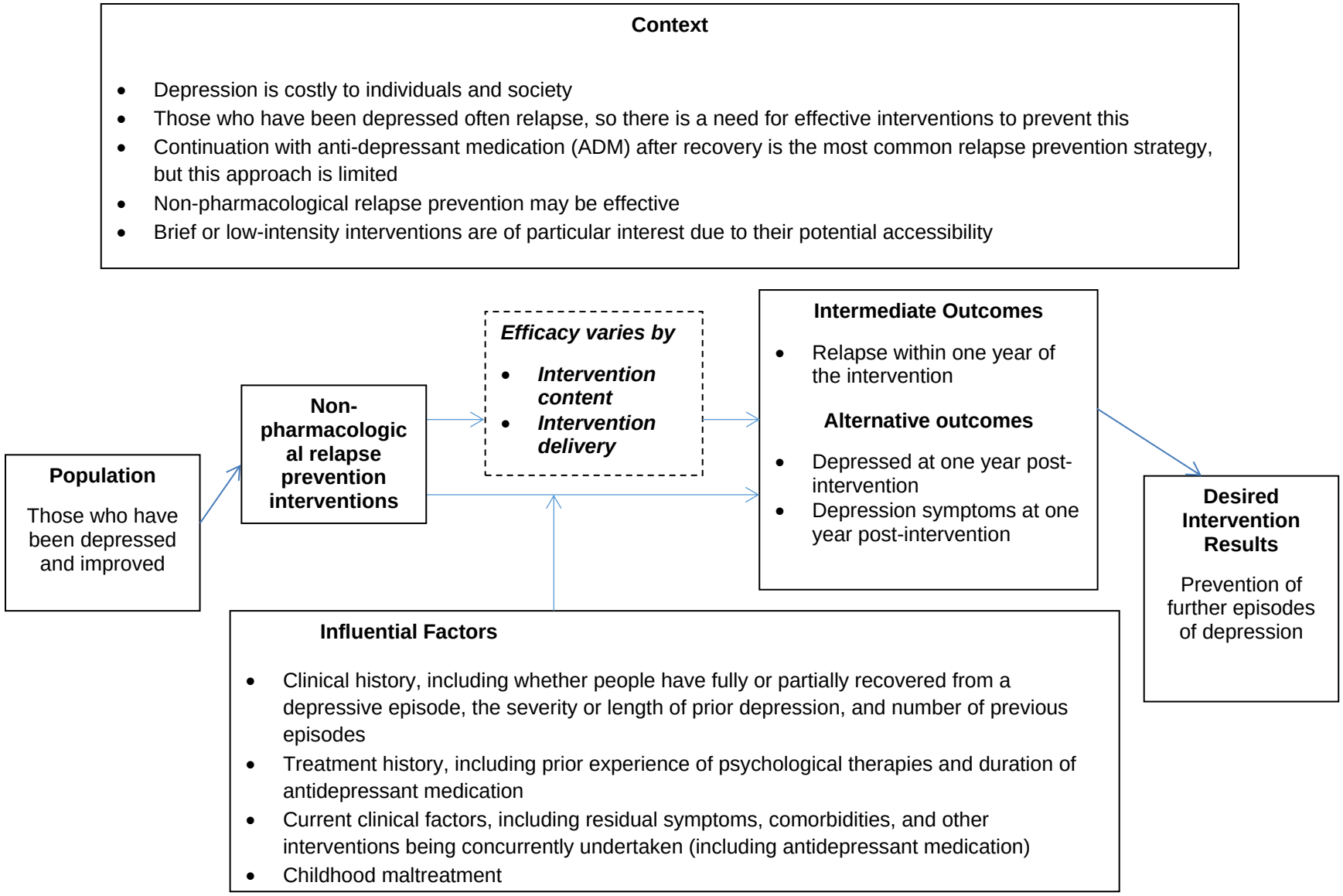


Figure 3: Conceptual Framework linking key assumptions and proposed mechanisms of action for a systematic review of non-pharmacological relapse prevention interventions

Aims of this review

This review will evaluate evidence for non-pharmacological interventions to prevent relapses in those who have recovered from depression. The first aim was to describe the research that exists in this field, and highlight any potential gaps in evidence. The second aim was to examine the efficacy of these interventions.

This chapter includes the evidence that was available up until 2013, prior to the development of the intervention that I will present in this thesis. A narrative summary of changes in the field based on updated searches are included in the discussion in Chapter 7 (as recommended by MRC guidance in developing complex interventions, Craig et al., 2008).

Method

This is a systematic review and meta-analysis that followed a pre-specified protocol. This protocol was registered in a public database prior to any work being undertaken (Clarke, Pilling, Kenny, & Mayo-Wilson, 2011). Prospective registration of protocols for systematic reviews is recommended (Moher et al., 2015) in response to evidence that there were biases in the reporting and publishing of reviews (Booth et al., 2011). Addressing these biases is particularly important given the use of systematic review evidence in informing policy and practice (Booth et al., 2011).

The review was published in December 2015 (Clarke, Mayo-Wilson, Kenny, & Pilling, 2015), and covered evidence that was published up to 2014. In this chapter I present the evidence up to 2014 as it formed the basis of the development of the intervention that I will present in this thesis. In accordance with MRC guidance in developing complex interventions (Craig et al., 2008), I will update the review in the evaluation of the pilot trial (and present a summary of changes in Chapter 7).

Definitions of terms

'Recovery' was considered to be a reduction in symptoms to below a diagnostic threshold in a clinical interview or validated assessment tool. Given the lack of consensus on the exact

time periods to distinguish ‘remission’ from ‘recovery’ (see Chapter 1), the review included both, and stated the exact criteria each trial used, including (where possible) their definition, operationalisation and time period. In this way this review provides a summary of the inclusion criteria trials used and a check of the appropriateness of comparisons between studies. Systematic variation in the eligibility criteria used by studies in this review may indicate areas for future research. Although other reviews have excluded people with ‘partial’ recovery (a high level of residual symptoms), this review does not, as level of residual symptoms is just one of several potentially important ‘influential factors’ that could impact outcomes (see Figure 3).

Relapse was defined as a change in the status of a patient, from recovered (fully or partially) to depressed. For the purpose of the review this was defined as meeting accepted diagnostic criteria on the basis of a clinical interview, or by meeting a diagnostic threshold on a validated measure. If study authors used an un-validated or self-report measure of relapse alone, the study was not included in the meta-analysis. Service utilisation alone (e.g., admission to hospital) was not taken as an indicator of relapse.

Non-pharmacological interventions were defined as any intervention that did not include the administration of a drug. So ‘advice on medication’ would be included, whereas combination therapy with fluoxetine and relapse prevention psychotherapy would not be included (unless the control arm was fluoxetine and so the study arms differed only by a non-pharmacological intervention).

A control was defined as any intervention that did not fall under the focus of the review (non-pharmacological relapse prevention). This could include active interventions such as clinical management, antidepressant medication or non-specific support, as well as evaluation-only controls. A broad range of controls were acceptable as, despite having different descriptions and setting for delivery, there could be significant overlap in the care received between control group types (for instance evaluation-only controls could seek treatment from primary care professionals, which could include medication/clinical management/non-specific support).

Eligibility criteria

Trials were included if adults in (full or partial) recovery from depression were randomised to either

- A non-pharmacological intervention aimed at reducing relapse of depression (this aim could be implied through the inclusion of depression relapse in the study's outcome measures), or
- Any comparator condition,
- And were followed up for a minimum of 1 year after randomisation.

Studies were excluded that

- Had fewer than 10 people in one of the study arms

Studies were only included if they randomised participants who had recovered. This meant studies that randomised to acute treatment were excluded, even if they then followed participants after recovery (to look for 'enduring effects' e.g. Hollon et al., 2006).

Search strategy

The databases searched were Embase, MEDLINE, PsycINFO (using the Ovid interface), CENTRAL, and ProQuest from inception to 04 December 2013 using a sensitive RCT filter without language or publication status restrictions. The search was focussed on all terms associated with two concepts: 'depression' and for 'relapse/recurrence/long-term' (for full search strategies see Appendices A, B and C). The search did not specify any particular types of intervention, so as to identify of all randomised trials which looked at a depression intervention without assuming, a priori, what research would exist. Tests of pharmacological interventions were removed during screening. Citations were screened by two authors independently and disagreements about inclusion were resolved by discussion with a third author. Reference lists and citations (using SCOPUS) of included studies and some excluded studies were also searched, and I contacted study authors of all included studies.

Data extraction

Data from each study were extracted by one review author and checked for errors by a second. Double data extraction though desirable is not necessary and sufficient for accuracy of data extraction, and in the absence of adequate resources, exploratory checking of the data is preferred (Day, Fayers, & Harvey, 1998). Information was also extracted on the content and delivery of the intervention being tested, as well as trial start dates and locations. Information about the clinical history of the population was extracted where available, as this is linked to baseline risk of relapse. Where possible information was extracted on how many people had relapsed, not relapsed, or not provided sufficient information, when this was measured relative to randomisation, and how it was defined and measured. Additional data or information about study methods were provided by study authors for 45% of the included studies, indicated with a + following the study name in the Study Characteristics Table.

The interventions were grouped into types of interventions. Where there were several trials of the same type of intervention, I conducted a meta-analysis of the number who had relapsed in intervention versus control groups. Studies with more than two relevant arms were split into two-way comparisons as follows:

- When there was more than one eligible intervention, the control group was divided to make up sufficient two-way comparisons.
- Where there was one eligible intervention but more than one control group, the control groups were combined to make up one two-way comparison.
- Factorial trials were treated as separate two-way comparisons.

Data analysis

Meta-analyses were conducted using Review Manager (RevMan) Version 5.2 (http://ims.cochrane.org/revman) for all of the pre-specified time points where sufficient study data were available. Relative risks and 95% confidence intervals (CIs) were calculated and combined using Mantel-Haenszel methods. When relative risk cannot be calculated, we will calculate odds ratios. Standardised mean differences (SMDs) and 95% CIs will be calculated

for continuous measures and combined using inverse variance methods. Random-effects models will be used because studies included different interventions and populations. Study drop-outs were assumed to have relapsed, in order to obtain conservative measures of treatment effect and to minimise methodological differences in the meta-analysis. This approach was adopted as some studies reported their outcomes on an intention to treat basis, with drop-outs assumed to be relapsed, and data was not available to form a completer analysis. This approach was the only one which allowed a consistent approach across all studies.

Risk of bias was assessed for included studies, and the quality of the evidence available. Trials were assessed using the Cochrane Risk of Bias Tool (Higgins, Green, & Collaboration, 2011) with regard to our outcome of interest, relapse of depression. Confidence in the outcome for each subgroup was rated according to GRADE criteria (Balshem et al., 2011) and incorporated into the interpretation of results.

Results

Trial flow

There were 20,531 potentially relevant citations and 389 papers were retrieved for full-text review. Of these, 29 trials were eligible for this review, and 22 trials were included in the meta-analysis (7 trials either did not report or provide usable data on request).

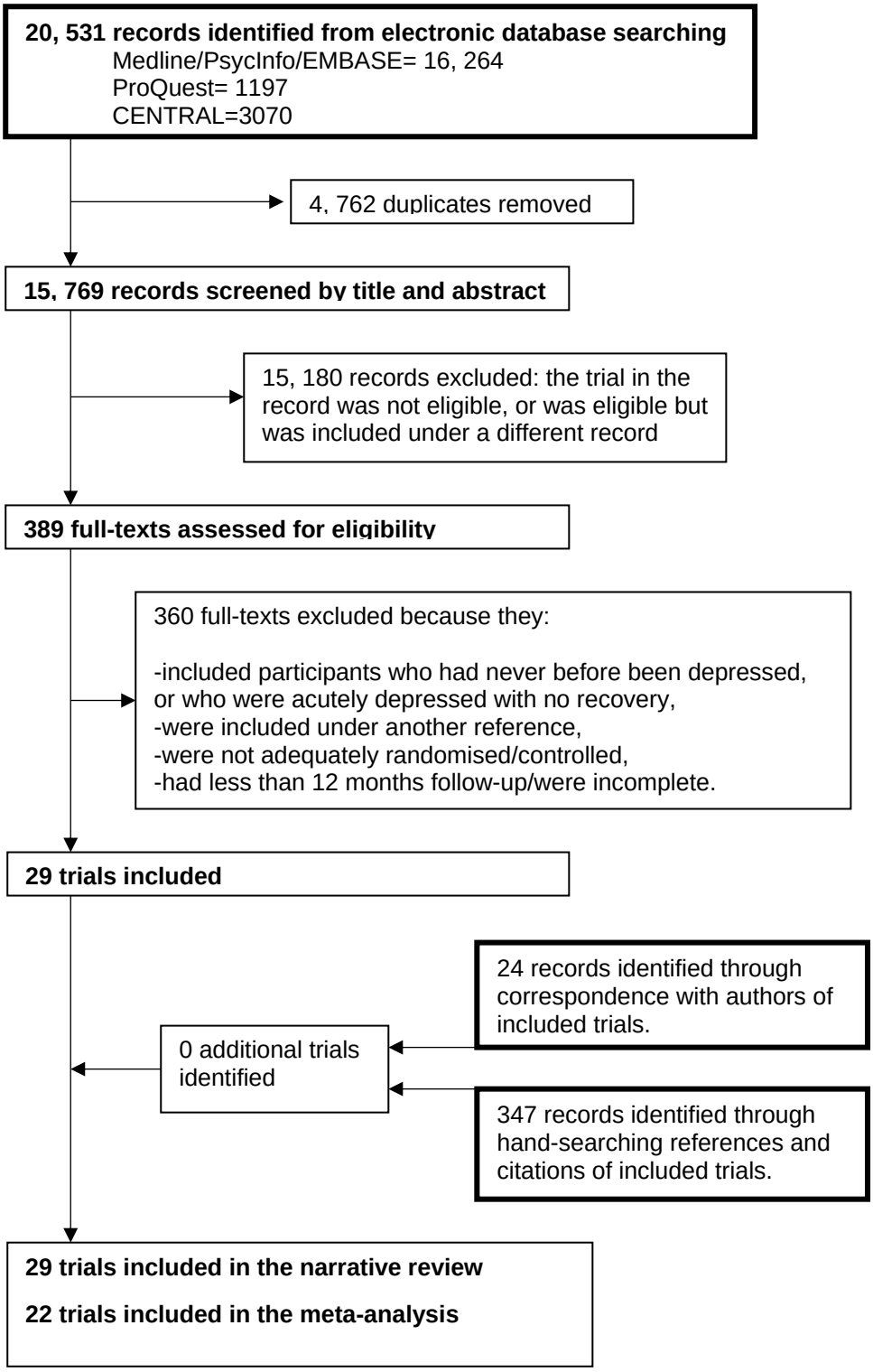


Figure 4: PRISMA flow diagram of study selection for a systematic review of non-pharmacological relapse prevention interventions for depression

Excluded studies

360 articles were assessed using the full-text and excluded. The primary reasons for this are included on the PRISMA diagram (Figure 4) and explained in detail below. Reporting the reason for exclusion of each individual study would not be accurate, as studies may have had

several reasons for exclusion but the sifting process may only record one. Instead, the reasons for exclusion from most to least common are reported, with the associated proportion of studies which were excluded based on this reason.

Acute treatment and its impact on relapse

Participants were acutely depressed with no recovery. Approximately 40% of the excluded references examined interventions that were delivered when a person was symptomatic and aimed to reduce depressive symptoms, so were not 'relapse prevention' according to our criteria that participants had to have experienced some recovery prior to the intervention. Acute treatments with enduring effects could be considered relapse prevention, but were not within the scope of this review (and are reviewed elsewhere: Hollon, Stewart, & Strunk, 2006).

Included under another reference

Study included under another reference: approximately 15% of the excluded references were of papers where the same trial had been written up elsewhere. Where included studies had multiple references, the one with relapse outcomes reported for the longest follow-up were used as the main study reference, and other references used where extra information was needed about the trial.

Not adequately randomised/controlled

Approximately 15% of the excluded references were not RCTs according to our criteria. Sometimes participants were not randomised to the relapse prevention intervention (they may have been randomised earlier, as in (Hollon et al., 2005) or there was no control group (for example if all participants received a relapse prevention intervention, and arms differed by antidepressant medication, as in (Wilson, Scott, Abou-Saleh, Burns, & Copeland, 1995).

Primary prevention of depression

Participants who had never been depressed. Approximately 15% of excluded references examined prevention of first episodes of depression, rather than depressive relapse.

Had less than 12 months follow-up/were incomplete.

Approximately 5% of the excluded references were on-going studies were identified from protocols or conference abstracts that could potentially be included in this review and could not be excluded based on currently available information. Of these, I expect three will be relevant, all focussing on MBCT:

Kuyken et al. (2010) describes plans for the PREVENT trial: a randomised trial comparing MBCT (with tapering antidepressant medication- ADM) to maintenance ADM in the prevention of relapse or recurrence of depression over 24 months. The trial will recruit 420 patients with recurrent depression from primary care.

Shawyer et al. (2012) describes plans for the DARE study: a randomised controlled trial comparing MBCT to supported self-monitoring (under real world conditions) in the prevention of relapse or recurrence of depression over 24 months. The trial will recruit 204 participants who have had 3+ previous episodes of depression from primary and secondary care.

Williams et al. (2010) describes plans for a three-armed randomised trial comparing Mindfulness-Based Cognitive Therapy (MBCT) with both Cognitive Psycho-Education (an equally plausible cognitive treatment but without meditation), and treatment as usual (TAU). The trial will recruit recurrently depressed patients and examine relapse of depression and suicidal thoughts up to 12 months post

Study characteristics

The 29 eligible trials were conducted in the USA (n=12), the UK (n=6), the Netherlands (n=3), Italy (n=2), Canada, Denmark, Germany, Sweden and Switzerland (all n=1). They included 4216 participants; the size of individual trials varied (range 31 to 485 participants, median 124), with a ‘mood management’ trial of 485 participants, (van der Meer, Willemsen, Smit, Cuijpers, & Schippers, 2010) and four CBT trials with fewer than 50 participants. Most trials included male and female adults without age restriction, although four trials limited inclusion to adults aged 55 years or over. Characteristics of the studies are summarised in Table 1, below.

Study Number	Lead author, year	N	Mean age (SD)	Mean previous episodes (SD)	Acute treatment	Pre randomisation/ eligibility	% on ADM at	Relapse prevention intervention	Intervention Length	Comparison	Criteria used to measure relapse	Weeks of follow-
	CBT											
1	Bockting 2005	187	44.7 (9.5)	*3-4 (IQR ± 3.8)	Any	2+ recent episodes, remission for 10 weeks-2 years	51	Group CT+ TAU	2 h/week for 8 weeks	TAU	DSM-IV diagnosis of MDE (SCID)	104
2	Fava 1994	43	46.1 (2.8)	----	ADM	Residual symptoms	100	CBT + discontinuing ADM	40 mins/fortnight for 20 weeks	Clinical management + discontinuing ADM	RDC-defined MDE	104
3	Fava 1998	45	46.0 (10.8)	3.6 (0.8)	ADM	3- 5 months remission	100	CBT + ADM	30 mins/fortnight for 20 weeks	Clinical management + ADM	RDC-defined MDE (CID)	104
4	Hollandare 2013 +	84	45.3 (12.8)	5.96 (9.1)	Psycotherapy + /ADM	Partial remission	50	Internet-based CBT	Internet modules & 10 weeks of email support	Non-specific email support	Diagnosis of depression (SCID)	114
5	Jarrett 2000 +	31	41.2 (10.5)	----	^^^CT	Atypical features and treatment response	0	Continuation CT	10 sessions over 35 weeks	Evaluation only	RDC-defined MDD OR Patient had more treatment	104
6	Jarrett 2001 +	84	42.7 (10.5)	3.4 (0.2)	^^^CT	Responders who completed 20+ CT sessions	0	Continuation CT	4 X 1 h/fortnight then 6X 1h/month	Evaluation only	DSM-IV diagnosis of MDD (LIFE 25)	104

7	Jarrett 2013	241	42.7 (11.8)	*4	^^^CT	Responders who were high risk	0	Continuation CT	4 X 1 h/fortnight then 6X 1h/month	Clinical management + fluoxetine or placebo	DSM-IV criteria for MDD (SCID)	140
8	Paykel 1999	158	43.27 (10.9)	*37% had 3+	8+ weeks of ADM	2-18 months remission, high residual symptoms	100	CT + clinical management	16 sessions over 20 weeks + 2 sessions 6 and 14 weeks later	Clinical management	DSM-III-R criteria for MDD for at least 1 month AND Minimum symptom score	68
9	Stangier 2013	180	48.6 (11.6)	7.4 (8.3)	Any, no CBT in the past year	3 + previous episodes, 8+ weeks in remission	75	Maintenance CBT	16 50-minute sessions over 8 months	Manualized psychoeducation	DSM-IV diagnosis of MDE (LIFE)	87
10	Wilkinson 2009 +	45	74.0 (7.3)	3.0 (1.9)	ADM	Remission for 2+ months and remain on ADM	100	Group CBT	8X1h30 over 10 weeks	TAU	MADRS score of 10+ at 6/12 months	52
	MBCT											
11	Bondolfi 2010 +	60	----	*4 (range 3-18)	ADM, CBT <5 times	3-months withdrawal from ADM	0	MBCT + TAU	8 X 2 h/week + 4 sessions each 3 months	TAU	DSM-IV diagnosis of MDE (SCID)	60
12	Godfrin 2010 +	106	45.7 (10.6)	----	Any	3+ previous episodes, 8+ weeks in remission	68	MBCT + TAU	2h 45m /week for 8 weeks	TAU	DSM-IV diagnosis of MDE	56

13	Kuyken 2008 +	123	49.2 (11.2)	6.4 (3.0)	ADM for 6+ months	In full or partial remission	100	MBCT + tapered ADM	8 X 2 h/week + 4 sessions each 3 months	Maintenance ADM	DSM-IV diagnosis of MDE (SCID)	65
14	Ma 2004 +	75	44.5 (8.9)	3 (2)	ADM CBT <5 times	12+ weeks remission with no ADM	0	MBCT + TAU	8 X 2 h/week + 2 sessions at 1 and 6 months	TAU	DSM-IV diagnosis of MDE (assessments "modelled on the SCID")	52
15	Segal 2010	84	44.1 (10.9)	4.7 (2.3)	^^^ADM	7 months clinical remission	100	MBCT + tapered ADM	8 X 2 h/week + 1 day + optional 1 h/month for trial duration	ADM / Clinical management + placebo	16+ on the HRSD-17 assessed twice then criteria for MDD measured with SCID, OR LIFE	86
16	Teasdale 2000	145	43.3 (10.0)	*median is 3 or 3.5	ADM CBT <5 times	12+ weeks remission with no ADM	0	MBCT + TAU	8 X 2 h/week + 4 more sessions over trial duration	TAU	DSM-III-R criteria for MDE (SCID)	60
17	Williams 2013 +	274	43 (12)	80% had ≥5	Any, exclude successful CBT	3+ recent episodes, remission for 8 weeks	≈45	MBCT+TAU	Individual pre-class, then 8 X 2h/week	Cognitive psychological education + TAU or TAU	Criteria for MDE ≥ 2 weeks (SCID)	61
	IPT											

18	Frank 1990	128	40.2 (10.9)	----	^^^ADM and decreasing IPT	20+ weeks relatively symptom-free	100	mIPT (+ placebo/ imipramine)	Monthly sessions	Medication clinic (+placebo/ imipramine)	RDC-defined MDD AND independently confirmed minimum symptom score	156
19	Frank 2007	131	30.6 (10.3)	----	^^^IPT (+ ADM if needed)	12-24 weeks treatment	24	IPT	Weekly/twice monthly/monthly sessions	None	DSM-IV diagnosis of major depression	104
20	Reynolds 1999 +	124	----	----	^^^Nortriptyline and IPT	Clinical response	100	IPT (+ placebo/ nortriptyline)	50 mins/month	Medication clinic (+ placebo/ nortriptyline)	RDC-defined MDE (structured psychiatric interview)	156
21	Reynolds 2006 +	116	76.8 (5.7)	*59% had 1	^^^Paroxetine and IPT	Clinical response	100	IPT (+ paroxetine /placebo)	45 mins/month	Medication clinic (+ paroxetine/ placebo)	DSM-IV diagnosis of depression (SCID)	104
	Care programs											
22	Apil 2012	136	65.6 (8.3)	4.4 (7.0)	Any	No current psychotherapy	46	Stepped Care Program	Symptom dependent for trial duration	TAU	DSM-IV diagnosis of MDE (MINI 5.0) OR Medical records show any additional treatment	52
23	Hansen 2012	268	*medis	----	Hospitalisation	Discharged	----	Specialised outpatient program	Symptom dependent for 52 weeks	TAU	Not measured (they looked at hospitalisation)	4-5 years

			38.4-38.7									
24	Hunkeler 2013	66	----	----	----	----	----	Web delivered care- and self-management program	----	Usual specialty mental health care	PSR every 2 weeks using LIFE	----
25	Katon 2001+	386	46.0 (12.6)	0.8 (0.4)	ADM	High risk of relapse	81	Relapse prevention program	Varied for 52 weeks	TAU	LIFE	52
	Other											
26	Brown 2001	179	45.1 (9.3)	----	Any (no current treatment)	Smoker	0	CBT+ smoking cessation treatment	8 X 2h over 6 weeks	Smoking cessation treatment	Not measured	52
27	Klein 2004 +	82	45.0 (11.4)	2.5 (1.6)	^^^CBASP	Incomplete remission	0	CBASP	Monthly sessions for 52 weeks	Assessment only	DSM-IV diagnosis (checklist) AND Minimum symptom score AND Clinical interview	52
28	Van der Meer 2010	485	43.8 (10.0)	*47% had 1	Any	Smokers with depression >1 month ago	0	Mood management + smoking cessation counselling	1X 30 minutes and 9X15 minutes over 91 days	Smoking cessation counselling	Not measured	52
29	Weissman 1976	150	39 (----)	----	^^^ADM	Clinical response to 6-8 weeks acute treatment	100	Therapy (+ amitriptyline/placebo/no drug)	1-2 sessions/ week for 8 months	Minimal contact (+ amitriptyline /placebo/no drug)	Not measured	87

Table 1: Study Characteristics of 29 included trials, including participant numbers and eligibility, acute treatment pre-trial, and trial design and follow-up

*= Not ‘mean (SD)’ ---- = not measured/reported ^^^ = in earlier stage of the trial += authors provided extra data for this review

NB the acute treatment column shows any treatment received before randomisation to relapse prevention or comparison. If this was delivered within an earlier stage of the same relapse prevention trial it is marked ^^^.

ADM = antidepressant medication, CBASP = Cognitive Behavioural Analysis System of Psychotherapy, CBT = Cognitive Behavioural Therapy, CT = Cognitive Therapy, MBCT = Mindfulness-Based Cognitive Therapy, TAU = Treatment as Usual

Criteria used to measure relapse: CID= Clinical Interview for Depression, DSM= Diagnostic Statistical Manual, LIFE = Longitudinal Interval Follow-up Evaluation, MDD= Major Depressive Disorder, MDE= Major Depressive Episode, RDC= Research Diagnostic Criteria, SCID = Structured Clinical Interview for DSM Disorders, MADRS Montgomery-Asberg Depression Rating Scale, HRSD, PSR = Psychiatric Status Rating

All included trials randomised participants who were not currently depressed to the intervention or control arms. The acute treatment that preceded randomisation is detailed in the Study Characteristics Table. Eighteen trials recruited people who had previously recovered from depression outside of a research context. Ten trials delivered acute treatment and then randomised people to receive relapse prevention or a comparator. To examine these studies uniformly, randomisation to relapse prevention is used as the baseline.

Control conditions included ‘evaluation-only control’, and ‘treatment as usual’, as well as 'active' interventions (which was defined as interventions specifically administered for the trial). However, there was considerable overlap in the content of these controls; for example, antidepressant medication was used in control groups described as ‘treatment as usual’ and as ‘clinical management’, as well as those described as ‘medication’ arms. There was a large difference in control event rate for relapse across the trials (for 12-month data, range= 0.2-0.79, IQR= 0.41-0.63).

Types of Intervention

The majority of included studies evaluated psychological therapies: cognitive behavioural therapy (CBT) (studies 1-10 in Table 1); mindfulness-based cognitive therapy (MBCT) (studies 11-17); and interpersonal psychotherapy (IPT) (studies 18-21). All were structured, time-limited interventions, except for IPT which was delivered monthly throughout the entire duration of follow-up.

The next most frequent type of interventions was service-level programs (studies 22-25 in Table 1). One study tested a primary care relapse prevention program that consisted of 2 visits and 3 phone calls with a depression specialist aimed at enhancing medication adherence, monitoring potential prodromal symptoms and developing a relapse plan (Katon et al., 2001). Other trials evaluated a stepped care program (Apil, Hoencamp, Haffmans, & Spinhoven, 2012), referral to a specialised outpatient intervention program (Hansen et al., 2012), and a web-delivered care-management and self-management program (Hunkeler et al., 2012).

The remaining trials tested psychotherapies that did not fall under the scope of the groups already

mentioned (studies 26-29 in Table 1). One trial tested 'cognitive-behavioural analysis system of psychotherapy' (CBASP), which is a psychological intervention usually used to treat chronic depression (Klein et al., 2004). This has similarities to CBT but did not fulfil our criteria to be grouped with CBT: largely due to the elements of analytic therapy and interpersonal therapy that its program includes. Similarly a trial of an early variant of IPT was not included in the IPT subgroup (Weissman, Kasl, & Klerman, 1976) as it pre-dated the current definition of IPT and extensive development was done to the intervention after this point. Two trials looked at mood management additions to smoking cessation treatment (Brown et al., 2001; van der Meer et al., 2010). These studies were eligible as they recruited people with a history of depression, randomised to a non-pharmacological relapse prevention intervention (mood management), and collected depression outcomes over the course of at least 1 year. They had a specific focus on smokers, but this is similar to other included studies which had a focus on a particular population of people who had recovered from depression. They did not provide data that could be used in the meta-analysis.

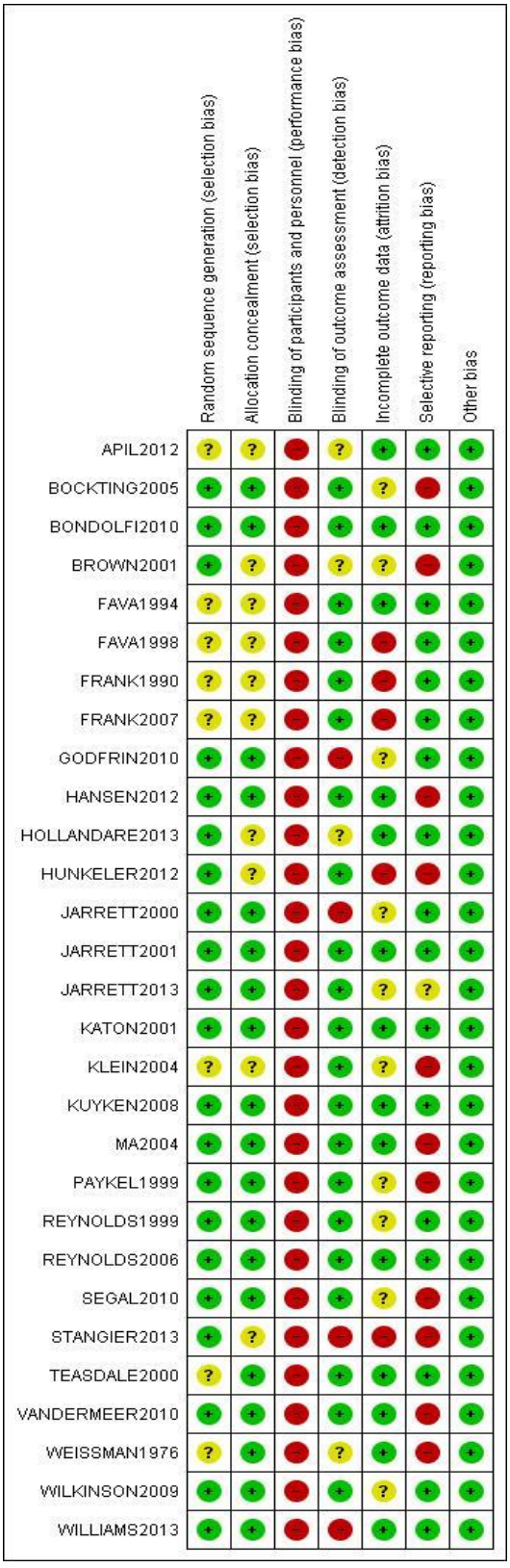
Risk of bias assessment

To assess risk of bias in a standardised and systematic way across studies, the Cochrane Collaboration Risk of Bias Tool (Higgins, Altman, et al., 2011) was used. Full risk of bias assessments for each study are summarised in Figure 5: Risk of bias assessments for .

Random sequence generation and allocation concealment were either at low risk of bias or there was insufficient information to assess risk. It was not possible to conceal the intervention from participants or providers those delivering it, so all studies were at high risk of bias for masking *per se*. The majority of studies used masked outcome assessors. Half of the studies had a low risk of bias from attrition; however, half were unclear or high risk of bias because of uncertainty about drop-outs, or because of high levels of attrition. There was a high risk of bias for selective outcome reporting in studies that included drop-outs as relapsed. If they did not provide separate numbers for participants who identified as relapsed, or for whom there was no information, this meant it wasn't

possible to assess whether there was a differential drop-out between intervention and comparison groups.

Figure 5: Risk of bias assessments for 29 trials included in this review



Legend: Assessment of validity of included studies according to the Cochrane Collaboration risk of bias assessment tool.

Low risk of bias in green with +, high risk of bias in red with −, unclear risk of bias in yellow with ?

Meta-analyses

The variation in control event rate (for 12-month data, range= 0.2-0.79, IQR= 0.41-0.63) meant relative rather than absolute risk reduction was preferred for the meta-analyses. All comparators were included within the same meta-analysis and the effect of the 'control type' explored post-hoc.

12 months

For the four main intervention groups (CBT, MBCT, IPT and service-level programs) data were available for 26 two-way comparisons at 12 months. For the three psychological therapies (see Figure 6) compared with all controls, the average risk of developing a new episode of depression by 12 months was reduced by 25% for CBT (RR= 0.75; 95% CI 0.64 to 0.89, I^2 = 8%), 21% for MBCT (RR= 0.79, 95% CI 0.69 to 0.91, I^2 = 0%) and 22% for IPT (RR= 0.78, 95% CI 0.65 to 0.95, I^2 = 0%). These psychological therapy subgroups were not statistically different at 12-month follow-up (Chi^2 = 0.21, df = 2 (P = 0.90), I^2 = 0%).

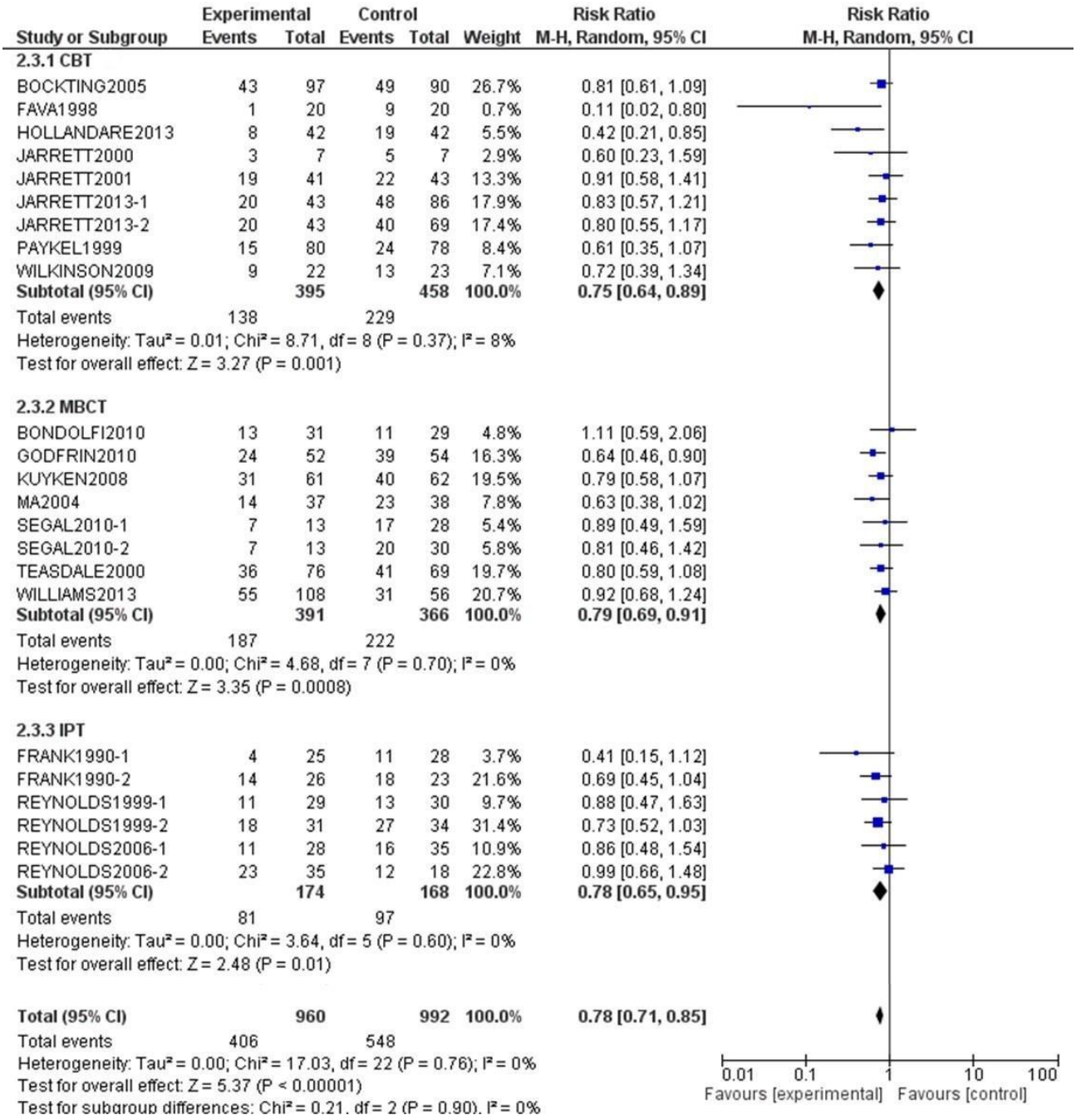


Figure 6: Forest plot off relapses in the 12-months post-randomisation in intervention vs. control groups for CBT, MBCT and IPT

For service-level programs (which included multiple interventions and service organisation) did not reduce the risk of developing a new episode of depression by 12 months (RR=1.00, 95% CI 0.81 to 1.23, $Chi^2 = 1.28$, df = 2 (P = 0.53); $I^2 = 0\%$). Results for specific programs within this group included a stepped care program (RR=1.26, 95% CI 0.74 to 2.15), a specialist outpatient program (RR=0.85, 95% CI 0.57 to 1.28) and a 'relapse prevention program' (RR= 1.01 95% CI 0.77 to 1.33). Data were

not available for the subset of relevant participants within a study of a web-delivered care-management and self-management program (Hunkeler et al., 2012).

One trial, of continuation CBASP, had a large effect but a relatively small number of participants (N= 82) and a large confidence interval (RR=0.12, 95% CI 0.02 to 0.91).

24 months

Data for relapse at 24 months were available for seven of the ten CBT studies, all six of the IPT comparisons, but none of the other trials (see Figure 7). The effect for CBT at 24 months was similar to the effect at 12 months but with greater heterogeneity (RR=0.72, 95% CI is 0.57-0.91, I^2 = 63%), but the effect of IPT was not sustained (RR=0.92, 95% CI is 0.81-1.05, I^2 = 0%).

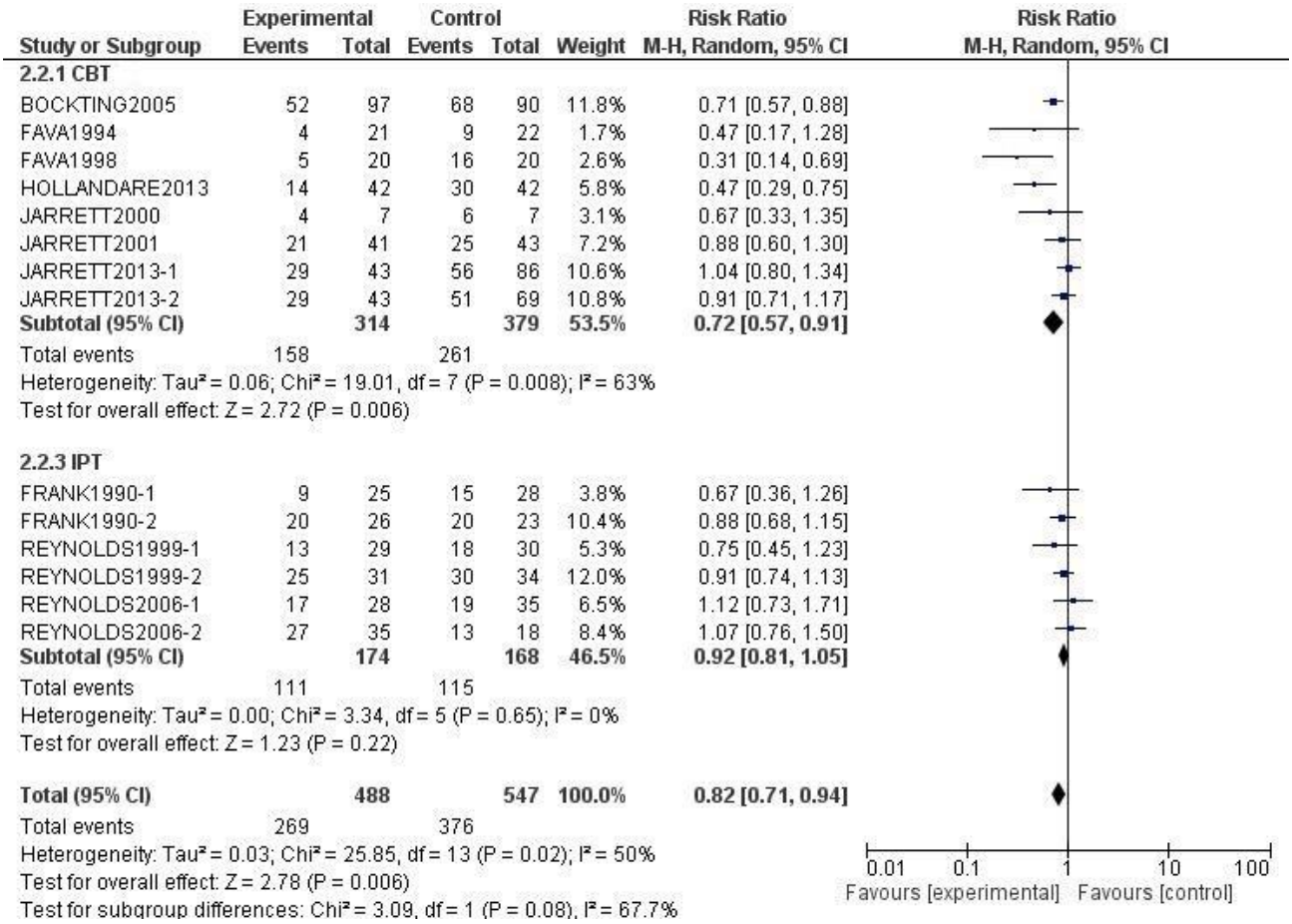


Figure 7: Forest plot of relapses in the 24-months post-randomisation in intervention vs. control groups for CBT and IPT

Attrition

Fifteen trials (1421 participants) reported drop-out at 12 months, which was the time-point with the most available data. There was no evidence of an important difference between intervention and comparison groups (RR= 1.15, 95% CI 0.85 to 1.52, I^2=0%).

Comparators

12-month data were used to assess the impact of treatment-as-usual or active comparators (data were limited at 24-months). At this time point, interventions reduced risk of relapse compared with treatment as usual (RR= 0.79, 95% CI 0.70 to 0.91) and active comparators (RR=0.77, 95% CI 0.68 to 0.87). There was no evidence of a difference between these groups (chi^2 = 0.12, df = 1 (P = 0.73), I^2 = 0%).

Publication bias

Publication bias refers to the finding that "investigations in which statistically significant differences between treatment groups have not been observed are less likely to be reported in scientific journals" (pp 374, Hetherington, Dickersin, Chalmers, & Meinert, 1989). Reporting bias could not be assessed statistically or using a funnel plot because there were too few studies and insufficient variation in study size (Hopewell, Loudon, Clarke, Oxman, & Dickersin, 2009). There are two particular areas of concern for risk of bias in this review. Firstly, inconsistent prospective registration of therapy trials, particularly in earlier years, means it is possible there are other trials that have been conducted but remain unpublished, and a small number of medium-to-large studies could change the conclusions. Secondly, the studies we identified and included were conducted by a limited group of researchers, particularly within the IPT sub-group.

Quality of the evidence

The GRADE rating criteria (Balshem et al., 2011) were applied for relapse to each type of intervention. Evidence was generally of low quality, which indicates that results may change following

further research (Guyatt et al., 2008). Reasons for downgrading were inconsistency of results, indirectness of evidence, imprecision and reporting bias.

Discussion

This review suggests that psychological interventions (specifically MBCT, CBT and continuation IPT) delivered when an adult has recovered from an episode of depression may reduce the risk of experiencing another episode within the following year by 22% on average (95% CI 15-29%). This compares with an efficacy reported for continuation antidepressant medication of 32% in the same time period (95% CI of 23-44%, calculated on the basis of 35 of 181 ADM and 108 of 180 placebo participants relapsing, Geddes et al., 2003).

The risk of relapse in the control arms varied considerably between studies (for 12-month data, range= 0.2-0.79, IQR= 0.41-0.63), which means any measure of absolute risk reduction should be interpreted with considerable caution (Akobeng, 2005). However, as an indication of the clinical utility of these interventions, the number-needed-to-treat (NNT) is 9 for the study population with the lowest baseline risk (Paykel et al., 1999), and 4.76 for the study population with the highest baseline risk (Reynolds et al., 1999). This estimate may be conservative given that the comparator groups were often active interventions, and given the conservative adjustment of drop-outs being counted as relapsed. Considering the suffering associated with an episode of depression, and the potential for an extended period of recovery to itself have a protective impact, this represents a potentially important effect.

However, longer-term evidence for the efficacy of these psychological therapies was limited: there was evidence for a sustained effect for CBT at two years, but the effect was not sustained for IPT, and there was no evidence available for MBCT.

There was no evidence that the service-level interventions had a reliable impact on relapse at 12 months (RR=1.00, 95% CI 0.81 to 1.23) with all individual studies reporting effects whose 95% CI spanned the line of no effect.

Interventions

CBT

There was considerable variation in the CBT relapse prevention trials in terms of the nature and duration of the intervention, and in the inclusion of participants who had had a variety of acute treatments. Generally, the authors of CBT trials had adapted standard CBT for acute depression into a relapse prevention intervention, and used their own manual in their own trials. This meant there was some heterogeneity between these interventions, particularly in terms of the length and frequency of sessions. Sessions were between 30 and 90 minutes and spanned periods of 8 to 35 weeks.

Most studies treated people individually, but two trials tested the intervention delivered to groups of 8 people (Bockting et al., 2005) or 4 people (Wilkinson et al., 2009). Assuming one therapist delivered each group, the therapist contact hours per person in these studies was 2 and 3 hours respectively. This compares with 5-7 hours (Fava et al., 1994, 1998), 10 hours (Jarrett et al., 2000, 2001) and 13-15 hours (Paykel et al., 1999; Stangier et al., 2013). Group formats are often chosen in an attempt to reduce costs, and may particularly suitable within relapse prevention where patients have no current pathology (Bockting et al., 2005). However, the time and work it takes to get participants into groups also has to be considered, as well as the potential to lose people or have gaps in treatment due to lack of flexibility: if a person cannot attend a one-to-one session this can be rearranged, whereas this is not possible with a group. That being said- the experience of the group environment may in itself be therapeutic, with participants sharing experiences and feeling understood.

One study tested a CBT intervention that placed relatively little demand on therapist time (Holländare et al., 2013). Participants were provided with a series of internet-based self-learning modules and given email support over a period of 10 weeks. Although a formal cost analysis is beyond the scope of this review, it seems likely that this would be cheaper than, say, the 10 sessions of individual face-to-face CBT offered in the three Jarrett's studies (5, 6 and 7 in Table 1), although reduction in cost does not necessarily mean an intervention is more cost-effective. The populations included in these

studies appear similar on clinical diagnosis and treatment history. The internet based, guided self-help CBT was effective in this individual trial, with a risk reduction of 58%, but there was a large level of uncertainty around this estimate (95% CI 15% to 79%] and replication would be needed in further studies.

MBCT

There was considerable homogeneity in the structure and content of MBCT with all trials following the same manual (Segal, Williams, & Teasdale, 2002) and offering eight weekly two-hour sessions to groups of between 9 and 15 people. However, there was some variation in the number of additional sessions offered, from none (Godfrin & van Heeringen, 2010) to monthly sessions for the trial duration (up to 16, Segal et al., 2010). There was also a high level of consistency in the way MBCT trials were structured and conducted, with two studies explicitly replicating Teasdale et. al's (Teasdale et al., 2000) methods (Bondolfi et al., 2010; Ma & Teasdale, 2004).

However, the consistency in eligibility criteria has meant that, in contrast to the CBT studies, MBCT has largely been tested in people who have responded to medication, and not in those who have experienced or responded to previous psychological intervention. Four trials explicitly exclude those who have experienced CBT, and of those that did not, two required participants to have remitted on antidepressant medication (see Table 1). There are several issues with this. Firstly, effectiveness may be limited to participants who recovered by means of pharmacological treatment. Secondly, the efficacy of MBCT may be a non-specific effect of psychological treatment. Some support for this can be found in a recent study (Williams et al., 2013) which found no difference in the efficacy at 12 month follow-up, of MBCT compared to cognitive psychoeducation (an attenuated version of MBCT with the meditation component removed).

IPT

IPT trials adopted a homogenous approach to the prevention of relapse, by offering maintenance sessions of IPT. All participants had IPT for the acute treatment of their depressive episode prior to randomisation.

All IPT trials provided monthly sessions for the duration of follow-up (either two or three years), except for one (Frank et al., 2007) that randomised participants to different frequencies of IPT: weekly, twice monthly, or monthly for the two-year trial. Two focused on older adults (Reynolds et al., 2006, 1999). As older adults are at an increased risk of relapse (Mitchell & Subramaniam, 2005, (Arean & Ayalon, 2010), the majority of patients within this meta-analysis could be considered high risk.

Whilst the reduction in relapse was similar to that seen for CBT and MBCT at one year follow up, any benefit associated with IPT was not present at two years despite the intervention being maintained over the two-year period. To give a numerical indication of the possible clinical impact of IPT in this group at 2 years, there is an NNT of 15, but with a large degree of uncertainty around this estimate (95% CI 6.25 to 33.33). All IPT trials were conducted by research groups from the University of Pittsburgh (USA).

Service level programs and other interventions

The fourth group of interventions reviewed were service-level programs, for which evidence of efficacy at one year was not demonstrated. This group consisted of only four trials, each of a different approach, for only three of which were able to identify efficacy data. They examined service provision, and apart from support and a focus on medication adherence did not explicitly focus on relapse prevention. A specific approach to relapse that is somewhat different to standard treatment approaches may be worth pursuing.

The remaining trials were of interventions not tested elsewhere (see studies 22 to 29 in Table 1). They did not appear to be effective, other than in one trial of CBASP (Klein et al., 2004). Of 42 participants given maintenance CBASP, one relapsed, compared to eight of 40 control group participants. The population of this study were those who had responded to treatment in an earlier

acute phase trial for people with chronic depression. Although independently developed, some consider CBASP to have key similarities to CBT, and that it should perhaps be viewed as a new variant of CBT (Power, 2013).

Influential factors

In the conceptual framework for this review I specified factors that may influence the efficacy of relapse prevention interventions, including clinical history, treatment history, comorbidities, and childhood maltreatment. I was limited in my capacity to explore these factors as our data was at a study rather than individual level. This meant that I could only examine variation in terms of the average over the study population rather than looking at individual differences. A meta-regression approach was considered but there were insufficient numbers of studies with consistent reporting of factors to be explored.

Clinical factors that have been identified as potentially important in relapse such as number of previous episodes (Bulloch, Williams, Lavorato, & Patten, 2013), levels of residual symptoms (Monroe, 2010), and psychiatric and physical health comorbidities (Hardeveld et. al 2010), did vary between trials. For example two of the MBCT trials required participants to have experienced three or more episodes of depression, whereas others, such as Vandermeer et al.'s mood management study (van der Meer et al., 2010), included participants who were recovering from their first episode. However, the absence of consistent reporting on these baseline characteristics across trials meant it was not possible to make a reliable statistical comparison. Recommendations on the reporting of randomised controlled trials aim to improve this consistency in the future (Moher, Schulz, Altman, & CONSORT Group (Consolidated Standards of Reporting Trials), 2001; Schulz, Altman, Moher, & others, 2010). I was not alone in continuing to experience this problem (Biesheuvel-Leliefeld et al., 2015), and access to individual patient data from trials may enable more sophisticated exploration of these issues (Lo, 2015).

There was some systematic variation in the intake populations of these trials, particularly in the acute treatment that had been received. This may be important as there are standard relapse prevention elements within acute treatment such as CBT, but not in others such as medication. Information about acute treatment prior to randomisation was widely available due to being part of linked trials, or being part of the studies' eligibility criteria. This means the included studies provide evidence that CBT may be effective for people who have received prior CBT to treat their acute episode, but also evidence that both CBT and MBCT may be effective as standalone interventions (that is, where participants were not treated with the same intervention in the acute phase). Further exploration of whether MBCT is effective in people who have received CBT or other psychological interventions is recommended, perhaps by broadening the eligibility criteria for MBCT trials to include those with a wide range of past treatment experience. Evidence for continuation IPT was all from studies whose populations had received IPT combined with medication for the treatment of their acute episode.

Strengths and limitations of this review

I have reported the review according to PRISMA recommendations (Moher, Liberati, Tetzlaff, & Altman, 2009, PRISMA Checklist in Appendix D), and believe it has several methodological strengths. Firstly, I pre-registered a protocol (Clarke et al., 2011), which is recommended to promote consistent conduct by the review team, and to ensure accountability, research integrity, and transparency of the eventual completed review (Moher et al., 2015). I conducted a comprehensive search of literature databases without specifying certain interventions, as well as contacting experts in the field to ensure coverage of the relevant research. I used two independent researchers to sift titles and abstracts of studies for inclusion, and checked data extraction for errors (Day et al., 1998). I assessed risk of bias and rated strength of evidence using recommended and widely used assessment tools (Guyatt et al., 2008; Higgins, Altman, et al., 2011).

I used patient numbers rather than reported effect sizes in our analysis, attempting to obtain these from study authors when they were not reported. I then applied a consistent method of analysis to all included studies, meaning our estimates of effect were not biased by variations in the design of

included trials. I was consistent in my treatment of drop-outs, used a clinically consistent point of randomisation, and compared data at the same point in time rather than using the last follow-up available. This resulted in a conservative estimate of treatment benefit and importantly may have allowed for a more accurate assessment of the relative evidence for CBT, IPT and MBCT. This allowed us to draw out potentially important differences in these interventions and trials which had not been possible in previous reviews (e.g. Biesheuvel-Leliefeld et al., 2015).

The limited number of trials and the difference in populations and trial designs meant it was not possible to statistically explore patient or treatment factors that might be associated with variation in outcomes. I also did not make any direct comparison against medication. This was because I was not confident that the use of medication was limited to only to control arms that explicitly tested medication. To illustrate the extent of the issue: some trials required participants to have had medication, some required them not to have had medication, some delivered medication themselves, some didn't control medication use but did measure it, and some had no information about medication use whatsoever. There was a similar picture within the relapse prevention stage, with some trials requiring participants to continue with, or discontinue their medication, not allowing participants to start medication, having no medication requirements but measuring their use, or not controlling or measuring medication use. The fact that I could not completely control for the use of medication is a limitation of the review.

Data from individual patients within trials in this review may allow for further exploration of relevant factors, including previous treatment (drugs or psychological) and specific psychological relapse interventions, the chronicity of the disorder and other possible indicators of relapse (e.g. (Kuyken et al., 2016). An understanding of the role of these factors could lead to more targeted, appropriately sequenced (in relation to both psychological and pharmacological interventions), and effective interventions. From a psychological perspective the focus should be on understanding the differential benefits of different treatments and the mechanism by which they exert their effect. Larger trials of psychological therapies, particularly ones that directly compare different interventions within one trial,

are warranted, but equally wide inclusion criteria in future trials would allow for subgroup analyses to explore these factors and identify other potentially important factors.

This review focussed on RCTs of a reasonable size, so provides evidence that the course of depression can be influenced by interventions, but doesn't cover the range of interventions that may have been tested using other study designs, or that have not been tested in scientific studies. There may be further information on relapse prevention in experimental studies, in the clinical experience of psychologists, doctors, or other professionals, and there may be strategies that people who have experienced depression are employing day to day to prevent their own relapses.

Implications for future research

Some have suggested (Rodgers et al., 2012) that brief self-help interventions may be as effective as formal psychological interventions for some people, thereby reducing both the burden and cost of treatment, yet the vast majority of the interventions identified were therapist intensive and lengthy (see Table 1). Although the review was not limited to psychological interventions, the majority of trials tested these. Current evidence suggests that, particularly given the fact that there are barriers to accessing healthcare services with depression (Hirschfeld et al., 1997), physical exercise, building networks of social support, psychologically informed self-help and engaging in meaningful activities could be a useful route to preventing relapse (NICE, 2009). Given the need to target people who are currently at least partially recovered, and to reduce the possibility of future episodes of illness, these interventions may be more flexible and more readily adapted for widespread use in relapse prevention. Seeing how they measure up to standard psychological interventions may well be an important avenue to pursue in the development of new effective ways to limit the suffering associated with this widespread and damaging disorder.

The influential factors identified may have had impacts on our estimates of efficacy that cannot be explored fully given our study level data and insufficient number of studies consistently reporting these factors (as mentioned above), and given the variation in study designs used within this review.

Restrictive inclusion criteria may have limited the generalisability of some findings, for example the MBCT trials selected populations who had not had (successful or very much) CBT. These populations may therefore not be representative of those who are offered MBCT within the NHS. There are further concerns that groups such as older adults are often excluded from research trials but are recipients of NHS care

Given the uncertainty about the exact impacts of the proposed influential factors on relapse rates, wide inclusion criteria may be recommended for future research. This has several advantages (as detailed in Yusuf, Held, Teo, & Toretsky, 1990), 1. Easier screening and recruitment which increases the feasibility of a large trial, 2. Large studies have less random error and so overall results are more reliable, 3. Results are more widely applicable, 4. Larger studies with less homogenous participants provide the opportunity for subgroup analyses. This last point is particularly important given the uncertainty around risk of relapse.

Conclusion

Psychological therapies delivered following recovery from depression, including CBT, MBCT, and IPT, may reduce risk of relapse after one year by 22%. For CBT this effect is maintained after two years. This is not dissimilar to that previously reported for continuing medication, but without the need for continued treatment throughout the follow-up period. The difference in effectiveness between interventions and the mechanisms by which these interventions exert their effect are not well understood, nor is the most effective and efficient way to deliver them. Further research into interventions after recovery from depression is warranted, particularly with regard to accessibility. Future research may use broad eligibility criteria in order to ensure findings are applicable to clinical populations, and to allow for exploration of the potential impacts of influential factors and mechanisms by which they exert their effects.

Chapter 3 A complex systems approach to relapse prevention

Abstract

Introduction: Evidence from randomised controlled trials supports the idea that the course of depression can be changed by interventions, and that both pharmacological and various psychological interventions can reduce the risk of relapse following recovery from depression.

Objective: To explore the process by which relapses might be prevented.

Complex systems approach: The preservation of mental health following recovery from depression is a dynamic long-term process involving complex interactions between biological, psychological and social factors and continual interaction with potential environmental stressors. These interactions at times result in depression: the 'emergent phenomena' that we are looking to reduce or prevent. Within the human system there are several potentially important mechanisms underlying depression at different 'levels of explanation', such as disrupted monoamine transmission and impaired cognitive control. These mechanisms are not mutually exclusive, and are not linked to depression in a linear causal relationship, but may nevertheless be useful as targets for relapse prevention interventions. I propose developing an intervention based on this 'complex systems' approach, which targets mechanisms that a) have evidence to link them with depression, and b) are theoretically possible for an individual to effect within their everyday life and routine activities.

Discussion: I have detailed an approach to relapse of depression which is based around some of the fundamental properties of complex systems. This approach will be used to inform the development of a relapse prevention intervention. The next steps are to explore the possible content of this intervention, and how it might be delivered.

Introduction

Depression is a debilitating and distressing disorder, which often has a relapsing and remitting course. So far in this thesis I have presented a summary of the classification of depression, its prevalence, and the approaches that are available to change the course of the disorder. Effective treatments can help people to recover from an episode of depression, but people who have comorbid disorders, have recently recovered, or have high levels of residual symptoms, may be at particular risk of relapse (Buckman et al., 2018). The focus of this thesis is to look at what could help people to maintain their recovery over time.

There are several interventions that appear to be effective in reducing the risk of relapse for those who are offered them. Chapter 2 presents a systematic review of non-pharmacological interventions that have been tested in randomized controlled trials, the strongest in the hierarchy of medical evidence (Piantadosi, 1995). This review predominantly identified trials of formal psychological therapies with structured intensive contact with a therapist (8 to 20 sessions), although one trial adapted therapy to be delivered online (Holländare et al., 2011). Most interventions were delivered individually , but some, such as MBCT were delivered in groups (e.g. Williams et al., 2013). The meta-analyses support the efficacy of cognitive behavioural therapy (CBT) in preventing relapses up to two years after recovery, across various populations and following various acute treatments. There was support for the efficacy of Mindfulness-Based Cognitive Therapy (MBCT) up to one year, although study populations were mostly limited to people who had remitted using antidepressant medication, or who had not experienced cognitive therapy. There was some evidence for the efficacy of maintenance IPT at one year but not at two years despite continued booster sessions.

The risk reduction following these therapies were indistinguishable at 1 year, (Clarke et al. 2015) despite their different therapeutic targets and proposed mechanisms of action. CBT focusses on dysfunctional thoughts and their relation to feelings and behaviour (RR=0.77, 95% CI=0.64-0.89), MBCT focusses on directing attention (RR=0.79, 95% CI 0.69 to 0.91), and IPT focusses on resolving interpersonal difficulties (RR=0.78, 95% CI=0.65 to 0.95). Continuing to take antidepressant medication also reduces relapse risk, yet has a proposed mechanism of action at

that is biochemical rather than directly cognitive or psychological. In trials that have directly compared psychological therapies to medication, the risk reductions are very similar (RR 0.075 95% C I0.001–0.149, Biesheuvel-Leliefeld et al., 2015).

However, in a recent dismantling trial, removing the mindfulness element of MBCT did not reduce its efficacy in preventing relapse (Williams et al., 2014), and a trial comparing relapse prevention focused CBT with manualized psychoeducation also found no difference in outcomes (Stangier et al., 2013). This calls into question the actual mechanisms by which relapse prevention interventions exert their effects, and the degree to which the mindfulness and cognitive components are necessary elements of the therapies. Kazdin argues that, given several studies which identify therapeutic changes linked to CBT in the absence of, and prior to any cognitive changes, CBT is likely not working through the cognitive mechanism its proponents originally envisaged (Kazdin, 2007). We might better think of these as therapeutic 'targets' rather than being the actual mechanism of action behind the reduction in relapse risk. It might be that bringing a more long-term focus into interventions improves relapse prevention (which is a long-term issue), in those in Chapter 2 this may be by reducing any residual symptoms or simply extending the time where someone is having input.

There also might be gains to be made through looking whether there is any additional focus on relapse prevention as separate from acute treatment. Although MBCT was designed specifically for relapse prevention, all of the interventions identified are firmly within a clinical psychology model with illness or illness prevention at the core, and perhaps a focus on wellbeing and building resilience could be extended. The 'Positive Psychology' movement highlights there are undeveloped avenues of research within the world of psychology such as into positive moods and what makes people flourish, and it is possible existing interventions perform well at knowing "*how to bring people up from negative eight to zero but not as good at understanding how people rise from zero to positive eight."*(Gable & Haidt, 2005).

The Lancet commission's recommendations for the future of psychological therapies highlights mechanisms as both an area that has been lacking clarity within psychological therapies research, and an important focus for future interventions (Holmes et al., 2018). However, the fact

that no single relapse prevention strategy stands out as ‘superior’, and the fact that the actual mechanisms of treatment effect are not clear indicates that the process by which wellbeing is maintained is complex, and that depression is not a simple ‘mechanical’ issue with one solution. I will therefore discuss mechanisms but aim to do this with the caveats mentioned above, and to specify whether I am referring to ‘therapeutic targets’ or ‘*proposed* mechanisms of action’, throughout this chapter. A systems approach could explore the potentially complex and interacting mechanisms behind relapse prevention at a broader level, with the key issue of the long-term process of relapse prevention at the core.

A whole system approach to relapse prevention

Relapse prevention can be looked at as the avoidance of an episode of depression or deterioration at a specific point in time, or equally the long term process by which mental health is maintained (Slofstra et al., 2017), involving interactions between many factors and with potential environmental stressors (Pincus & Metten, 2010; Tschacher & Haken, 2007). As such, a systems approach, which looks at the way system components work together and the properties of the system as a whole over time (Boulding, 1956), may provide an insight as to how relapses occur and may be prevented. In contrast to the linear ‘cause and effect’ focus which often characterises the disease model of mental illness, systems approaches such as the biopsychosocial model of health (Fava & Sonino, 2008) may be appropriate for a long-term approach as it focusses on the whole person, and takes into account potentially important factors from different and varied domains of a person’s life.

> *The next level is the "human" level that is of the individual human being considered as a system.* General systems theory (Boulding, 1956)

A complex interaction between biological factors (including genetics), psychological factors and cognitive biases, and social factors all play a role in helping people to stay well (Fava & Sonino, 2008). A systems approach lends itself to characterising this as it considers how and why system components interact and link to certain outputs over time. In this chapter, I will begin to consider

how wellbeing is maintained over time, and, given various important and interacting factors, how relapses might be prevented.

Objectives

In this Chapter I aim to elucidate the process by which wellbeing is maintained and relapse of depression prevented within the framework of a complex systems theoretical approach. I will firstly explore more general theory related to complex systems and their characteristics. I will then relate this to relapse of depression by exploring some proposed mechanisms underlying depression and its treatment at a biological, psychological and social levels of analysis, as well as a combined model. Finally, I will present an approach to relapse prevention that instantiates this approach with therapeutic targets drawn from the models discussed.

Systems approaches

Systems can be classified according to their external interactions (open/closed) and their complexity (simple/complex). A person who is at risk of relapse of depression would be classified as an 'open' system because of interactions with surroundings. This system could also, along with most living things, be considered complex, although the concept of complexity is 'slippery' as it does relate to some extent to the place from which you view the system (Bar-Yam, 2002). Examples of systems that could be studied as complex might be a city, an ecosystem, or a neural network. A key defining characteristic of complex systems is that (with increasing complexity) the interrelations between system components become difficult to model and thus the system seems to take on a 'life of its own'. Other key characteristics have been identified:

> *Complex systems have several defining characteristics including the tendency to be self-organising, be sensitive to initial conditions, and make non-linear phase transitions (to jump quickly from one position to another very different position); the existence of emergent properties; and the importance of interaction effects and feedback (Shiell, Hawe, & Gold, 2008).*

In order to explore the meaning of some of these system properties before I apply them to depression, I have provided examples from other complex systems in Table 2.

Table 2: Four properties of complex systems, their definitions, and an illustrative example

Property	Definition	Example
Emergence	There are properties or behaviours that emerge from the system that are greater than the sum of its parts.	The structure (or cooperation) of an ant colony (Drogoul & Ferber, 1994). Each ant acts by selecting a task based on reacting to the stimuli around it, but over the whole colony a set structure and apparent co-operation emerges.
Non-linearity	A change of output is not necessarily proportional to a change in input.	The number of cars in a city increases up to a certain number (say, 10, 000 cars) with no consequence and traffic continuing to flow freely. Above this critical point, there is a rapid slowing of traffic and complete standstill when the number of cars reaches 11,000.
Spontaneous order or self-organisation leading to **States of equilibrium**	Complex systems have a tendency to become globally coherent. They have feedback loops that can either dampen change or accelerate change. The order reached is then self-sustaining (states of equilibrium)	When heating some water in a pan the water is initially in a state of equilibrium. The state is in equilibrium and the temperature slowly increases, and then a self-organised pattern (convection) occurs and the water heats very rapidly (Demic & Cheng, 2014). The water then stays around boiling temperature.
Capable of change: adaptation, growth:	These systems learn and adapt, and are continually interactive, "whereby 'interactive' refers to the system-environment circularity" (Tschacher & Haken, 2007).	Natural selection is often described as a process that is causally related to a species' survival. However as well as being a 'cause' it is also a consequence of the ability of an organism and it's traits to survive and reproduce in a particular environment, and "*It is these functional effects that are ultimately responsible for the trans-generational continuities and changes in nature*." (Corning, 2002)

Applying properties of complex systems to depression

I will now consider the four properties of complex systems detailed in Table 2 (above) and explore how they might relate to depression, and the process by which wellbeing is maintained and relapses prevented.

Emergence: Depression (as well as wellbeing or resilience) is an emergent property of the human system, in that it is a phenomenon that cannot be directly linked to and explained by the sum of the parts of the system (Pincus & Metten, 2010). **Emergent phenomena** only occur from complexity: a less complex system such as a robot would not exhibit mental health.

There are several implications of viewing depression in this way, the most important perhaps is that we cannot directly target emergent phenomena, we must target something within the system the emergent phenomena derive from, and then observe the impact of this change on the phenomenon. Relapse prevention may be better compared to dealing with a traffic jam (the emergent phenomena), rather than simply a blocked road. The 'traffic jam' can be targeted in multiple ways (traffic lights before the obstruction, people using a smartphone app to reroute to avoid the obstruction, radio announcements asking people to avoid the area), whereas an obstruction can be directly removed. There are probably multiple different ways to prevent relapse, as appears to be the case from the variety of pharmacological and psychological interventions which reduce relapse risk (as described in Chapter 2 and in the Introduction to this Chapter).

In order to attempt to reduce this emergent phenomenon we must first observe and monitor it. Using the classification of depression that I described in Chapter 1, the emergent phenomenon of depression and wellbeing may be simply represented by this graph of depression plotted over time (See

Figure 2: Illustrative figure of a common trajectory of depression and how this thesis will approach relapse prevention on page 45).

Most research uses a categorical or threshold 'indicator' of this phenomenon such as 'relapse of depression' (a period of time spent above the threshold for depression after a period below the threshold) or 'meeting criteria for depression' (a depression symptom score that reaches a certain

cut-off). However, looking at the whole trajectory of the emergent phenomenon also has potential value. It could be used to clarify the aim of an intervention: to make any depressive episodes less severe (a shallower bump in the line), of shorter duration (a narrower bump), or to maintain a steady wellness state and prevent fluctuations from this (a consistent low line), or all of the above. There are then specific methods of analysis which can be used to examine the whole 'biopsychosocial resilience' trajectory: time-series analysis, state space grids, catastrophe modelling and network modelling (Pincus & Metten 2010). Certain questions lend themselves to examining the dynamics of the emergent phenomena, such as whether there appears to be a 'downward spiral' as reported by people who experience depression, in that a gradual decline turns into a rapid descent, or whether stress has an additive impact on relapse risk (Levine et al., 2020). Details about the trajectory of depression and wellness may have implications for when the best time is to intervene.

This complex systems approach focusses more on whether the emergent phenomenon changes, rather than assuming the cause of change. In this way it is perhaps a pragmatic approach, and can be seen as valid given that we do not know the exact driver of change in existing interventions (e.g. removing the mindfulness element of MBCT does not reduce its efficacy, Williams et al., 2014).

Non-linearity: Emergent phenomena arise from complex interactions between system components in a non-linear process. We would expect that an input or change to one of the system components may then accelerate change and lead to system-wide impacts, or may lead to minimal impact, but not that there would be a 1:1 cause and effect relationship. For example, rather than viewing an obstruction in the road as the 'cause' of a traffic jam, a person could observe that the traffic jam is caused by: a narrow road with a large and unexpected obstruction; the time of day meaning roads are busy and cars are unable to re-route to other roads after being directed to do so using satellite navigation technology; the timing of local traffic light systems that directed them towards the obstruction; etc.

Taking this approach, we would not expect there to be a linear relationship between the 'causes' or risk factors that have been identified (and summarised in Chapter 1), and consequent relapse

of depression. Factors such as the number of previous episodes a person has experienced may, at a group level, increase our accuracy at predicting relapses, but the extent to which we could ever expect to predict emergent phenomena using one 'factor' is necessarily limited within a systems approach. There are implications for our expectations from treatments: given non-linearity of the system, the fact that antidepressant medication which exerts its influence on one part of the post-synaptic neuron then results in a reduction of the emergent phenomena of depression in anyone at all may be seen as a large effect. However the increase in the effectiveness of medication when provided alongside 'clinical management', and prescriber effects, and the fact that placebos with no 'active' medication can reduce depression (Fournier et al., 2010) illustrates the expected complexity around this effect. It has been suggested that key nodes within the system can be identified as therapeutic *targets* (Pincus & Metten, 2010) without assuming or proposing that they are in fact the actual therapeutic *mechanism*. This is a flexible approach: it assumes there are several possible routes to influence the system as a whole. I will take this approach and later in this chapter look to models of depression to identify potential target areas from biological, psychological or social models (or all of the above).

Spontaneous order or self-organisation (that is then self-sustaining in **states of equilibrium**): Non-linearity means that we do not expect to observe a risk factor linking with an emergent phenomenon in a 1:1 relationship, however there are some patterns that can be observed in how systems change. We would expect complex systems to become globally coherent through feedback loops that either dampen or accelerate change: also called global coherence or 'order for free' (Kauffman, 1996). Karl Friston proposed that this adaptation means minimising 'free energy' by optimising predictions around interactions with the external world:

> *Adaptive agents must occupy a limited repertoire of states and therefore minimize the long-term average of surprise associated with sensory exchanges with the world. Minimizing surprise enables them to resist a natural tendency to disorder* (Friston, 2010).

There are several studies that suggest that both mental health and depression are 'attractor states' (states which systems tend towards). Hosenfeld et al., (2015) investigated this through using time series plots and frequency distributions of the DSM-IV symptoms of their study cohort

over the course of two years. They found high bimodality coefficients (BC>.55) for 66% of the sample, and classified 90% of the symptom distributions as bimodal. This corresponds to our diagnostic criteria: as described in Chapter 1, a diagnosis of depression depends on experiencing symptoms consistently and to a significant severity, continuously over a certain period of time

Once a state of equilibrium is reached this is then robust and somewhat resistant to change. If we imagine that for everyone, mental health and depression are attractor states, albeit with different 'pulls', and explanation for the prevalence of relapses of depression may be that acute treatment does not push the system far enough into a state of wellness equilibrium. Indeed, evidence that relapses are more common for people who are close to the threshold for depression on recovery, and for a shorter period of time (Buckman et al., 2018) supports this. Treatment often focusses on reducing and resolving depressive symptoms, however people's experience of recovery and wellbeing goes much further than simply the absence of depression symptoms. In a systematic review Leamy and colleagues (2011) identified 97 papers that examined the concept of recovery, and collated these into a conceptual framework which included 13 characteristics that people gave to describe recovery. These were not absence of depression symptoms, but rather positive constructs such as connectedness, hope and optimism for the future, identity, meaning in life, and empowerment (Leamy, Bird, Boutillier, Williams, & Slade, 2011)

The self-organisation that occurs, and the resultant state, depends on system components (and therefore will vary between people). For example, it has been argued that if a person's network of depression symptoms is closely linked, they are more likely to relapse, as small changes in the system could lead to onset of depression. For others, whose depression symptoms are less closely related, it may take more of an outside influence to push the whole system into spontaneously organising into a depressed state (van Borkulo et al., 2015). Similarly the concept of centrality of symptoms might suggest that changes to 'fatigue' or 'feelings of worthlessness' would have a broader impact on the whole network of depression symptoms than if there were changes in more peripheral, less connected symptoms (Fried et al., 2016). It may also be that repeated experiences of depression increases the 'pull' of it as an attractor state for individuals (see the next section on change).

Capable of change: adaptation, growth: People who have recently recovered from depression may be susceptible to relapse because they may not be fully in a 'well' equilibrium state yet, but also because they have experienced an equilibrium depression state before and have adaptations to it. A fundamental property of all open complex systems is that they learn and adapt, and are continually interactive, "whereby 'interactive' refers to the system-environment circularity" (Tschacher & Haken, 2007). In terms of depression, this has biological plausibility: neurons "that fire together, wire together" (Hebb, 1949), and so all experience impacts the brain. This raises the question of whether an input such as a medication can have intended changes, as a recovered equilibrium state may be reached but then removing that medication may unsettle the system. This fits in with the finding that, although continuation antidepressant medication is effective at reducing risk of relapse, this effect is not maintained following discontinuation of medication, and in fact people then relapse at the same rate as prior (Berwian et al., 2017).

Systems adapt and learn, so although the experience of depression will have had impacts on the system, continued 'health' of the system will also be 'remembered'. This hypothesis is consistent with the finding that life events are less likely to precipitate episodes of depression as more episodes are experienced (Kendler et al., 2000). The aim of relapse prevention interventions may then be to maintain help a person to maintain the 'well' state for longer in order for the system to learn and adapt to this state.

Models of depression at different levels of explanation

Up to this point I have described an overarching approach: to look at the properties of complex systems and apply this to our understanding of, and approach to, relapses of depression. This can then shape our understanding of how they might be prevented. In summary: a) there may be multiple different mechanisms underlying relapse; b) it is unlikely that there will be a linear cause and effect relationship between any one change within the system and risk of relapse; c) people may be less likely to relapse if they are in a robust state of wellness, and d) if this wellness is maintained for longer periods any adaptations to a depressed state may be reduced. If systems behave in a non-linear fashion and are difficult to model, the approach we might take is to target any potentially important mechanisms, and then measure the impact on the emergent

phenomena in order to assess empirically the link between that particular mechanism and depression. Translating this approach into a relapse prevention intervention therefore requires a closer examination of the potential mechanisms underlying relapse of depression.

To add some additional complexity: mechanisms may reflect a process at different 'levels' of explanation (Holmes et al., 2018). It may be true that flooding synapses with serotonin reduces depression and that improving cognitive control through MBCT reduces depression, and these processes might be entirely independent of each other, or have any level of interaction. To give another example, the 'mechanism' behind the maintenance of depression at a psychological level might be that dysfunctional negative schemata directs attention towards negative stimuli and this leads to more depressed mood. The 'mechanism' at a biological level might be changes in the monoamine circuits in the amygdala, ventral striatum, and perigenual anterior cingulate cortex lead to more depressed mood. Both of these may be true but even if so, one does not determine the other.

Marr and colleagues described this concept, that there are multiple 'levels' at which to approach or explain human processes, using the analogy of a cash register (Marr, Ullman, & Poggio, 1982). The cash register's function is to add up the total amount of money to be demanded of the customer, and to calculate the change they should receive (the computational level). This level of analysis has its own rules, such as addition and subtraction. In order to perform its function, the cash register can use one of several possible representations and algorithms (the algorithmic level): for example, using Arabic numerals or using binary number representation. The cash register must have some 'hardware' (the implementation level), which could take several different forms.

In terms of mental health, the computational level may be thoughts or feelings and their function within a social world (psychosocial), the algorithm level may be the patterns of representation in the brain such as neuronal firing, blood flow, and neurotransmitter activity; and the 'hardware' may be the brain and body. Each of the 'levels of explanation' are inter-related but also independent to some extent: the hardware cannot be inferred from the computation or algorithm

(and vice versa). Relationships between the levels can, however, be explored and tested empirically.

Of course, a cash register is a comparatively closed and simple system compared to our example, but these levels can serve as a structure to examine models of depression at different levels of explanation. A 'model' is defined as a simplified representation of a process (so several potential mechanistic processes), and it is important from the outset to note this distinction between a model of a process, and the process that it seeks to represent, so as not to "confuse the map with the terrain" (pp. 354, Pincus and Metten 2010). Models of depression may feed into our understanding of the individual mechanisms occurring within the wider system, and hence may point towards therapeutic targets. I will firstly detail some models from within the psychosocial, psychological or cognitive, and biological levels, and then go on to describe a model that attempts to integrate between levels using empirical evidence to justify any links.

At the psychosocial level, models of depression offer 'maps' of the interplay between person and environment. Social and societal factors are often used as predictors of poor health outcomes, such as the link between childhood maltreatment and later depression (Vythilingam et al., 2002). Therapies such as interpersonal psychotherapy are focused at this level, and are effective at treating depression (Cuijpers et al., 2011). Interestingly, life stress (or negative life events) has been linked to first episodes of depression but then is decreasingly important when it comes to further episodes (Monroe & Harkness, 2005). Perhaps interpersonal stress can cause a first episode of depression, then as the system adapts to the depressed state lower levels of stress are required to push a person back to that state.

At the psychological or cognitive level, models of depression centre around a person's thoughts and feelings. Beck's cognitive model, describes depression as arising from three mechanisms, the 'cognitive triad' (negative views about the world, oneself and the future), negative self-schemas, and errors in logic (Beck, 2005). There is an interplay with behaviour: seen as intrinsically linked with thoughts and emotions. Within a psychodynamic model depression begins through the processing of a loss, and through the interplay between different parts of the self (including with repression). This approach has led to the development of several effective

interventions, such as CBT and psychodynamic therapy, or behaviour activation, which characterises depression as a disorder of avoidance and so aims to increase activities (Martell et al (2010).

At the 'biological level', models primarily 'map' depression in terms of our hardware. There have been several suggested biological mechanisms underlying depression, such as insufficient or too much serotonin (Carver, Johnson & Joormann, 2008; Harmer, 2008; Nordquist & Oreland, 2010), problems with monoamine transmission more generally (Booji, Van der Does & Riedel, 2003; Rosier, Elliot & Sahakian, 2012), or genetic polymorphisms in the 5-HTTLPR gene (Clarke et al., 2010; Rosier et al., 2012). The role of inflammatory processes is also the subject of considerable research (Kohler, Krogh, Mors & Eriksen Benros, 2016; Rohleder, Wolf & Wolf, 2010; Maes et al., 2009), as well as the impact of physical health (McPhie & Rawana, 2015). The 'disease' model is perhaps the most prominent, where symptoms are seen as the manifestations of an underlying pathogenic process, with (potentially) a linear uni-directional relationship between a pathological process and the resultant mental illness. The medical approach has resulted in the development of effective drug treatments such as tricyclics like amitriptyline, and more recently selective serotonin re-uptake inhibitors (Lopez-Munoz & Alamo, 2009).

Integrating mechanisms from different levels of explanation

I have described models of depression at different levels of explanation, which may be seen as different maps of the same terrain. Integrated models seek to represent processes at more than one level of explanation within a single model. Within a healthcare setting, clinicians may aim to take the gold standard 'biopsychosocial' approach, and consider the whole person that is coming to ask for help or support. We know that there are myriad complex interactions between these levels. Genetics play a role in depression (NICE, 2010), but this is not a purely biological role, as environmental factors may impact genetic expression (Nestler, 2013) and genes may also shape behaviour of the individual and those around them (Viding & McCrory, 2020).

Several of the proponents of the models described above argue for incorporating their work into, and linking to findings from other levels. For example, Aaron Beck has argued that evidence from

neurobiological studies of depression should be integrated with the cognitive model, and has proposed a model to do this (Beck, 2005). In this model, he incorporates findings from neuroimaging studies using cognitive tasks. The focus remains predominantly at the psychological level, but biology is incorporated. Similarly, Jon Roiser and colleagues have proposed a model of onset and maintenance of depression that incorporates similar elements, (Roiser, Elliott, and Sahakian 2011).

Extended cognitive neuropsychological model of depression

The extended cognitive neuropsychological model of depression (Roiser, Elliott, and Sahakian 2011) brings together potential mechanisms from multiple different levels of explanation, and describes the evidence that supports each mechanism as important in either the onset or the maintenance of depression. Figure 8, below, illustrates the core components of the model.

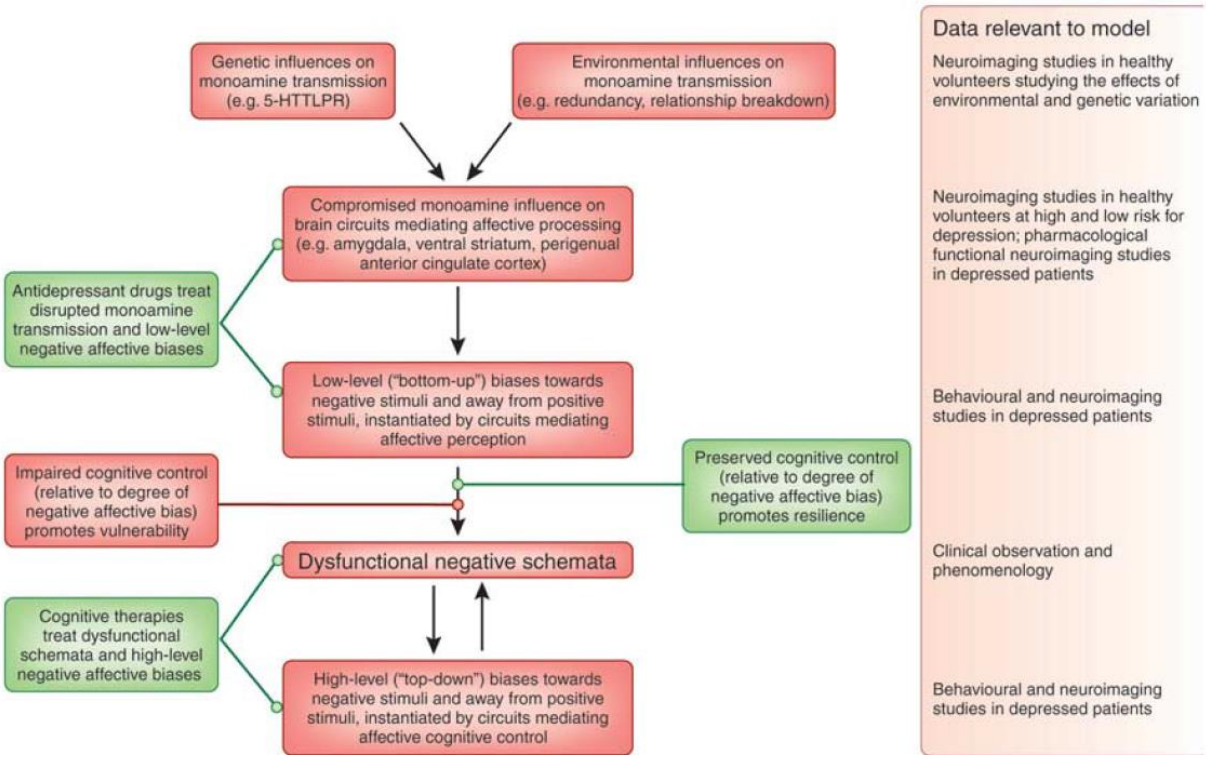


Figure 8: The extended cognitive neuropsychological model of depression from Roiser et al., 2011

In this figure, the red boxes indicate factors contributing to the development and/or maintenance of depressive symptoms. Genetic and environmental influence are linked to compromised monoamine influence. This does not impact mood directly, but changes low-level biases away

from positive stimuli and towards negative stimuli, then resulting in dysfunctional thoughts (or 'schemata'). In this way the model links the hardware (influences from genes and environment on the body) with algorithmic (affective processing biases) and social levels.

The green boxes indicate factors that relate to recovery from depression. The two boxes on the left relate to areas where treatment is effective at reducing depressive symptoms: antidepressant drug treatments (which are suggested as treating disrupted monoamine transmission and low-level biases), and cognitive therapies (which are suggested as treating dysfunctional schemata). Rather than simply looking at associations or correlations between components of the model (as with the red boxes), interventions which seem to change the behaviour of the system give better evidence that the model includes mechanisms or causal links.

The authors retain a primary focus at the level of the algorithm (cognitive control balanced with affective biases), and attributes the 'core' cause of depression at this level. I will however attempt to incorporate multiple mechanisms from this model as therapeutic targets rather than focus on one core 'cause'. This is given: that depression emerges from multiple mechanisms (emergence), that the role of each is unpredictable (non-linearity) and likely to be different in each individual as a result of past experience (adaptation). It is also in line with the uncertainty previously described around the validity of these mechanisms themselves.

I propose taking key elements from the extended cognitive neuropsychological model of depression but focusing more broadly than cognitive biases, onto **any** element of the model that in theory could be modifiable by an individual within their everyday life. There are several parts of this model which, purely theoretically, a person who wished to reduce their risk of depression could attempt to target outside of a healthcare or supported setting. As explored in Chapter 1, accessibility has been identified as particularly important in relapse prevention. For example, at the highest level of the model illustrated, it is not possible to change your own genetics but it is possible to have control over some environmental influences on yourself. This may be through avoiding risk, or increasing positive environmental exposures. There are further parts of this model which may be within a person's sphere of influence: a person could choose to take

antidepressant medication, seek out activities which strengthen cognitive control and/or modify affective biases, and reduce negative or increase positive schemata.

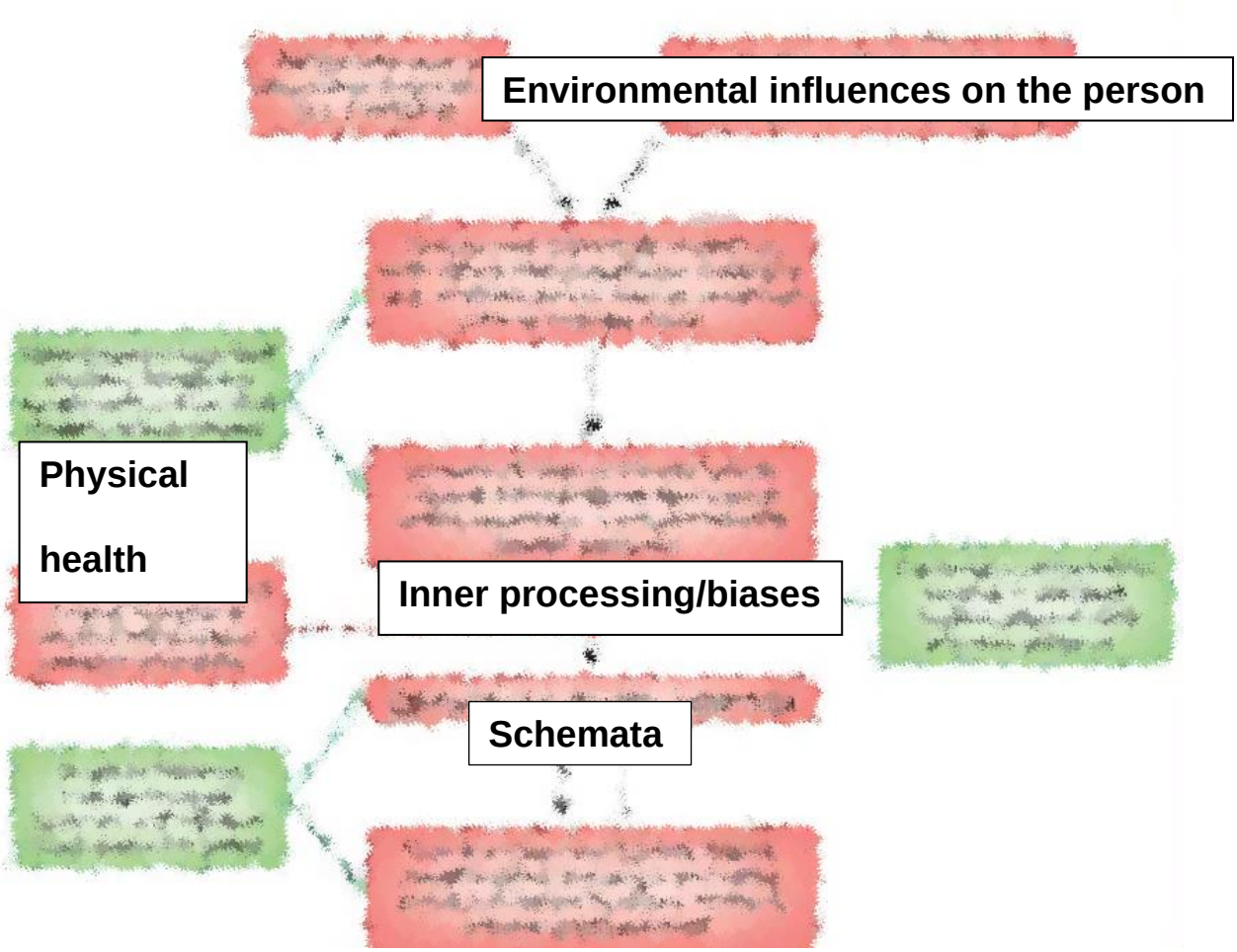


Figure 9: Four potential therapeutic target nodes for a novel relapse prevention intervention, derived from and overlaid on Roiser et al.'s (2011) extended neuropsychological model

Note: The extended neuropsychological model is blurred out here but presented in full in Figure 8. The four target nodes highlighted here are placed over the part of the model from which they were derived.

Long-term change

I have therefore identified four nodes from the model above which may be targeted by individuals in their relapse prevention efforts. However, this model misses a key element of relapse prevention which is that it is a long-term process. Indeed, many models of depression at do not specifically focus on temporal effects: the impacts of experiencing depression and the potential

differences between primary prevention, acute treatment, and relapse prevention. Fundamental to relapse prevention itself is prevention of a change over time, so consideration of how the system changes and adapts is key. Indeed, it has been argued that an additional level of explanation should be added to those from Marr if we are to move beyond explaining more simple closed machine-like systems:

> *"I am not sure that Marr would agree, but I am tempted to add learning as the very top level of understanding, above the computational level. [...] Only then may we be able to build intelligent machines that could learn to see—and think—without the need to be programmed to do it." Tomaso Poggio, Vision (David Marr. 2010. The MIT Press), Afterword, P.367*

The 'scar' hypothesis suggests that each episode of depression causes a psychological and cognitive 'scar', and that this increases risk of future depression (Zeiss & Lewinsohn, 1988). Attempts to demonstrate a 'scar' at a psychological level have not always been successful (Beevers et al., 2007). The 'kindling' is the counterpart of the 'scar' hypothesis, but at a more biochemical level. It suggests that neurocognitive changes arise during the course of depression and that relapses may be a function of these (Monroe & Harkness, 2005). There is some evidence to support that neural pathways associated with depression become stronger during a depressive episode (Vidailhet, 2010).

The accessibility and variety of intervention targets should therefore allow for more people to be able to make sustained changes that fit into their everyday lives, therefore having more of a long-term protective effect from reversion to a 'state' of being depressed, or allowing people to better adapt to a 'wellness' equilibrium state that is then resistant to change. Additional to the natural impact of people choosing for themselves what would fit within their lives and results in positive mental health for them, some habit formation techniques might be useful to provide people with a strategy on exactly how to implement changes in a way that is likely to be long-term.

A complex systems model of depression and proposal for intervention

The schematic below represents the system which I am focussing the relapse prevention intervention on, and its characteristics. When describing an intervention approach it is important to define the 'problem space': and explain exactly what system the intervention is designed to influence (Bar-Yam, 2002). It differentiates this intervention from, say, an early phase pharmaceutical intervention which may aim to target a system of biological processes within a body as it's whole problem space, or perhaps a public health intervention whose target system is the population of a country. I have not used a causal loop diagram as is often used to describe systems, as I am not proposing specific causal relationships beyond the body being impacted by environment and being the basis of thoughts, feelings and behaviour. Instead, the properties of interactions within the system are described. The physical body is represented by a dashed circle due to it also being itself an open system within this problem space. I will consider depression an 'emergent phenomenon' of this system.

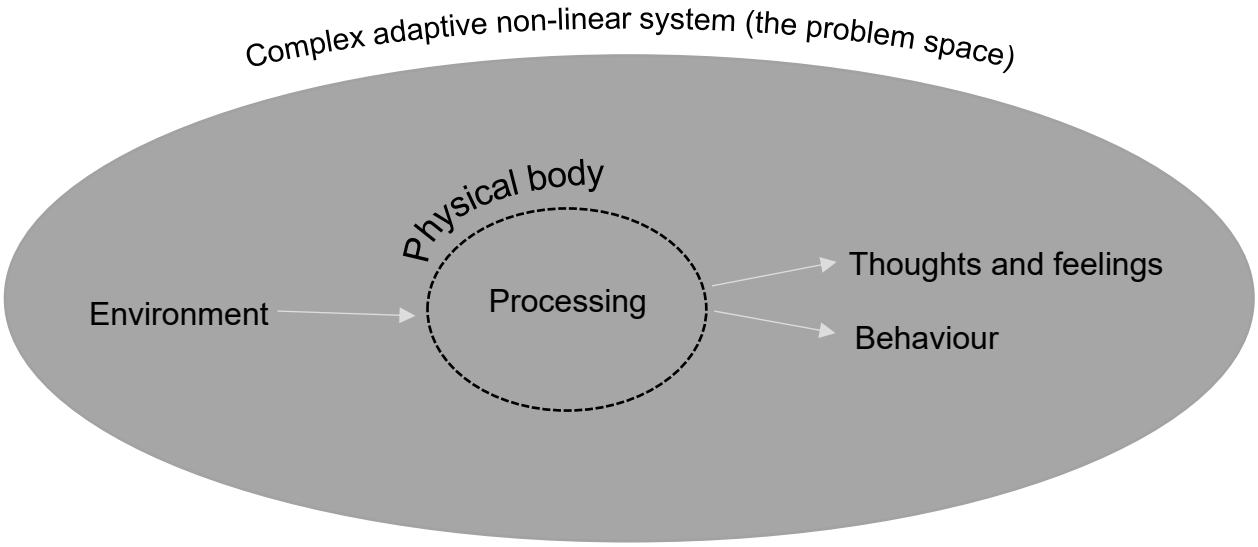


Figure 10: Schematic of the problem space for the novel intervention, and approach to relapse prevention

Grey shading indicates properties of self-organisation, spontaneous order and adaptation which are present throughout the complex adaptive non-linear system. This highlighting and focus on complex system characteristics is in contrast to a more simplified model which specifies each interaction.

There are three key areas of uncertainty in relapse prevention: the risk factors for relapse (see **Introduction** and earlier in this chapter), the extent to which these risk factors represent causal mechanisms, and the mechanisms by which existing interventions (reviewed in Chapter 2) exert their effects. Given this uncertainty I propose an approach to relapse prevention that is pragmatic and flexible, and built upon potentially important mechanisms in relapse prevention, and a consideration of the properties of complex systems.

The aim of the relapse prevention intervention is to help the system to maintain a 'wellness' equilibrium state. This is the individual who has recovered from depression and encompasses their physical body, their thoughts feelings and behaviour, their environment, and the interactions between these elements. This is a 'complex adaptive non-linear' system, meaning it has certain properties as described above: self-organisation, spontaneous order and adaptation. The potential future depression is an 'emergent phenomenon' derived from this system, its components, and internal and external interactions.

This approach leads to three intervention principles:

1. *To provide an intervention for people who are well,*

The intervention's intended population are people who are well (starting state). As such the intervention content will be centred around wellbeing (and not mental health problems or 'symptoms'), the language used will be non-medical, and activities suggested will be 'everyday' (and not based in clinical settings or on specific to mental health problems).

2. *The aim of which is to 'practice' wellbeing,*

There is evidence that if people have a longer period of recovery and fewer residual symptoms this is linked to an increased chance of maintaining recovery. It is suggested that people can protect their state of wellbeing through repetition of activities that enhance wellbeing as their system learns and adapts to this (ideally equilibrium) state, and as such there will be a focus on individual choice with a view to what could fit into a person's life long-term, and also on habit formation as a strategy to 'practice' wellbeing with little effort in the longer term.

3. *With key targets that have well evidenced links with the emergent phenomena of depression.*

There are multiple valid approaches to protecting mental health. The intervention will suggest four broad therapeutic targets that have been linked to relapse (or 'nodes' within the system):

- environmental or external influences on a person (proposed to impact monoamine transmission),
- automatic processing (including cognitive control and affective biases),
- conscious thoughts, feelings and behaviour ('schemata'), and
- Physical health.

Discussion

I have detailed an approach to relapse of depression which is based on the fundamental properties of complex systems. Importantly, that they have emergent phenomena which have a non-linear relationship to system components, and therefore relapses of depression may occur unpredictably with multiple possible interventions or even levels of intervention which could be used. Risk factors for depression and relapse may give us some idea at the group level who might be at an increased risk, but at an individual level will be limited in their predictive power. We know that relapses are more common soon after recovery, and when a person has residual symptoms (Chapter 1), which suggests that people's state of wellness following recovery might be precarious, and not an established 'equilibrium' state that is then resistant to change. Risk of relapse may be higher for people who have had multiple previous episodes although this evidence is less clear (Buckman et al., 2018), but given we know that systems learn and adapt, we might expect the experience of being depressed to increase future risk. However, we might also predict that practising wellbeing over time may then reduce the risk of future deteriorations in mental health. The aim of a relapse prevention intervention may therefore be on enhancing wellbeing, and establishing a wellness equilibrium state (which then provides some protection from future deteriorations).

I have explored some of the models of depression which provide multiple mutually inclusive mechanisms by which depression is caused or maintained, or wellbeing is maintained. A complex systems approach that targets four nodes from Roiser and colleagues' extended cognitive neuropsychological model (Roiser et al., 2011) is described. Activities which repeatedly have a positive impact on the system may have long-term impacts (though inducing adaptations to a non-depressed state, or through helping them to achieve a longer-term equilibrium). Of course, though targeting these mechanisms, within a systems framework we would not assume a) that the mechanisms targeted are the actual mechanisms by which any effects are brought about, and b) that there will be a linear relationship between a change in one mechanism and resultant emergent phenomena of wellness or a deterioration. By structuring an intervention using this model with target nodes with well evidenced links to relapse risk, the effects of it could then be used to explore the interrelations between these nodes within individual systems over time, or potentially across systems.

Strengths and limitations

A complex systems approach to relapse prevention attempts to address complexity and incorporate the implications of how systems operate, which may be missing from models of depression which focus more on individual mechanisms. For example, one key characteristic of complex open systems is that they learn and adapt, which seems important to highlight given that I am focussing on people who have an experience in common: depression and recovery. Long-term preservation of mental health also suits a systems approach, as the process by which mental health fluctuates or is maintained over repeated experiences is a key part of this.

By incorporating elements of biomedical, psychosocial and cognitive explanations into a relapse prevention approach this offers flexibility, which may be valid given that there is not as yet a 'stand-out' best (or better) approach to relapse prevention in terms of outcomes. Individual differences in lifestyle may then be incorporated so, for example, someone who does not have access to psychological therapy could take a different approach, or someone who is not able to exercise is able to identify the best long-term strategy for them. I have also identified that existing relapse prevention interventions largely focus at the level of conscious schemata (they are largely

psychotherapies), and there are several other domains within the cognitive neuropsychological model where mechanisms could be targeted, such as external influences on monoamine transmission and the balance between attentional biases and cognitive control.

It has been suggested that mechanisms of treatment effect often overlap with mechanisms underlying the onset or maintenance of a disorder (Holmes et al., 2018), however we cannot assume this overlap (e.g. headaches are not caused by a lack of paracetamol). I would argue that by considering the functioning of systems we can develop hypotheses that might be more likely to be valid and might move away from the more unidirectional cause and effect explanations. Take the (now disproved) 'serotonin' hypothesis which suggested that depression is (at least in part) caused by diminished serotonin on the basis of treatments such as selective serotonin reuptake inhibitors successfully treating depression. If you consider the properties of the brain as a system which self-regulates and which would respond when a synapse is flooded with a neurotransmitter the presynaptic cell might compensate by producing less of the neurotransmitter and/or the post-synaptic cell receptors might reduce sensitivity. If you consider this element of the behaviour of the brain as a system it could be hypothesised that SSRIs could work through neuronal adaptation reducing sensitivity to serotonin in the brain, which would explain the delay of several weeks between starting SSRIs and their antidepressant effects (NICE, 2010). This example illustrates that consideration of how systems work may lead to quicker gains in interventions.

Although the complex systems approach attempts to more realistically reflect a whole system and its processes and interactions as well as it's component parts, it remains a simplified model of a system, but with fewer specified interactions, directions of effects and emphasised parts than existing models (Roiser et al., 2011). It is also limited in its aim to increase or improve wellbeing, but with nodes derived from a model of depression, and without as detailed a characterisation of 'wellbeing' as of depression and relapses.

Of course, the approach to relapse prevention detailed in this chapter remains theoretical, and it remains to be set-out how this could be delivered as an intervention, whether this would be feasible, and what the clinical impact would be. The next chapter will seek to "identify the

components of the intervention and the underlying mechanisms" (Campbell et al., 2000) exploring activities that may provide a positive influence on each of the potentially important mechanisms described above, and how these may be put together to be offered as an intervention for people who have recently recovered from depression. I will focus on feasibility and acceptability from the outset, and describe an intervention that could move to the next stage in the continuum of increasing evidence, and be tested in an exploratory trial.

Conclusion

I have set out a complex systems approach to relapse of depression and will use this as the basis for the development of a new relapse prevention intervention. It emphasizes the adaptability of systems, and the potentially system-wide influences from multiple separate 'routes' into the system. Understanding the processes underlying depression can be at several levels of explanation: including biological, psychological and social. Integrated models such as those that highlight the interactions between cognitive elements and neuropsychological evidence can be used to highlight targets for interventions.

Chapter 4 Development of a brief wellbeing-focussed intervention to be offered after recovery from depression

Abstract

Background: A complex systems approach to relapse prevention may offer a practical framework by which to develop a novel relapse prevention intervention. The approach has a wellbeing and non-medical focus, and suggests that repetition of wellbeing activities and long-term behaviour change could be protective against future reversions to a depressed 'state'. Four 'nodes' are suggested as therapeutic targets.

Objective: To design an intervention according to this complex systems approach.

Methods: In order to identify intervention components that are likely to influence outcomes, behaviour change and habit formation research was explored to look at a style of intervention delivery that models participants as the experts in their own mental health. Activities that could be feasible for individuals to incorporate into their everyday lives with evidence they may have a positive impact on the four target 'nodes' are explored. Finally, written intervention materials and delivery protocols were developed with a focus on acceptability through consultation with IAPT clinicians, service users and the public, and clarity (using a think-aloud paradigm with four volunteers who interacted with the PRotect materials).

Results: The PRotect wellbeing intervention provides self-help options for people who have recovered from depression. The intervention content is detailed in a workbook, and engagement with the material is supported through an introductory phone call, a 2- hour group workshop, and a 20-minute review phone call one month after the workshop.

Discussion: The intervention aims to be feasible to deliver in IAPT services, acceptable to clinicians and clients, and to help people to maintain their wellbeing after recovery from depression.

Introduction

Although many people will stay well after recovery from depression, some will relapse. The risk that this will happen is heightened if a person has residual symptoms and risk is higher soon after recovery: perhaps a brief or 'incomplete' recovery means a person has not fully reached a robust state of wellness. Given that complex systems learn and adapt rather than remaining static, I predict that experience of a certain 'state' such as depression is 'remembered' by a system, and this could increase the chance that a person would return to that state. Perhaps interventions have largely focused on reducing symptoms (rather than building wellbeing) and have stopped at the point of recovery (or crossing the depression threshold), and going beyond this may reduce relapse risk. An intervention that aims to build wellbeing over the long-term may be more likely to help a person to establish a wellness 'equilibrium state', which is then resistant to change. The term 'wellbeing' has no consensus definition but is generally considered to include the presence of positive and absence of negative emotions/moods, satisfaction, fulfilment, and the ability to function well (*Well-Being Concepts, HRQOL, CDC*, 2018). Service-users have argued that these ideas are needed for 'recovery' to be better described than simply the absence of illness: citing elements such as fulfilment and meaning as fundamental to wellbeing (Leamy et al., 2011).

We know that offering additional intervention after the resolution of depressive symptoms can improve long-term outcomes (Biesheuvel-Leliefeld et al., 2015; Clarke, Mayo-Wilson, Kenny, & Pilling, 2015; Geddes et al., 2003). Continuation antidepressant medication reduces risk of relapse, as do psychological interventions (Biesheuvel-Leliefeld et al., 2015), but without the associated side effects and the potential need for prolonged treatment (Andrews, Thomson Jr, Amstadter, & Neale, 2012; Fava, 2003). The strongest evidenced of these is relapse-prevention focused cognitive behavioural therapy (CBT; Clarke et al., 2015; Vittengl, Clark, Dunn, & Jarrett, 2007) which can offer an additional 25% reduction in risk of relapse to depression over the course of up to two years (Clarke et al., 2015). However, there are many more approaches to relapse prevention outside of the healthcare domain that have not been tested in large randomised controlled trials, and it is common for people access their own 'self-help' activities outside of healthcare systems (Gartner & Riessman, 1982; Norcross et al., 2000).

Accessibility of interventions

Accessibility is a priority for innovations in psychological interventions (Holmes et al., 2018), and feasible interventions are more likely to result in actual improvements in health (Craig et al., 2008). The psychological relapse prevention interventions that have been reviewed in this thesis generally take up a significant amount of psychologist and patient time (see Chapter 2). Brief interventions may be more suited to healthcare services with high demand and limited resources, as well as to service users, who have already recovered from their depression and may not want to invest a lot of time and energy continuing with psychological intervention. Currently most resource focusses on acute treatment of mental health problems, although there is increasing focus on longer-term outcomes following treatment, and relapse prevention (Ali et al., 2017). Given this, a low-intensity intervention to offer in addition to acute treatment may be a realistic option for moving towards longer-term treatment strategies.

Few low-intensity interventions have been tested for this use: a comprehensive health technology assessment (Rodgers et al., 2012) identified only one (non-randomised) study of them. Indeed, in the systematic review searches I conducted for chapter 2 there was only one study where CBT had been adapted to increase access (through delivery over the internet with 10 weeks of email support, Holländare et al., 2011). However, interest in the area is increasing with several studies beginning after that review was conducted (Cook & Watkins, 2016; Holländare et al., 2013; Klein et al., 2018; Krijnen-de Bruin et al., 2019; Watkins & Cook, 2016).

In a number of health care systems, the need to increase access to psychological interventions has led to the introduction of guided self-help interventions, which are less costly to offer than formal psychological therapies, and could therefore be accessed by people who otherwise may not have received care. The English healthcare system's 'Improving Access to Psychological Therapies' (IAPT) program explicitly addresses the problem of access through the provision of low-intensity interventions: psychological therapies delivered with limited support from a Psychological Wellbeing Practitioner (PWP; Clark, 2018). Guided self-help is offered to people who do not have a severe mental health problem, so may also be suited to people who have recovered from depression and so have few or no depressive symptoms. The large numbers of

people being seen within IAPT services (a large portion of the approximately one million people referred annually) means that focussing a relapse prevention intervention for delivery within these services may increase reach and impact. In this chapter I will develop a brief, accessible relapse prevention intervention which is based on the evidence about relapse risk (Chapter 1), evidence that post-recovery interventions can reduce relapse risk (Chapter 2), and complex systems theory as an overarching approach (see Chapter 3).

Key considerations for intervention development

Complex interventions are those with a number of components that are inter-related and may work both together and independently to impact a health outcome. Just as in all complex systems, there may not be an easy-to-define 'active ingredient' which is the linear cause of a health outcome. Developing complex interventions will continue to be a key part of addressing mental health problems, particularly as a focus on psychosocial interventions (which are often complex) and on adapting effective interventions to be delivered through technologies (whose efficacy can then not be assumed) has been recommended (Holmes et al., 2018).

Guidance into how these interventions should be developed and evaluated has been provided by the Medical Research Council (MRC) and updated over the years since 2000, with the most recent guidance commissioned by MRC and the National Institute for Health Research (NIHR) published in 2021 (Skivington et al., 2021). It seeks to emphasize that the intervention development process should be viewed as dynamic and iterative. The phases of research presented in the original framework (2000, below) are not intended to be discrete sequential units as there is a need for these phases to feed into one another, and the continuum of increasing evidence may not be followed through all phases.

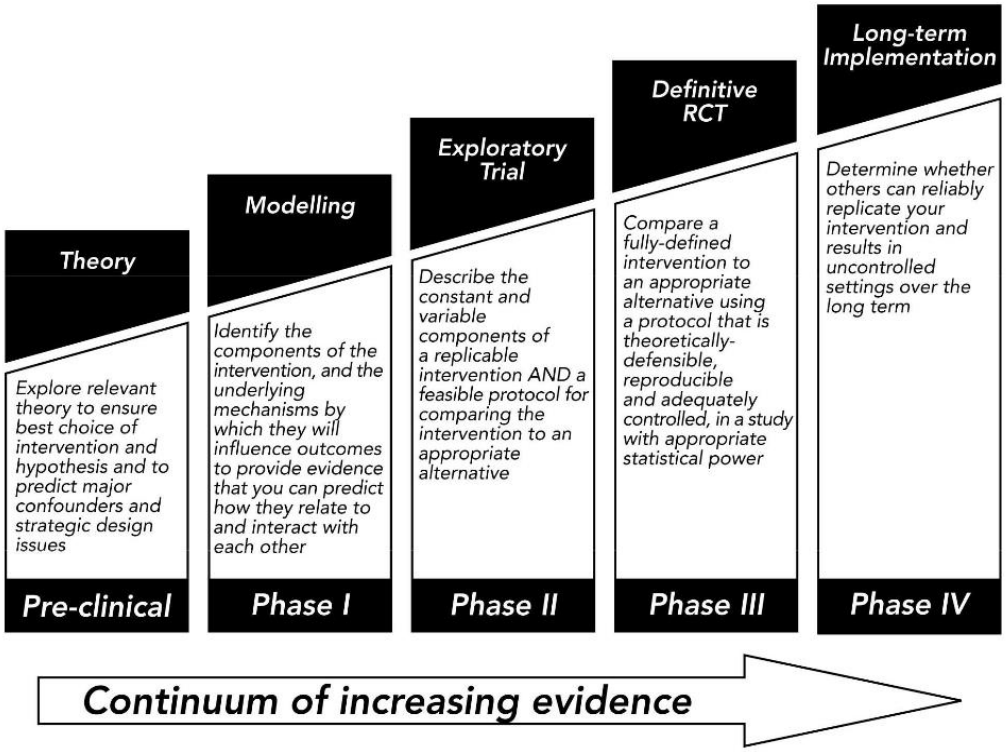


Figure 11: Flow diagram of the continuum of increasing evidence in healthcare, from MRC guidance, 2000

An appropriate and well supported model of relapse of depression helps to inform intervention development, and makes it more likely to be effective and/or able to inform theory (Campbell et al., 2000, Craig et al., 2008). Throughout, guidance has stressed the importance of a focus on feasibility, and on developmental studies prior to large-scale evaluations (Hallion & Ruscio, 2011). The MRC guidance advises that as well as the content of delivery, the method of delivery may be an important means by which an intervention exerts its effects.

A phased approach to the development and evaluation of complex interventions (those that include several components including most psychosocial interventions) is recommended, albeit with the caveats mentioned above from the 2021 guidance. Chapters 1-3 of this thesis form the 'preclinical phase' of complex intervention development. I now move on to Phase I: defining components of the intervention and how they will link to change, and the first part of Phase II: defining intervention design and exactly how it will be delivered. I will focus on feasibility throughout, with the aim of piloting the intervention (Chapter 5).

Objective

I will firstly describe core principles of the intervention that link to changing the course of depression and the evidence base for potential intervention activities that may affect the four therapeutic targets identified. I then report on the development work undertaken with the IAPT service focussing on the delivery of the intervention. This chapter aims to report on the evidence base and development work that led to the design of the PRotect intervention (with a focus on feasibility from the outset), before describing the final intervention design to be taken forward. Finally, I will describe the PRotect intervention in full according to guidance on better reporting of interventions (Hoffmann et al., 2014).

Phase I: Identifying components that may influence outcomes

The first section of intervention development I report in this chapter relates to Phase I of the MRC guidance for the development of complex intervention. It states this phase aims to*: "Identify the components of the intervention and the underlying mechanisms by which they will influence outcomes…."*. In this section I will explore the core principles of the intervention and how they may influence outcomes. I will then go on to describe activities that aim to target the mechanisms I have identified as potentially important, and evidence for this link.

Core principles of the intervention

To provide an intervention for people who are well.

The first is that people are well (the first core principle of the intervention) and are in a good position to make their own judgements about their health. The intervention will be tailored to people who are well in terms of both the language used, the suggested activities, and the style of delivery. The language will be non-medical and focus on wellbeing (rather than symptoms, risk, warning signs, or mental illness). The suggested activities will fit into people's everyday lives and not be based within clinical or healthcare settings. The style of delivery will be non-directional, with clinicians offering choices to participants but not 'prescribing' a certain course of action. In this way the style of delivery models self-efficacy: a belief that you are in control of your own mental health. Self-efficacy has been linked to better effective long-term health behaviour change

(Strecher et al., 1986). Perhaps treatments that focus on symptom reduction, illness or dysfunction risk leaving people close to the threshold of depression, and therefore at increased risk of relapse. It may be important to also focus on positive constructs such as connectedness, hope and optimism for the future, identity, meaning in life, and empowerment, which have been identified by services users as key parts of recovery (Leamy, Bird, Boutillier, Williams, & Slade, 2011).

The aim of which is to 'practice' wellbeing

The overall aim of the intervention is to support and encourage people to 'practice' wellbeing, with the prediction that systems adapt and learn over time and that repeated protective activities will provide a continuous impact on the system. This is supported by evidence that people have been in recovery from depression for longer are less likely to relapse. There will be a focus on learning, and that activities should be explained and explored within the intervention but then applied outside of this in normal life. Intervention materials and delivery should therefore reflect this split, and each component should include an activity as well as discussion of ways to introduce the principle outside of the therapeutic environment. Habits (behaviours that are automatic and take little effort to maintain) could be key to establishing long-term protection. Research into habit formation has identified that habits do not become unlearnt, but rather can be replaced with another habit. By examining how healthy habits, such as going for a walk every day, are successfully formed and maintained, researchers have identified some important steps (Gardner, Lally, & Wardle, 2012; Lally & Gardner, 2013; Lally, Van Jaarsveld, Potts, & Wardle, 2010). These can be summarised as: 1. Make it small, 2. Use a cue, 3. Practice repeatedly. Actions will be effortful to start with and become less so over time.

With key targets that are well supported in their links with the emergent phenomena of depression.

The intervention will include activities which aim to target potentially important mechanisms underlying depression. It should be noted that within a complex systems framework we may *target* these mechanisms but would not assume they are then the therapeutic mechanism behind

which any change in depression comes about. Equally the wellbeing focus and style of delivery may be important in bringing about change, alongside any number of other factors, and the interactions between these factors (non-linearity). The spontaneous order we see in complex systems means that there is not one part at fault that should be fixed or must be targeted, rather there are lots of inter-related parts. As the impact of targeting certain nodes is unpredictable, I would expect that it is the individual person who has the most evidence, potentially through previous experience, about which nodes are most closely related to positive mental health outcomes for them, and which changes are most likely to fit into their own lives in the long-term.

Style of delivery

Behaviour change research focuses on how an intervention might result in a change is someone's behaviour that then continues outside of the intervention setting, which may be useful in the field of relapse prevention where there is an attempt to move from 'treatment' to everyday life and continued recovery within the everyday world. There are several ways to approach behaviour change interventions, which can be summarised in terms of their function (see Michie et al., 2011 for a review and resulting behaviour change framework).

Table 3: Four intervention functions and definitions relevant to this thesis, taken from Michie, Stralen and West, 2011

Intervention function	**Definition**	**Examples**
Education	Increasing knowledge or understanding	Providing information to promote healthy eating
Training	Imparting skills	Advanced driver training to increase safe driving
Modelling	Providing an example for people to aspire to or imitate	Using TV drama scenes involving safe-sex practices to increase condom use
Enablement	Increasing means/reducing barriers to increase capability or opportunity	Behavioural support for smoking cessation, medication for cognitive deficits, surgery to reduce obesity, prostheses to promote physical activity

Given the scope of the novel intervention which is the focus of this thesis, I will focus on education, training and modelling. Although I hope the intervention is also 'enabling', it does not itself 'increase the means' or 'reduce barriers' over and above training so I do not label it as such. Rather people may take what they have learnt through the intervention and use this for

enablement and possibly environmental restructuring in their own lives (Michie, Stralen, & West, 2011). The PRotect intervention will aim to meet these intervention functions as follows:

Education: through detailing some of the theory and evidence base for each target node. Information about a broad variety of resources people can seek and use outside of the intervention will be explored.

Training: through including practical interactive tasks to illustrate every node. In order that people might 'practice' wellbeing. The intervention focusses on everyday activities that fit into normal life, rather than require specialist support. Providing information about habit formation provides participants with tools to embed activities into the long-term with decreasing effort in order that small changes can have big impacts over the long-term (Lally & Gardner, 2013).

Modelling: through the style of delivery of the intervention. A modelling style of intervention delivery will be achieved through an emphasis on individual choice, with the participants assumed to be the expert at all times. Specifically, this means:

- Describing wellbeing activities through sharing 'tips' from people who have recovered from depression about what helps them, not recommendations.
- Participants who have the common experience of recovering from an episode of depression, sharing tips with each other in a group setting.
- Highlighting the different routes that are options and might maintain wellbeing, and highlighting that some will not be chosen. The intervention is also careful to acknowledge that its participants are not depressed, and may not become depressed again.
- Facilitators using a 'hands-off' style, minimising direction and instruction, using a motivational interviewing (Hettema et al., 2005) rather than overtly directive style of communication. Facilitators share their own personal experience and as such are not prescribing for others, directing or educating but rather are modelling behaviour).
- Motivational interviewing is also used in phone calls, which aims to enhance readiness for change (Hettema et al., 2005) and which has been used to encourage engagement with relapse prevention treatment in substance use disorders (Grow, 2013).

- Participants taking the most active role in a) planning for themselves and b) advising others in the group and as such model behaviour for each other

Targeting the four nodes: Intervention activities

Although we have a model of depression with strong evidence linking some mechanisms within this model to risk of depression, the evidence about how best to target these nodes is more mixed. Here I will summarise evidence for activities or interventions that may provide some protection to wellbeing in each of the four target areas identified in the complex systems model I propose in Chapter 3. In some areas evidence is preliminary from small reports or trials, and in others there is well established evidence from relevant guidance or from systematic reviews.

- **Targeting environmental influences:** This involves identifying influences in the temporal, physical, or interpersonal environment that are within the control of the person and that have a positive impact. This will be different for each person and involve personal reflection to identify appropriate actions.
- **Targeting processing biases:** Affective biases and their relation to cognitive control have been the subject of experimental work in depression, and there are interventions that aim to modify cognitive biases. I summarise cognitive bias modification systematic reviews, as well as evidence that mindfulness may be protective through impacting attentional direction.
- **Targeting schemata:** The field of 'positive psychology' includes several activities that purport to support or strengthen positive schemata (thoughts and behaviours). I present systematic reviews of these interventions, and the types of constructs and activities that are suggested.
- **Targeting physical health:** There is a large body of evidence that supports the link between physical and mental health. I describe advice and practical activities that people could undertake who are wishing to maintain or improve their physical health (from the National Health Service's advice and resources).

Environmental influences

The cognitive neuropsychological model of depression (Roiser, Elliott, & Sahakian, 2011) suggests that negative influences from the environment compromise monoamine transmission, and this then combines with genetic influences on monoamine transmission to influence brain circuits that mediate affective processing. They suggest this leads to negative low-level biases in information processing. Rather than focussing on any unidirectional relationship between 'cause' and effect, the complex systems approach would identify environmental influences as a potentially important 'node' in the system that could be amenable to therapeutic intervention.

The negative environmental influences suggested by Roiser and colleagues are redundancy, and relationship breakdown: the endings of positive environmental influences (work and relationships). To target this node within a relapse prevention intervention, I suggest that by increasing positive environmental 'inputs' to the system, other unintended negative influences may be diluted, and the system as a whole may be more likely to remain in equilibrium.

Providing a positive environmental influence

There is evidence of positive impacts on mental health from a person's temporal environment (e.g. hobbies), physical environment, (e.g. housing), and the interpersonal environment, (e.g. social networks). These could be targeted in various ways:

'Temporal' environment

- Planned, regular activities (including work or volunteering)
- Planned alone-time or down-time
- Hobbies

Physical environment

- Improving your home, bedroom or own space
- Noticing or looking for visually pleasing things
- Spending time outdoors in nature or in another pleasant space

Interpersonal environment

- Relationships with people/social networks/contact with people

- Peer support groups

These activities are necessarily subjective as they rely on an assessment of the impact external factors have on a person's mood or wellbeing. Each individual person must assess what external factor influences them in a positive way. This assessment may be based on reflection: activities than an individual knows from their own life experience has a positive impact on them. This will vary hugely, for example one person may find contact with their family has a negative or neutral impact on them, whereas someone else may find their mood is boosted after, say, a phone call with their sister. The approach to this route within the intervention will be firstly psychoeducation about the principle of external influences, followed by individual reflection and personal planning of ways to increase positive environmental influences.

Processing biases

The second route to relapse prevention is in working on the balance between low-level biases and cognitive control. Cognitive abnormalities are a core feature of depression, and biases toward negatively toned emotional information are common (Clark et al., 2009; Sahakian & Morein-Zamir, 2011). The low-level biases may be influenced by monoamine activity, and contribute to the forming of positive and negative schemata (Roiser, Elliott, & Sahakian, 2011). Cognitive control can also moderate the effect of low-level biases (Roiser, Elliott, & Sahakian, 2011). Some have argued that this balance between cognitive control and processing bias is the key mechanism underlying the onset of depression (Roiser, Elliott, & Sahakian, 2011), however I would argue that causal unidirectional relationships are not often seen complex systems, and this mechanism is probably just one part of a more complex picture of depression risk. This is then better described as a node within a complex system which may be more or less important for different people and at different times, but may be worth targeting.

Modifying processing biases

To target this node within a relapse prevention intervention, I suggest two possible types of activity. The first is an activity that aims **to preserve or improve cognitive control**, such as mindfulness. A review of the impact of mindfulness meditation practices on objective measures

of cognitive functions found that early phases of mindfulness training were associated with significant improvements in selective and executive attention (Chiesa, Calati, & Serretti, 2011). Strengthening cognitive control may allow people to 'over-ride' the processing biases that may put them at risk of depression.

The second is an activity that aims **to moderate or change processing biases**, such as attentional or interpretation bias modification procedures. The field of interventions to moderate or change processing biases is in its infancy, but there have been several proposed interventions with evidence of an impact on processing biases, and mixed evidence of an impact on mood. A meta-analysis of cognitive bias modification training studies found that it can have a medium effect on biases (g=0.49), with a larger impact on interpretation biases (g=0.81) than attentional biases (g=0.29, Hallion & Ruscio, 2011). This translated to a small effect on depression and anxiety symptoms, which was reliable in studies which looked at reactions after exposure to a stressor (g= 0.23, Hallion & Ruscio, 2011). They found that the effect was larger where people participated in multiple training sessions, suggesting that the system may be adapting and learning through the repetition of these sessions. Reviewing attentional bias modification procedures, Mogoase et al (2014) also found a small effect on anxiety symptoms (g=0.26). A further review of 49 trials found small effects in non-clinical samples, but these effects do not appear to be clinically important, and the available studies were small and at risk of publication bias (Cristea, Kok, & Cuijpers, 2015).

It should be noted that the participants in most studies included in these meta-analyses did not have clinical levels of depression and anxiety, which is the case for my conceptualisation of a relapse prevention intervention delivered after recovery from an episode of depression. Similarly, although the impact of these interventions on immediate mood symptoms is low or unclear, this does not reduce the likelihood that they may prevent relapse. If we consider a population who have low levels of symptomatology (who are 'well'), a medium impact on a processing bias may be more important than any impact on short-term mood. Current mood state was not identified as an important precipitant or risk factor for relapse of depression in the evidence reviewed in Chapter 1. There is some limited preliminary evidence from small trials to support this assertion.

For example, one study recruited participants who had experienced recurrent depression and recovered, and examined the effects of an attentional bias modification procedure on outcomes more closely related to risk of depressive recurrence: residual depressive symptoms and cortisol awakening response. They used an active control condition, and found an impact in the month following the procedure, suggesting that this procedure could be seen as a “cognitive vaccine” against depression (Browning, Holmes, Charles, Cowen, & Harmer, 2012).

Versions of cognitive bias modification training programs are available to the wider public via online programs and smartphone ‘apps. This makes these strategies feasible for a person to implement within their life. These tasks can be conducted in everyday situations without a therapist or professional’s supervision. They do not require people to be in a certain mood or to examine personal feelings or experiences, hence they “circumvent the practical and psychological requirements” that are often present for formal psychological therapies (Yiend et al., 2014). Although evidence for the effectiveness of these activities on biases and on mental health outcomes is sparse, they are also in the public domain and people are free to undertake them if they wish. Future research may investigate people’s experience of using these programs, whether they feel they are effective, and perhaps whether a randomised controlled trial is feasible and warranted. One limitation of this route is that it is difficult to explain and understand as it relates to processes that we are not consciously aware of and that only appear within strict experimental paradigms. Careful consideration about how to present this route, particularly with the input of the target population, might be necessary to counter this.

Thoughts and behaviours/actions

The third route to relapse prevention is in targeting (conscious) thoughts and behaviours, the rationale being that conscious thoughts contribute to our positive or negative schemata. Dysfunctional negative schemata are present when a person is depressed, and it is common to have negative views of themselves, the world, and the future (Beck, 2005).

Working on positive thoughts

Rather than simply the absence of negative views, the field of 'positive psychology' focusses on desirable views and strengths. Tasks aim to increase "positive feelings, positive behaviors, or positive cognitions, as opposed to ameliorating pathology or fixing negative thoughts or maladaptive behavior patterns" (Sin & Lyubomirsky, 2009, p.469). They may help to build positive 'schemata' just as relapse prevention CBT challenges negative schemata (Beck, 1991). Choosing to add positive thoughts or actions (or as described previously: environmental influences) that are within control may then dilute the impact of any negative events that are unforeseen and outside of our control.

There have been two systematic reviews of relevance in this area. These are of positive psychology interventions: "treatment methods or intentional activities aimed at cultivating positive feelings, positive behaviors, or positive cognitions" (Sin & Lyubomirsky, 2009). In 2013 Bolier and colleagues (Bolier et al., 2013) conducted a systematic review of randomised controlled trials of positive psychology interventions, and identified 39 studies with 6,139 participants. Most studies reported the interventions were effective in increasing subjective or psychological wellbeing or reducing depression symptoms, and their meta-analysis found small effects (SMD 0.2-0.34) of the interventions, some of which were maintained after 6 months. There was considerable variation in the quality of studies, the lower quality studies reported higher efficacy, and there was evidence of publication bias.

The review provides a comprehensive overview of the types of positive psychology interventions that have been studied. Most were delivered in a self-help or guided self-help format. The tasks focus on constructs such as optimism, gratitude, kindness, hope and compassion. They found that individual delivery was most effective, then group, then self-help. An earlier systematic review (Sin & Lyubomirsky, 2009) identified a slightly higher effect size, which may be due to the fact that they also included mindfulness based interventions. They recommend:

- That people should regularly practice and keep a record of positive strategies, incorporate them into their everyday lives, and turn these strategies into habits. This resulted in greater improvements in wellbeing and reduction in depressive symptoms in included studies (Seligman, Steen, Park, & Peterson, 2005).

- Multiple and different positive psychology activities can be beneficial (rather than needing to focus on one)
- People from individualistic cultures may benefit more from positive psychological interventions (Lyubomirsky et al., 2011), so cultural background should be considered.

Types of activities

Many positive psychology tasks are easily accessible and feasible to implement in everyday life (for a list of books and analysis of their content, see: Seligman, Steen, Park, & Peterson, 2005). See table 4 for some of the more frequently tested examples of positive psychology constructs, and associated tasks and references.

Table 4: Frequently discussed positive psychology constructs, associated tasks and references/studies

Construct	Task	Example references
Gratitude	-Counting your blessings	Emmons & McCullough, 2003; Seligman et al., 2005
	-Expressing gratitude	Seligman et al., 2005
Kindness	-Practicing kindness	Otake, Shimai, Tanaka-Matsumi, Otsui, & Fredrickson, 2006
Hope/personal growth	-Setting personal goals	Green, Oades, & Grant, 2006; Sheldon, Kasser, Smith, & Share, 2002
	-Using personal strengths	Seligman et al., 2005; Sheldon & Lyubomirsky, 2006

It should be noted that evidence here is of mixed quality and there are issues with small studies, lack of long-term follow-up, and publication bias. As such they cannot be presented as evidence-based interventions despite some trials, but might be appropriately presented as suggestions for people to see for themselves if they find them helpful or unhelpful, with the agency remaining with the individual to assess this for themselves. The reviews are also limited in their definitions of 'positive thoughts and behaviours' and they note that they have excluded interventions designed to improve physical well-being (health). This is the final proposed target of the intervention.

Physical health

The fourth and final route to relapse prevention is in system-wide care of the physical body, as physical and mental health are intrinsically linked. The physical body is the ‘hardware’ on which the environment exerts its impact, and that the emergent property of mental health and depression depend on. Potential mechanisms include ones at a biological level: stimulating neuroplastic processes implicated in depression, reducing inflammation, psychological: increasing self-esteem and self-efficacy, and social: increasing social support and being more able to fulfil social roles (Kandola et al., 2019) It is linked with our risk factors for depression in Chapter 1, and also the comorbidities in Chapter 2.

This route is perhaps the most easily explained, and the concept of taking care of physical health is fairly universally understood. In the UK, the National Health Service offers healthcare and along with Public Health England, runs campaigns and provide guidance for people looking to maintain or improve their physical health. They look to the best available evidence from a very large body of research to produce their guidance, which I will include items from in the intervention. Activities to choose could include:

- Managing and treating physical health problems in line with medical advice
- Eating a balanced and nutritious diet. NHS advice includes trying to eat your ‘5 a day’ of vegetables and fruit, and drinking plenty of water.
- Exercising. NHS advice includes how to start activities such as walking or badminton, or tools are available such as the ‘couch to 5k’ podcast, which guides people to begin running.
- Reducing harm such as stopping smoking, reducing alcohol use and avoiding drug misuse.

A flexible approach suits this route: the different aspects of physical health will be relevant to different people. For examples, exercise may be very important for someone who finds it has mood boosting effects on them, but less relevant to other people, for example if they have a very active job, or have a physical health condition that prevents them increasing physical activity.

Phase I Conclusions

I have linked the target mechanisms identified in Chapter 3 with activities that people might choose to undertake. Given uncertainty about: a) the importance of each target area in any one individual's mental health; b) the differential importance of these target areas on mental health in general, and c) the effectiveness of everyday activities in modifying each of these target areas, the intervention will ask people to choose the most important activities for them. In this way co-production will occur within the intervention.

Phase II: Defining intervention delivery methods and materials

The next stage in developing this intervention is in deciding exactly how the principles detailed above will be translated into practice. This intervention will seek to change people's behaviours such that additional activities provide a positive influence to the target nodes specified above. The intervention will also seek to set-out ways in which those behaviours will become habitual, so that they are maintained over the long-term and so provide a continued positive influence on the system.

IAPT research

IAPT services are the largest providers of evidence-based psychological therapies for depression or anxiety in England. Given the need to focus on feasibility and accessibility of relapse prevention, the delivery of this intervention was based on what is possible within IAPT services. To research this, I had several formal and informal conversations with IAPT staff where I explored existing intervention delivery methods, and the current approach to relapse prevention within services.

Individual therapy was the most commonly employed mode of delivery of therapy. It generally involved face-to-face contact with a staff member, often in a GP surgery clinic or IAPT offices, and could last between 20 minutes and one hour per session (although telephone appointments were also available). Group therapy was also offered and generally involved a commitment to attend a series of group sessions on a weekly basis. Acute treatments delivered within the service largely fell into two categories: high intensity and low-intensity (guided self-help), although 'books on prescription' were also available ('unguided' self-help). Workshops were offered to people in

addition to their high or low-intensity treatment, covering topics such as perfectionism, self-esteem, stress and low mood. Clients were generally free to sign up for whichever one-off standalone workshop they felt would be useful.

Existing relapse prevention approaches in the IAPT service were described as mixed, with some clinicians completing ‘staying well plans’ with their clients during treatment, or talking about warning signs, triggers, and when to seek help. Relapse prevention was always part of acute treatment and there were no standalone relapse prevention interventions at the time. Given tight time-frames within which to deliver acute treatment, whether relapse prevention work happened, and the extent of it, varied between clinicians and between individual clients.

Table 5: Record of intervention development work and contributions

Aim	Date	Time	Intervention Development Work	Attendees
IAPT research	21/05/2013	13.20-17.00	Shadowing low-intensity work	Katy Lucas
	18/10/2013	16.00-17.00	Meeting with Camden Research Lead	Hannah Deakin
Developing intervention core principles	08/11/2013	9.30-11.30	Clinical advisory group	Islington: Andre Lynam-Smith, Emma Poon. Camden: Hannah Deakin, Ailsa Lee, Sherry Rehim.
	19/11/2013	12.30-14.00	Service-User Forum/advisory group	Steve Pilling, Ailsa Lee, Jenny Rowden, 5 service users
	19/11/2013	16.00-17.00	Individual clinical adviser	Heidi Thomas
Assessing and choosing feasible delivery methods	06/01/2014	13.00-14.00	Islington North team meeting	Islington North staff, I arranged attendance with Laura Cole
	10/01/2014	13.00-14.00	Islington low-intensity meeting	Islington North and South low-intensity staff, I arranged attendance with Laura Cole
	15/01/2014	09.15-11.00	Camden North meeting	Camden North team, I arranged attendance with Alastair Bailey and Hannah Deakin. Kay Frost chaired the meeting.
	06/02/2014	11.30-13.00	Camden South meeting	Camden South (Hunter street) team, I arranged attendance with Katy Lucas
	06/02/2014	15.30-17.00	Camden Low-intensity meeting	Camden North and South low-intensity staff, I arranged attendance with Hannah Deakin
	07/07/2014	11.00-12.00	Meeting with Camden Research Lead	Tarun Limbachya
	07/08/2014	15.30-17.00	Camden PWP forum	Around 16 Camden PWPs- chaired by Emma Hawkey
	31/10/14	ongoing	Shadowing IAPT workshops	-
Refining of written materials	16/11/2014	19.00-21.00	Young professionals focus group	4 young professionals: Ben Ives, Megan Duffy, Victoria Stephens, Jess Lewis
	25/3/2015	19.00-20.30	Consultation on intervention plans	Depression alliance group
	26/10/2015	N/A	Sense checking	Email: GC and JW
	26/10/2015	N/A	Normalising design of materials	Consultation with magazine editor (AW)
	Various dates	4 X 1 hour	Think-aloud studies	Four anonymous volunteers

Delivery of the intervention core principles

In the initial stages of intervention development I worked with a clinical advisory group, and a service-user advisory forum on the core principles of the novel intervention. During these meetings I presented background research and existing interventions, the proposed core principles, and the proposed 'targets' (as developed in Chapter 3, see Appendix E for the presentation). Participants asked questions during the brief presentation, and this was followed by feedback, a discussion, and sharing individual expertise. These sessions were audio-recorded and feedback incorporated into further development of the intervention. There was a particular focus on the relevance of the proposed targets, and the extent that they 'made sense' and aligned with service user experience.

The service users in particular commented that they liked the non-medical language and the wellbeing focus. Their understanding of the four routes was explored, and the 'targeting processing biases route' was felt to be the least easy to apply to everyday experience. Two groups agreed that a good way to present this route in everyday language was to describe it as 'training your brain'. They felt that similarly when you go to the gym to train your body, you do not know the exact changes that are happening, say, within your muscles but you are aiming for an outcome which you can feel and appreciate. They felt the cognitive bias modification exercises were similar to gym exercises but for rapid and unconscious reactions within your brain.

Assessing and choosing feasible delivery methods

In order to ensure feasibility of delivery of the intervention, and to support potential future roll-out, I opted to choose a style and format of intervention delivery that fitted well within existing IAPT systems. Given that this intervention would be in addition to acute treatment offered by psychological therapies services which itself has problems with accessibility and being offered to all those who need it, I decided to design a brief, one-off intervention which could have future potential as an alternative to discharge. Accessibility and encouragement of engagement was considered important, particularly if a brief intervention was to result in behaviour change, and have long-term impacts. For this, having some contact with a therapist (a guided self-help rather

than a pure self-help intervention) may be important. In the two trials of internet-based relapse prevention previously mentioned, the one whose participants took 150 minutes of therapist support was effective (Holländare et al., 2011), whereas the one whose participants took an average of 17.3 minutes of therapist time found no sustainable effects of the intervention on relapse rates (Klein et al., 2018).

The IAPT workshop format fits in with these considerations. Workshops offered by IAPT follow a common format using power-point slides over the course of 2 hours with a break halfway through. There is evidence that a brief pre-treatment motivational interview can increase engagement significantly (Grow, 2013), which was deemed as important given the workshop is the primary method of delivering this intervention and so attendance was seen as important. I also proposed to have review calls after the workshop, but there was some disagreement amongst IAPT staff about whether holding someone on a caseload for an extended period would have too high an impact on staff, and some concerns that clients may become over-reliant. However, several clinicians felt that just a brief phone call could really help clients to feel supported and to encourage long-term behaviour change, and it was agreed that one follow-up call would be feasible and perhaps worthwhile.

As the workshops are guided self-help, I decided to produce a booklet to be given to people prior to the workshop. The workshop will then guide attendees through the written materials with extra activities and will be interactive to facilitate learning. The booklet may facilitate more long-term change as people can refer back to their plans, and are encouraged to do work outside of the workshop time. In order to encourage self-efficacy and emphasize the core principle that people are best placed to decide their own relapse prevention strategy, extra resources were provided at each workshop for people to select, and the booklet was kept to a minimum. The aim was for people to be active in their own personalisation of their wellbeing plan: for some people written materials help but for others, setting phone reminders or discussing ideas is more useful. Not including all materials within a large booklet models the principle that there is not ‘one size fits all’, and models empowerment, modelling being a key intended method of behaviour change of this intervention (see Chapter 3 and Michie et al., 2011). The style of the review call was also

designed to model this empowerment and self-efficacy by using a 'brief motivational interview' style (Grow, 2013) and by asking the participants if they have any 'tips' to pass on to others who have just recovered from depression.

Refining written materials

I developed a draft booklet to be given to participants of the intervention with several options for content, format, font and design. In order to develop the intervention materials and check their usability I conducted four 'think-aloud' experiments with the aim of refining intervention materials and to check their usability in a lab-based study (Nielsen et al., 2002). Four participants (2 male 2 female) volunteered to review the intervention materials. They were recruited through advertisement within the University Department. 'Think-aloud' paradigms (Nielsen, Clemmensen, & Yssing, 2002) treats verbal reports of participants as the data, rather than the processes underlying the verbal reports. The procedure was as follows:

- Make the participant comfortable
- Give a brief background and rationale for think-aloud procedures
- Observe the participant interacting with the written materials, and encourage them to 'think-aloud': to verbalise any thoughts they are having
- Prompt the participant after their initial use of the materials to then focus on each part of Using the booklet (observed behaviours)
- Present specific options for font, text, images and formats for review

The think-aloud experiments were audio-recorded and observations noted down during the process. The findings then were incorporated into changes to the design of the written materials. There was a particular focus on usability, clarity and any difficulties understanding, any particular likes or dislikes arising from interacting with the materials, and more detailed feedback on options for fonts, images, and layout. Following these modifications, a magazine editor provided feedback on the overall presentation of materials, and advised on ensuring the style was non-medical: advising that there should be lots of space around blocks of text, with a reading age around 13 and a 'notepaper' style of background on workbook pages.

Phase II Conclusions

IAPT services are well placed to deliver a variety of low-intensity interventions to the large numbers of people who may benefit from accessing this support, and in particular to deliver the wellbeing focused, non-medical intervention principles of the novel intervention which is the focus of this chapter. Their workshop style is the template format by which to instantiate the intervention core principles and target nodes, supplemented by a short, self-help workbook and additional activity ideas that people can choose as they wish within the workshop. Materials were refined through user testing in the 'think-aloud' paradigm and through editorial consultation. Engagement with the intervention and materials is encouraged through introductory and review calls which are non-directional and model the service user as the expert in their own recovery.

Results: The PRotect intervention

The PRotect intervention aims to present self-help options in a brief and accessible format that to people who have recently recovered from depression. The intervention follows a complex systems framework, where the focus is on enhancing wellbeing, and establishing a wellness equilibrium state (which then provides some protection from future deteriorations). It does not replicate a consideration of vulnerability, risk, or triggers that may have been part of acute treatment or may be contained in other relapse prevention interventions. The intervention acknowledges that there are different ways in which someone may improve their wellbeing, and these will be different for each individual. To support the establishment of wellbeing activities into 'everyday' life, and to enable the participation of people who wish to avoid medical terms, the intervention deliberately eschews any use of psychological or medical terminology. Here I describe the PRotect intervention in full, complying with guidance for the better reporting of interventions (Hoffmann et al., 2014).

Intervention delivery

The PRotect intervention content is contained in a self-help workbook. A short (<10 minutes) introductory phone call in the style of a brief motivational interview (Grow, 2013) is used to encourage attendance at a workshop which covers the workbook's contents. Review calls (<20

minutes) were offered to workshop attendees for one month later. The introductory phone calls followed a trial procedure document (Appendix F), with additional prompts list provided on the request of trial clinicians following training (Appendix G). The review phone call also followed a trial procedure (Appendix H). The workshop followed a PowerPoint presentation with loose script (Appendix I) and associated tasks.

The workbook

The workbook (to be found in full in Appendix J) introduces the concepts of the intervention. It suggests that participants consider:

- activities that have a positive impact on their mood (similar to elements of CBT and behavioural activation).
- activities that may 'train your brain' such as using cognitive bas modification or mindfulness practice.
- 'positive psychology' tasks such as taking a personality strengths questionnaire, or writing a note of thanks.
- ways to care for their physical health.

In order to facilitate long-term impact from a brief intervention, an evidence-based strategy for maintaining behaviour change through reinforcement learning is then introduced (Lally & Gardner, 2013). Finally, there are lined pages to make a wellbeing plan and then to review the wellbeing plan. The reading age for the booklet was kept below age 14 as per guidance on accessibility of health information, and the style was intended to be normalising (similar to a magazine or other non-medical text). Notebook-style papers were used for people to complete their own plan. The booklet content was kept as brief as possible (total booklet was 24 leafs long) so that people would personalise their own plans rather than seeing the booklet as comprehensive.

Introductory call

The introductory call was in the style of a brief motivational interview and used in order to encourage attendance at the workshop (Grow, 2013). In order to facilitate this style, a document

of introductory phone call ‘prompts’ was provided. The call was scheduled to last for ten minutes and included these components:

- **Introduce yourself and the intervention**

e.g. “I’m just phoning to introduce myself, and to give you a bit of an introduction to the PRotect wellbeing course you are being offered. Did you receive the letter and booklet about this?”

- **Ask about the participant (and identify any potential barriers to attendance).**

e.g. How are you feeling about coming? Do you have any concerns about it?

- **Arrange workshop attendance**

Workshop

The workshop is structured around the PRotect self-help workbook, with facilitators presenting information from the PowerPoint slides and leading activities such as a short mindfulness meditation and completing a personality strengths questionnaire (Seligman et al., 2005). The delivery style is intended to be normalizing, with workshop facilitators participating in activities alongside the participants. Facilitators do not make ‘recommendations’, but instead at (four specific) points within the presentation share an example from their own lives. A PRotect resource pack is available at each workshop for participants to review and select resources to take away, with flyers for local community groups, healthy recipes, advice on exercise from the NHS, print-outs about NHS recommended apps such as a mindfulness and meditation app, information about an NHS pod-cast ‘couch to 5K’ which guides people to safely start running, etc. The first half of the workshop includes a description of and activities around the four target routes to wellbeing. In the second half, habit formation tips are introduced, and each participant identified a behaviour change they would like to implement, and makes his or her own personalized wellbeing plan.

Room set-up

The room was set-up to have a poster in each of the four corners, and resources relating to that relapse route on a table in the corner. During the workshop there are several points where the

participants are asked to go to one of the four corners: to leave a post-it note with an activity they currently do that corresponds to that route, or during the ‘four corners’ task, where the group are asked to stand by their preferred and least preferred routes. The resources in each corner are there throughout the workshop, and participants are free to take any resources that interest them. In this was choice is emphasized and modelled: people do not have all resources in their own booklets but have to actively choose what they are or are not interested in.

PowerPoint slides

The PWPs were provided with PowerPoint slides for the workshop, as would be the case with other workshops they deliver within IAPT. However, they were encouraged to personalise 4 slides with examples from their own lives or experience. There was no protocol for workshop delivery, but rather instructions were included in the notes of the PowerPoint slides. This is because the normal way that PWPs are trained for workshop delivery is by watching a workshop, co-facilitating a workshop, and then continuing themselves. They do not have manuals for workshop delivery, but rather share PowerPoint slides. Providing a manual and extensive training may have resulted in a workshop that is not feasible to deliver within normal IAPT systems and not sustainable to roll-out. There were 22 slides in total.

The first slides were the standard ones used in all IAPT workshops. These explain what to do in a mental health emergency, some logistics for the day (e.g. location of toilets and fire alarm instructions), and ground rules. They then present a plan for the sessions of the day. The first half of the slides relate to the four routes, and for each route there are examples and a task to complete as a group. The second half of the slides relate to habit formation and planning changes.

Extra resources

During the workshop extra ‘resources’ (printed information) relating to each of the four routes were placed on tables around the room. Resources gave details of self-help activities and included leaflets for local social groups, mindful colouring or chocolate tasting activities, and recipes to cook healthy meals. Participants were free to take any or no resources away with them.

Review call

The review phone call focused on reviewing the experience of the workshop and the participant's personal wellbeing plan. It was delivered in the style of a brief motivational interview. The PWPs were instructed to:

- Listen to the clients experience of implementing their PRotect plan
- Normalise any feelings of discouragement
- Affirm small steps
- Build feelings of self-efficacy through exploring activities the clients are doing that help their wellbeing (small everyday activities).
- Allow the client to lead the way with thinking about ideas for the future
- Answer any questions about the PRotect course
- Encourage self-efficacy through signposting

Flexibility, and responding to the client's needs were emphasized as being important for this phone call. For this reason, the key topics to cover, and some sample questions were provided (rather than a detailed script). The call finished with the PWPs asking the participants what tips they would pass on to others who have recently recovered from depression, again in order that the intervention models self-efficacy and responds to participants as experts in recovery.

Discussion

In this chapter a complex systems framework for relapse prevention and evidence around behaviour change and activities which may reduce relapse risk were brought together with development work in therapies services. An intervention for use within these services was described. The complex systems approach suggests people can 'practice' at being well, and that relapse may be a particular risk if people are treated to close to the diagnostic threshold (which is inevitably a risky area), and if their treatment focussed on symptoms and symptom resolution there might be more to be gained from an additional focus on wellbeing and strengthening. I identified target routes from a cognitive neuropsychological model of the maintenance of depression. I then brought together evidence from systematic reviews or health guidance to

suggest activities within the theoretical framework, and focussed on positive or protective activities.

A relapse prevention intervention which moves from a focus on pathological to the positive, and from a guided treatment within a 'healthcare' domain, to one which focuses on long-term self-directed plans within the 'everyday' domain may help to bridge a potential gap between prior 'treatment' and everyday life going forward, and deliver long-term benefit from a low-intensity intervention. Delivering a relatively brief intervention immediately after treatment, whilst an individual is already in contact with therapists or services, engaged, and likely to be feeling positive about the progress they have already made may be justified if clinically effective.

Participating in a group-delivered workshop may help to normalise the experience of having depression and re-frame a person as expert in recovery rather than 'at risk' of relapse. The follow-up phone call may help to extent to concepts discussed in the workshop into everyday life. By asking the questions in both workshop and follow-up call about what they are doing to maintain their wellbeing, and what tips they would have for others, the mode of delivery of the intervention is intended to model the participants as actively maintaining their recovery and therefore to impact behaviour change. In this way the approach is different to acute treatment rather than just 'more', which may apply to some of the relapse prevention interventions identified in Chapter 2.

This intervention is likely to be relatively low cost given its length and its facilitation by PWPs within a group setting, and as such may be more likely to be provided as an additional intervention to the many people who recover from depression and routinely would be discharged from services. The omission of psychological and medical terminology may make this intervention accessible to people who have recovered using medication, who do not wish to engage in a psychological intervention or who do not identify as being at risk of mental illness (Gulliver, Griffiths, & Christensen, 2010). The style of delivery is somewhat of a departure from the normal IAPT style, with no recommendations provided. Training of the PWPs therefore needed to focus on the differences between this intervention and normal ways of working: completely free choice of activities, not giving advice, personal disclosure.

Strengths and limitations

This intervention was systematically developed from a relevant theoretical framework, and incorporated best available evidence into an intervention that would fit within existing services. There was a focus on feasibility of delivery from the outset, and it is hoped that this means the resulting intervention is more likely to improve health (Craig et al., 2008). It was designed following Medical Research Council (MRC) guidance for the development of complex interventions (Campbell et al., 2000; Craig et al., 2008; O'Cathain et al., 2019) and was refined through consultation with clinicians, people who have experienced depression, and non-experts (members of the general public).

The PRotect approach is holistic in that it considers the individual as a whole person with their own biological, psychological, and social world. It respects the knowledge and expertise of the individual person in knowing what is best for their own mental health, and what is possibly within their own lives. In contrast, some precision medicine approaches place the responsibility of personalising an intervention into the hands of the clinician or researcher.

A key limitation of the approach is the areas that are not covered as 'targets' within the intervention but which we know are linked to depression: many of which are detailed within the cognitive neuropsychological model of depression (Roiser et al., 2011) but have not been selected as within a person's 'control' such as influences from genetics or from the past. Childhood trauma has strong evidence linking it with a predisposition to depression, and this intervention at best ignores this impact, and at worse asks people to take actions themselves to prevent a condition that they be unable to prevent due to another person's actions towards them in earlier life. Careful highlighting within the intervention of the fact that there are other influences on our mental health than ones we control is essential, and it might be that some analysis of participant experience of the intervention can enable me to see whether the intervention led to people feeling empowered as intended, or overly responsible for something beyond their control. It also must be highlighted and reiterated that this intervention is not intended as a replacement of any acute treatments which may themselves have relapse preventive effects. For example, in this intervention a person cannot simply decide to undo the impact of childhood trauma within

their everyday life, but within a treatment setting with a professional such as during acute psychotherapy it might be that memories of childhood trauma can be modified and therefore some of the impacts of it can be reduced.

Conclusion

The PRotect intervention suggests self-help activities that are categorised into four routes to wellbeing, and presents these in a delivery style that is intended to model self-efficacy. Intervention materials focus on activities which may fit into everyday life, and which may provide some protection from relapses of depression. It may be feasible to deliver to people who have recovered from depression in an IAPT service, and this should be explored.

Chapter 5 Design, methods and analysis plan for a randomised controlled feasibility trial of the ‘PRotect' intervention in NHS psychological therapies services

Abstract

Background: The PRotect intervention is a brief guided self-help intervention, which aims to help people to maintain their recovery after depression. The design of a feasibility trial is presented which aimed to 1) test the feasibility of trial methods and of intervention delivery, 2) collect clinical outcomes for intervention and control arm participants, and 3) explore the experience of trial clinicians and participants.

Methods: This was a parallel-group randomised controlled pilot trial of the PRotect intervention compared with evaluation only (1:1 ratio). Participants were clients of two inner London IAPT services who had completed treatment for depression. Psychological Wellbeing Practitioners (PWPs) delivered the PRotect intervention: a short introductory phone call, a 2-hour workshop, and a 20-minute review call. Data were collected in relation to the three study aims as follows:

1. Monitoring of recruitment, randomisation, follow-up interviews, and intervention delivery from narrative descriptions, descriptive statistics, audio-recordings, and fidelity forms.
2. Presence of a depressive episode, level of symptoms of depression and anxiety, and a measure of functioning for all participants 3 and 6 months after entry to the trial.
3. Brief semi-structured interviews with all trial participants on completion of participation and a focus group of trial clinicians following trial completion.

Conclusion: This pilot follows similar methods as a proposed randomised controlled effectiveness trial, and as such will provide support to proceed using the proposed design, with adaptations, or suggest not to proceed.

Introduction

This chapter sets out the design and methods of a pilot randomised controlled trial of the PRotect intervention for adults who have recovered from depression. The sections are based on those recommended in *SPIRIT* (Standard Protocol Items: Recommendations for Interventional Trials) guidance (Chan et al., 2013), and some elements are reported as per the associated guidance for adaptations for pilot trials (Thabane & Lancaster, 2019) and the SPIRIT outcomes extension (Butcher et al., 2022). Although we are looking at feasibility outcomes, I have termed this a 'pilot trial' as it conducts part of the future RCT on a smaller scale to see if it can be done (Eldridge et al., 2016). Although there has been some overlap and disagreement as to where to use the words 'pilot' or 'feasibility' when describing trials over the years and across research disciplines, Eldridge et. al's 2016 conceptual framework provides a useful distinction which is in-line with current definitions from funding bodies such as the National Institute for Health Research. They describe 'feasibility' work, as any research undertaken in order to see whether a future study could be possible (and how). Pilot work is a more specific concept within the broader category of feasibility studies: "A pilot study asks the same questions but also has a specific design feature: in a pilot study a future study, or part of a future study, is conducted on a smaller scale." (Eldridge et al., 2016). Both feasibility and pilot studies can be randomised or non-randomised. Within this framework randomised pilot studies could also legitimately be called randomised feasibility studies, however I choose to describe this as a randomised pilot trial as it adds specificity about the fact I am conducting the future larger randomised controlled trial on a smaller scale.

This chapter focuses on the study design, methodology, and analysis decisions and omits some details on the administration and governance of the trial.

Background and rationale

People who have recently recovered from depression may be concerned about the possibility of future deteriorations in their mental health. There is some evidence that this

concern is justified, with depression literature largely agreeing that people who have experienced depression are at risk of further episodes, with evidence of relapse risk after 15 years of 85% in people who received specialised mental health care for a depressive episode (Hardeveld et al., 2010). However, taking a positive psychology approach (Aspinwall & Tedeschi, 2010), I would argue that the converse may also be true: that the improved mood, increased energy and heightened functioning associated with a recovery from depression puts people in a good position to take steps to protect their mental health, and perhaps to engage briefly in some further intervention despite being currently 'well'. Existing interventions with high-quality evidence to support their efficacy (from randomised controlled trials) are largely high-intensity psychological therapies (Clarke, Mayo-Wilson, Kenny, & Pilling, 2015), which may offer an additional 22% reduction in risk of relapse in the following year compared to acute treatment alone. However, there are several reasons that a low-intensity alternative which focuses on wellbeing and recovery (rather than risk) could be of benefit.

Within a complex systems-informed understanding of depression and relapse prevention, an intervention where the focus is on enhancing wellbeing, and establishing a wellness equilibrium state may provide some protection from future deteriorations (see Chapter 3). Existing interventions identified within the review were largely adaptations of acute treatments originally intended to reduce illness rather than increase wellbeing, which might perhaps leave people vulnerable. A focus on techniques to reduce or avoid 'symptoms' may help someone to be 'not depressed' and to sit somewhere close to the threshold for depression more than learning skills which move them further away from that threshold (see Chapter 1). Given perhaps 50% of the people who recover from depression will *not* go on to experience a relapse, a post-recovery intervention might a) be accurately described as aiming to 'protect recovery' (as well as prevent relapse) and b) might focus on the fact that people are recovered and that they may well maintain their recovery.

The fact that perhaps 50% of people will maintain their recovery after depression treatment also lends weight to the argument for a lower-intensity relapse prevention (or 'recovery protecting') intervention than those which were included in the Systematic Review in Chapter 2. Within a stepped care model, the least 'restrictive' (in terms of both participant and therapist time, Bower & Gilbody, 2005), or the 'least intrusive most effective' (NICE, 2009) intervention should be offered to people. For those who have recovered from depression and 'completed' treatment, most are currently offered no intervention, they are discharged from services and left to continue preserving their wellbeing without any ongoing direction. Given relapse risk some intervention is possibly justified, but it would seem there should be options at a lower intensity than existing relapse prevention interventions identified in Chapter 2, or indeed to people who have a current mental health problem.

The PRotect intervention

The PRotect (Protecting Recovery after depression) intervention was developed in response to this need for a low-intensity relapse prevention intervention with a wellbeing focus. It presents a variety of self-help interventions in a brief and accessible format that could be offered to people who have recently recovered from depression, with the aim of helping people to increase or preserve wellbeing, and therefore reduce the risk of a relapse. It was developed following Medical Research Council (MRC) guidance for the development of complex interventions (Craig et al., 2008) and was informed through consultation with clinicians and previous clients of IAPT services, and non-experts (for more detail on the development of the intervention see Chapter 4).

Whilst participating in the PRotect intervention, people are asked to make a wellbeing plan based on what is relevant to them as individuals and what is possible within their own lives (rather than being directed towards a certain plan or strategy by a clinician). The intervention acknowledges that there are different ways in which someone may improve their wellbeing, and these will be different for each individual. It suggests that participants consider four routes to wellbeing: 1) environmental influences that may have

a positive impact on their mood, 2) activities that may 'train your brain' or work on the balance between cognitive control and attentional biases such as 'cognitive bias modification' (Yiend et al., 2014) or mindfulness practice (Chiesa et al., 2011), 3) 'positive psychology' tasks (Bolier et al., 2013) such as taking a personality strengths questionnaire or writing a note of thanks (Sheldon & Lyubomirsky, 2006), and 4) ways to care for their physical health. These routes were selected on the basis of areas within the cognitive neuropsychological model of depression (Roiser et al., 2011) which are potentially modifiable in combination with a complex systems approach, as described in Chapter 4.

The activities themselves were selected on the basis of established or emerging empirical support linking them with the four routes. In terms of 'brain training', there are now several smartphone apps or online programs that target cognitive abilities and biases in automatic processing that that may be modified during mindfulness training (Chiesa, Calati, & Serretti, 2011) and that have been associated with risk of developing depression (Roiser et al., 2011). These appear to have some efficacy in improving mood (Mogoaşe, David, & Koster, 2014). The 'positive psychology' tasks which aim to increase "positive feelings, positive behaviors, or positive cognitions, as opposed to ameliorating pathology or fixing negative thoughts or maladaptive behavior patterns" (Sin & Lyubomirsky, 2009, p.469) have been linked to improvements in constructs such as personal growth, kindness, and goal attainment (Green, Oades, & Grant, 2006; Otake, Shimai, Tanaka-Matsumi, Otsui, & Fredrickson, 2006; Sheldon, Kasser, Smith, & Share, 2002) usually with small but durable effects (Bolier et al., 2013; Sin & Lyubomirsky, 2009). They may help to build positive 'schemata' just as relapse prevention CBT challenges negative schemata (Beck, 1991) and are presented online and in many popular books (for a list of books and analysis of their content, see: Seligman, Steen, Park, & Peterson, 2005). For some individuals, aspects of physical health which are within personal control, such as improving diet, participating in exercise, and managing

physical health problems may also be important in the maintenance of mental health (Paans et al., 2018).

In order to ensure that the impact of the intervention is long-term and hence may provide protection against relapse, participants are provided with an evidence-based strategy for maintaining behaviour change through “reinforcement learning” (Lally & Gardner, 2013). This strategy involves firstly identifying an intended habitual action, which should be as simple or small as possible (so ‘wear trainers’ would be better than ‘increase my daily step count’). Secondly people must identify a ‘cue’ for this behaviour: whether that be something in their daily routine or their physical environment, that is the indication that the intended habitual behaviour should be performed. Finally, people must commit to repeating the action whenever they encounter the cue: a pattern which is effortful at first but will become less effortful over time and repetition.

In addition to this, participants are offered a ‘review phone call’ one month after the intervention workshop in order to check back on their progress and remind of any plans that were produced during the workshop. It is hoped that this structure provides a sort of ‘step’ between acute intervention, which may have involved weekly or fortnightly contact with a therapist, and everyday life without intervention. To support the establishment of activities into ‘everyday’ life, the intervention deliberately eschews any use of psychological or medical terminology, a decision informed through consultation with people with experience of depression during intervention development.

An appropriately powered randomised controlled trial could be used to test whether the PRotect intervention is effective in increasing the chances that a person will stay well following recovery from depression. Randomised controlled trials are the highest level of evidence for treatment effectiveness within medicine (Balshem et al., 2011) given that they isolate the impact of an intervention through random allocation to each arm, and able to do so without the need for an understanding of individual participant’s baseline likelihood of each outcome. This fits in with a complex systems approach which posits that any risk factors may not relate to outcomes in an independent or predictable way

(non-linearity, see Chapter 3). Pragmatic (or effectiveness) trials (Roland & Torgerson, 1998) which compare interventions within a real-world setting are particularly useful in providing evidence that is directly applicable within healthcare services. This chapter presents the Methods and planned analyses of a pilot which sought to address key areas of uncertainty (Thabane et al., 2010) in order that a larger randomised controlled effectiveness trial could be planned (Avery et al., 2017).

Objectives

The first objective of this pilot is to identify whether a powered trial of the PRotect intervention would be feasible: whether people would engage with the research, be willing to engage with further intervention post-recovery, and whether the proposed intervention can be delivered. For a trial to be feasible it must be able to recruit and retain an adequate number of participants. Recruitment depends on the number of people who are eligible or referred to a trial, but also crucially a consent rate high enough that selection bias is minimised. Although CONSORT guidelines do not specify to report consent rates, it has been suggested that they should (Marušić & Buljan, 2020). Retention of 80% or more participants is recommended to minimise bias in outcome analyses (Page & Persch, 2013). Engagement with an intervention and its acceptability is also important in order that a future trial would be feasible and could actually be used to test the effectiveness of the intervention.

The second objective is to explore whether a future trial of the PRotect intervention could determine a difference in clinical outcomes. This involves collecting clinical outcomes for participants after they leave treatment, and seeing whether any difference between groups may be used to inform a power calculation for a larger trial. The clinical outcomes assessed in a pilot trial should reflect what would be in a future effectiveness trial. Outcomes are selected on the basis of their utility in producing evidence that could be interpreted within the context of the evidence base reviewed in Chapter 2 (relapse of depression according to diagnostic criteria), and so that the outcomes would be useful

to the services delivering the intervention (using measures the services routinely use or use to assess service delivery).

The final objective is to explored the experience of delivering and participating in the trial and intervention. A future trial could be informed by how the people involved experienced the trial methods and the intervention, whether they see it as beneficial and worth pursuing, and whether there were any changes to be made. The extent to which staff and patients understand, participate in, and can reflect on an innovation in healthcare determines how likely that intervention could be implemented in the long-term and normalised into routine practice (Murray et al., 2010).

The corresponding research questions are as follows:

1. Would a larger trial be feasible with similar trial methodology? Is the PRotect intervention feasible to deliver within an existing healthcare service?
2. Can we collect clinical outcome measures and could these measures be used to indicate effectiveness in a larger trial?
3. What was the experience of trial clinicians and participants?

Trial design

This is the pilot for a pragmatic parallel group individually randomised trial of the PRotect intervention following acute psychological therapy for depression and as such largely follows the proposed methods for the full trial but with a focus on feasibility rather than clinical effectiveness. The trial design, target participants, interventions, outcomes are first summarised here in order to provide context for the more detailed chapter sections that follow.

Participants: Participants were eligible if they had experienced, and recovered from depression according to either DSM-V diagnostic criteria (assessed for the 12 months prior to the trial using the Longitudinal Interval Follow-up Evaluation; LIFE), or scores on a self-report depression symptom measure moving from above to below the clinical 'cut-off' (Urtasun et al., 2019). Further eligibility criteria kept to a minimum. For example,

participants were recruited at the end of their acute treatment in an 'IAPT' therapies service but there were no requirements on the focus of their acute treatment.

Sample size: In order to assess feasibility of intervention delivery the intended sample size needed was for five workshops to be delivered to groups of 5-10 people. With estimated 30% attrition and 1:1 allocation ratio, 65-130 participants would be needed.

Intervention: The PRotect intervention includes provision of a self-help workbook, and guided support from an IAPT service through an introductory phone call in the style of a motivational interview, a group workshop, and a review call. The group workshop covered information and activities around four routes to wellbeing, and each participant made a personal wellbeing plan.

Control: Participants in the control arm are discharged from the IAPT service where they received their acute psychological treatment. Neither intervention nor control arm participants are restricted in seeking other intervention (for example they may have received and continue to receive antidepressant medication from their General Practitioner, or seek mental healthcare from other services). This 'evaluation only' control condition reflects the current routine practice for people who have completed their acute treatment in IAPT and are seen to have recovered from their presenting problem.

Outcomes: The rate of referrals to the trial (49 per month) combined with a 66% consent rate was used to indicate feasible recruitment, and 80% of participants at each follow-up point was considered good retention. Outcomes indicating feasible intervention delivery were 80% of those eligible completing their introductory calls, attending a workshop, and completing the follow-up call, and the length of calls in minutes and seconds being within +/- 20% of target length.

Study setting

The study setting was two inner London NHS Foundation Trust IAPT services, which provide psychological therapies services to the population of two boroughs. The services were involved in the trial in three ways: participants are recruited at completion of their

treatment with the services, PWPs currently employed within the therapies services deliver the intervention, and the intervention was delivered within the services' existing systems, with the delivery of the intervention largely managed by a PWP. It was important to test delivery of the PRotect intervention within a real-world setting, in order that a future powered trial is a 'pragmatic' (Roland & Torgerson, 1998) effectiveness trial.

Residents of the boroughs (Camden and Islington) include a much larger proportion between the ages of 20 and 39 than the national average, perhaps in part due to a large student population. The two boroughs are ethnically diverse, with 37.8% and 33.4% of their populations coming from an ethnic minority group (compared to 13.6% of the population of England). There are varied health needs in this population, with 26-30% of children living in low-income families, and differences in life expectancy of up to 10 years between the most and least deprived parts of the boroughs.

People living in these boroughs can seek treatment from the IAPT service if they think they might be experiencing a common mental health problem, by referring themselves directly via a telephone line or via the website. General Practitioners (GPs) and other professionals can also refer clients. The services are made-up of four teams as there are 'North' and 'South' teams in each borough. All have their own clinical and administrative staff, and operate out of different bases. The teams each cover the catchment area of certain GP surgeries within the two boroughs, and have close ties with these surgeries. They have a broadly similar make-up of staffing with other IAPT services which usually comprise approximately 60% High Intensity therapists (mixture of clinical and counselling psychologists, CBT therapists, and counsellors, including managers) and 40% Low intensity therapists, or 'Psychological Wellbeing Practitioners' (PWPs). In these boroughs (not partnership organisations) there were approximately 60 High Intensity therapists (including 8 trainees) and 44 PWPs (including 16 trainees).

People can refer themselves to these services either independently or on the advice of their GP. Indeed, around 60% of people with depression who come into IAPT have already been prescribed antidepressant medication, so must have sought help

elsewhere. IAPT services do not require a person to change their medication use, and IAPT delivered care proceeds largely independently of any medication a person is receiving. This will continue within this trial: medication use will be monitored (through self-report) but participants' medication use will continue or change independent to the trial recruitment and intervention delivery.

In the study setting there is a central referrals telephone line and email account which the two teams share. When a referral is received the administrator completes a triage call with the client where they ask for contact details, collect some basic psychological information, and book the person in for assessment. During the assessment, a PWP asks some more detailed questions about the reason that the person is seeking treatment from the service. If suitable, the person is then offered treatment within the stepped care model (Bower & Gilbody, 2005).

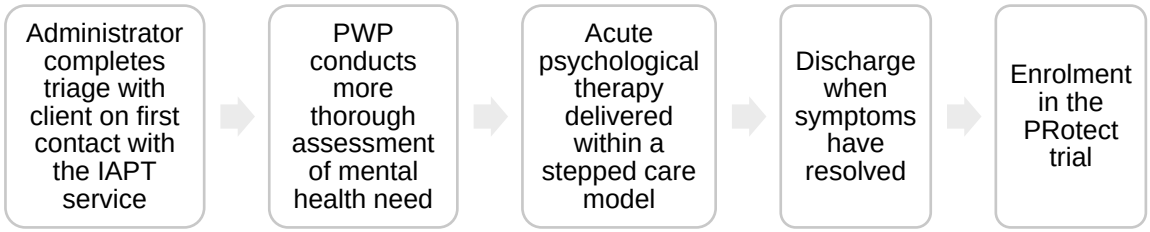


Figure 12: Flow diagram of the usual pathway through IAPT care leading to enrolment in the PRotect trial

Within this model, people are offered NICE recommended interventions with mild to moderate depression, generalised anxiety disorder (GAD), panic, stress and sleep difficulties might be offered 'low-intensity' interventions at a 'Step 2' level; and people with moderate to severe depression or anxiety disorders including obsessive compulsive disorder, health anxiety, social anxiety or post-traumatic stress disorder might be offered high-intensity intervention at 'Step 3' level. Step 2 interventions could include psychoeducation, behavioural activation, sleep hygiene, problem solving, or worry management delivered largely by 'Psychological Wellbeing Practitioners (PWPs). Step 3 interventions are often time-limited goal specific treatment usually using a cognitive-

behavioural therapy model, but may also be others such as counselling or eye-movement desensitisation and reprocessing therapy.

A key element of IAPT service delivery is routine outcome measurement. Clients are asked to complete a set of questionnaires, the 'IAPT Minimum Dataset', every other session. This includes a self-report measure of depression symptoms (PHQ-9), anxiety symptoms (GAD7), work and social functioning (WSAS) and questions about employment.

Eligibility criteria

Participants were eligible if they had recently completed IAPT treatment (within 1 month of screening), and had experienced and recovered from an episode of depression as indicated by:

- A score on the PHQ9 that had gone from 10 or above to below 10, and/or
- A remitted episode of depression according to DSM-V diagnostic criteria (assessed for the 12 months prior to the trial using the LIFE evaluation).

They also had to provide informed consent and demonstrate sufficient proficiency in English language to participate. Exclusion criteria were: current suicidal thoughts (reporting frequent "thoughts that you would be better off dead, or of hurting yourself in some way" on the PHQ-9); current co-existing drug/alcohol, psychotic or neurodegenerative disorder (no formal assessment, excluded if flagged in pre-screening or which became apparent during the LIFE interview); and current participation in another piece of research (through participant self-report).

PWPs 'Psychological wellbeing practitioners' (PWPs), who hold a nationally accredited post-graduate qualification in providing guided self-help interventions, were eligible to deliver the intervention if

- they had experience of delivering workshops in a similar format,

- they completed one additional 2-hour training session on the PRotect intervention delivered by researchers, which consisted of talking through the script and PowerPoint slides and reviewing the research evidence used in developing the intervention.

Interventions

The PRotect intervention content was contained in a self-help workbook, which was posted to all participants. A short (<10 minutes) introductory phone call in the style of a brief motivational interview (Grow, 2013) was used to encourage attendance at a workshop which covered the workbook's contents. Review calls (<20 minutes) were offered to workshop attendees for one month later. The introductory and review phone calls followed trial protocols, and the workshop followed a protocol with specified PowerPoint presentation and associated tasks.

Introductory call: The intervention began with an introductory phone call between the participant and the PWP. During this conversation, the PWP introduced the key concepts of the intervention. They also asked how and where the participant would like to receive the intervention manual, and when they could attend a workshop. They asked about any barriers to attendance (brief motivational interview). They aimed to make each call last for ten minutes, and a full protocol can be found in Appendix F. The PWP sought to audio record their side of the conversation (hence permission from the participant was not needed) where possible, and completed a fidelity form for each call (Appendix P).

The workshop: Workshops were held in a room with audio-visual equipment in a hospital conference centre from 5.30-7.30pm on a weekday. The workshop was structured around the PRotect self-help workbook (Appendix J), with facilitators presenting information from the PowerPoint slides, and leading activities such as a short mindfulness meditation and completing a personality strengths questionnaire (Seligman et al., 2005). The facilitation style was intended to be normalizing, with workshop facilitators participating in activities alongside the participants. Facilitators did not make

'recommendations', but instead at (four specific) points within the presentation shared an example from their own lives. The topic of personal choice and individuality was raised throughout, with an emphasis on choosing routes *not* to follow, as well as to follow. A PRotect resource pack was available at each workshop, and participants reviewed this and selected any resources they wished to take away. Resources pointed towards self-help activities and included leaflets for local social groups and recipes to cook healthy meals. In the latter half of the workshop, each participant identified a behaviour change they would like to implement and made his or her own personalized wellbeing plan. The mode of delivery was designed to encourage self-efficacy: clients were given completely free choice of activities, workshop facilitators did not make recommendations but did share their own experiences, and participants were asked to contribute advice for others who have recovered from depression. Participants booked review calls with one of their workshop facilitators (during the workshop) for one month later. The workshops followed PowerPoint slides (Appendix I). The facilitators sought to audio-record the workshop sessions if all participants consented to it being recorded (for consent form see Appendix R).

Follow-up call: Review calls were booked during the workshop for one month later, and reviewed the workshop and personal plan in the style of a brief motivational interview (Grow, 2013). The clinician modelled the participant as the expert by asking whether they had any tips for other people who had recently recovered from depression. The calls were 20 minutes long and a full protocol for the calls can be found in Appendix H. The PWPs did not audio-record these sessions but did make notes about the content of the call on the fidelity form (Appendix S).

Two PWPs were recruited to deliver the intervention from each of the four IAPT teams in consultation with service managers. The intervention was delivered across the two services, with participants from either service eligible for any workshop for two broad reasons. Firstly, to ensure groups were as full as possible: given the emphasis on sharing tips between group participants and for intervention costs to be minimised per participant.

Secondly, it was considered important that people moved away from the therapist who delivered their acute treatment given the intervention emphasises that people have reached a stage of recovery, and that the focus then shifts away from 'treatment' and towards habit formation and maintaining wellbeing.

In the control arm participants were offered 'treatment-as-usual', which for most people would have been discharge from the IAPT service without follow-up or any additional intervention. It should be noted that similarly to the intervention arm, people were free to seek treatment or intervention outside of the study, and in particular it is likely that several participants would have been provided with a prescription for antidepressant medication by their General Practitioners (given the large proportion of people who have received this on initial entry to an IAPT service). The use of antidepressants as well as other interventions is monitored rather than controlled in both arms.

This is proposed as the control for the larger effectiveness trial which would identify initially if there *is* any benefit of offering the PRotect intervention over the current routine discharge. Once this is answered further research might include active or attentional controls.

Interventions: modifications and monitoring of adherence

Clinicians delivering the intervention followed the services procedures and policies for risk management during delivery of the intervention. However the nature of this study, in that it recruited people who had been discharged from IAPT care, required an appropriate approach to managing risk across IAPT and GP services. After discussions with the service clinical lead, it was agreed that study participants were under the care of IAPT if they were receiving the IAPT intervention and so any risk issues would be dealt with within their service. Subsequent to the intervention and for the control arm the GP would be the person to report any risk issues to.

The intervention developer (KC) provided supervision throughout the study to assess and address any overt issues with delivery and to seek to maintain fidelity. In order to explore intervention receipt, we collated reports from the PWPs, fidelity forms completed

for introduction and review phone calls, a sample of audio-recordings, self-reported reasons for non-attendance at the workshop, and self-reported behaviour change after workshop attendance at 6-month follow-up. For the purposes of this pilot, intervention arm participants were asked to self-report use of intervention activities.

Outcomes

Nine feasibility outcomes were proposed:

Recruitment and retention

1. 49 referrals per month (calculated to enable recruitment of 32.5 people per month)
2. 66% ‘consent rate’ (people referred who then enrol in the study)
3. 80% completion of 3-month outcome assessments
4. 80% completion of 6-month outcome assessments

Intervention delivery and receipt

5. 80% of intervention arm participants complete introductory calls
6. Mean length of introductory calls between 8 and 12 minutes
7. 80% of intervention arm participants to attend workshop
8. 80% of people who attend workshop to complete follow-up call
9. Mean length of follow-up calls between 16 and 24 minutes

These outcomes are selected to be a stringent measure of feasibility in several ways. Consent rates are often calculated as number of consents/number eligible for the study, however here it is the number of consents/number referred to the study. This is to provide a more stringent measure which tests the whole system of referral and recruitment rather than just acceptability of the study. The outcome completion percentages (and attendance percentages) are selected as they are within the range recommended to reduce risk of bias (see Introduction). A similar +/- 20% figure was used as a stringent test of the feasibility of delivering calls to the time intended.

An embedded qualitative study was planned in order to explore any feasibility findings in terms of participant or staff experience, and also in order to identify any other important aspects of their experience that could be incorporated into future plans for a larger RCT. All participants recruited to this pilot trial, and staff delivering the intervention, were asked to share their experience following completion of their participation.

Participant timeline

The participant flow, from referral through to final outcome data collection is summarised in Figure 13 below, and in more detail later in this chapter.

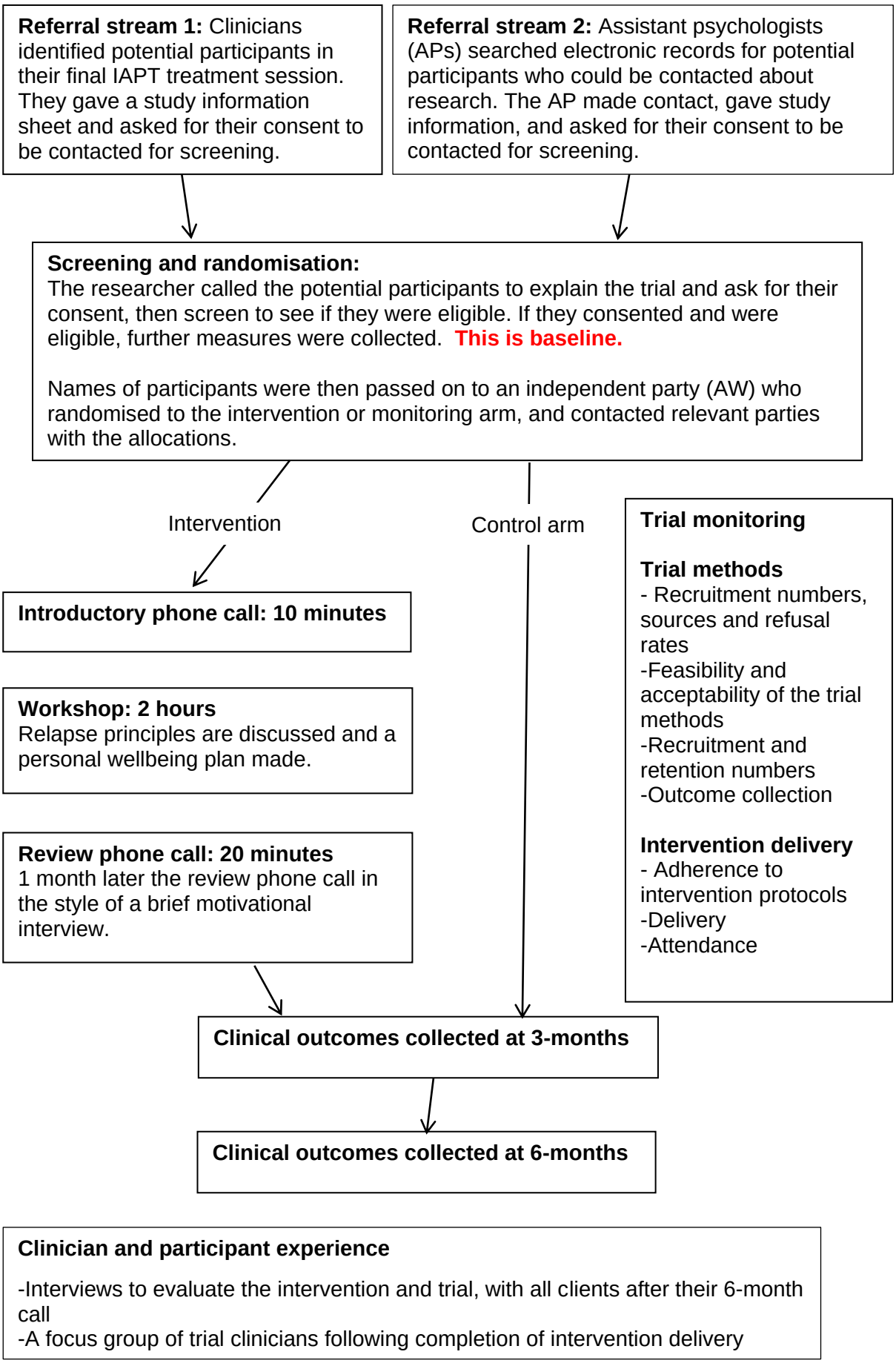


Figure 13: Flow diagram of pilot trial processes: participant recruitment, intervention delivery and data collection

Sample size

Given that a key aim of this pilot was to assess feasibility of intervention delivery, I sought to recruit sufficient participants for five workshops delivered to groups of 5-10 people. Drop-out is normally estimated at 20-30%, but could be at the higher end due to the fact that participants are 'well' on study entry and may not be available for the pre-scheduled workshop dates. For this reason, I sought to recruit 130 participants, which (with estimated 30% attrition) would leave 50 intervention and 50 control arm participants, at the higher end of what is needed to explore the study aims. Recruiting 65 participants would allow the lower estimate of five workshops with five people in each. This sample size was based on the need to assess the whole system of recruitment and random allocation to a group-based intervention within this individually randomised study, rather than simply on assessing acceptability of the study as a whole through raw numbers of participants recruited.

As this is a novel intervention, and there had only been one, non-randomised study of a low-intensity intervention in a similar population (Rodgers et al., 2012), there is no estimate for the predicted size of effect of the intervention. This pilot study could be used to provide an indication of effect for use in a formal sample size calculation for an effectiveness trial which compares outcomes between groups.

Recruitment

Strategies to ensure adequate recruitment

The study's IAPT services are actively engaged with multiple research projects and a strategy to ensure adequate recruitment was developed in response to the experiences staff described with other research studies. Thorough preliminary feasibility consultation was undertaken to build relationships with staff who went on to become more involved in the project, publicise the trial, to understand the system in which the intervention would be implemented and to troubleshoot potential problems before they occurred. This work began during the initial stages of the research project, and included shadowing clinicians,

having informal conversations with staff, and attending team meetings (for dates and details of meetings see Chapter 4). In summary:

- Staff were enthusiastic about recruiting for trials, and reported altruistic motivations or a general sentiment that it was a 'good thing' to support research.
- Although they did recruit for trials, they found it difficult to *reliably* remember to mention trials within busy clinics, particularly ones with complex inclusion criteria.
- They stated that it is not possible to take more than a few minutes from clinical contact time to recruit participants. The time set out for treatment is limited, and there were ethical concerns about taking away a person's treatment time.

They identified specific issues with previous research studies' design or management:

- They had not met most academics they were recruiting for. A feeling of distance between the staff and researchers, has in some studies meant that staff didn't feel able to ask the researchers questions, and that they were more likely to prioritise demands from within their own teams than from an unknown researcher.
- Research plans were at times not practical or possible within IAPT. A good understanding of the service and their systems may help researchers in either better planning research or in adapting their expectations.
- Some clinicians reported that trials with complex eligibility criteria were more difficult to 'bear in mind', and that some studies used eligibility criteria that did not translate easily into IAPT (for example based on information they would not collect routinely).

Several strategies were employed in the design and management of the PRotect trial in order to ensure adequate recruitment.

- **Being physically present**

The first strategy was to have a researcher physically present in services where possible through borrowing a free desk at each of the four offices, and working in these teams at least one session per week, and attending team meetings (whether presenting the study

or not). This allowed a consistent view of developments in the services, and for staff to approach me with questions or referrals.

To harness staff enthusiasm for research, I kept people informed of study developments through regular update emails thanking people for their contributions and noting progress, presented results to the group as early as possible, and offered to contribute to non-trial related work within the service such as presenting at the PWPs research reading group.

- **Recruiting and incentivising two trial clinicians from each team**

We recruited two trial clinicians from each of the four IAPT teams to be PRotect intervention facilitators, in order to extend the physical presence of the study within the whole service. When researchers were not present, there was still an ambassador from within each team with their own motivation or personal involvement in the trial. These trial clinicians were able to remind about the study and answer questions. The trial clinicians volunteered for the role, and their reasons for taking part were:

- A concern about what happens to their clients after they leave treatment.
- An interest in research.
- Continuing professional development and 'for the CV'.
- Variety: trying something a bit different.

In order to meet these expectations, I:

- Circulated fortnightly emails with an update about the trial progress. These focussed on what had been achieved by the service.
- Ensured the trial clinicians had honorary contracts with UCL so that they could become more involved in the research and carry out their own studies, as well as add the position to their CVs and have their contributions formally recognised.
- Gave extra responsibility for the conduct of the trial to recognise excellent work. One trial clinician became 'Intervention Arm Coordinator'.
- Offered opportunities for research and research mentorship in emails, and in person throughout the study, as well as access to resources within the University.

- Sent interesting articles or details of academic lectures to the trial clinicians.

Use existing IAPT systems wherever possible

We tried to adapt to use existing IAPT systems where possible. Clinicians used their own supervision arrangements for delivery of the intervention. The trial clinicians suggested that the best way to book review calls for people attending workshops would be to have a sign-up sheet available at each workshop.

Procedures for intake calls, office management, and supervision arrangements varied slightly between teams, and this knowledge from trial clinicians helped us to adapt trial procedures. I had continued meetings with PWPs and IAPT Leads to clarify issues such as whether delivering the intervention would count as a clinical contact, how to manage risk, and how to manage the trial participants in the computer records system. This approach fits in with our aim to test the intervention as closely as possible to how it would be delivered outside of a research trial.

Designing a process for referral that keeps service burden to the minimum

The largest potential barrier to the success of the trial would be a difficulty recruiting participants. The design addressed concerns about complex, non-IAPT eligibility criteria and difficulty remembering trials in busy clinics. We used a two-stage recruitment process, where IAPT staff were only responsible for giving trial information sheets to participants and asking if they would be happy to be contacted by a researcher. This meant they only had to comply with Data Protection Regulations (passing on a person's contact details), and not with complicated research consent procedures. This helped to keep the time and legal burden of referral to a minimum, and also ensure my own compliance with research consent procedures.

To supplement this, Assistant Psychologists searched clinical records for clients who may have been missed and not offered the trial. There is a field on the IAPT clinical record system which asks "Are you willing to be contacted about research". Approximately 40% of people had answered yes to this question, 20% had answered no, and 40% had not been asked. The AP contacted people if they had not been asked (and

asked this question initially) or if they had said yes, gave brief information about the trial, and asked for permission to pass their details on to me.

The fact that people had had the study information several days before being contacted for screening meant we had given sufficient time for them to consider their participation which is required for ethical research recruitment and for consent to be truly informed. This meant we were able to conduct the screening and baseline measures within that initial research call, minimising the burden on participants in terms of calls.

Referrals

Two referral streams were used for participant recruitment: clinicians identifying and approaching their own clients, and an Assistant Psychologist reviewing records and flagging potential participants (to clinicians or to researchers if that person had consented to be contacted about research). These two streams were needed as although it is generally understood that clients prefer their own clinician to approach them about research, this can place a burden on clinicians who might forget in busy clinical settings or who might prioritise time for treatment. It is usually considered ethical for a person within the clinical care setting (rather than an outside researcher) to make the first contact with a patient about research.

IAPT clinicians approached clients they thought might be eligible during their final treatment session. We asked clinicians to approach anyone who had had an issue with low mood or depression and had gone from above to below threshold on the PHQ-9 regardless of any other co-existing mental health problems, the focus of acute treatment, or medication use. I reassured that any further eligibility criteria would be applied by the researcher.

An assistant psychologist reviewed electronic patient notes to identify any further clients that might be eligible for the study, then contacted them by phone or email (unless they had stated they did not want to be contacted about research).

We provided referral forms IAPT clinicians could complete but emphasized that all we needed in terms of ethics and data protection was for them to give the client the information sheet (Appendix K), and ask if they consent to be contacted by a researcher (Appendix L). This meant clinicians who were in email contact with clients could pass details on this way, or speak to me in person if they saw me. If the client gave consent for their contact details to be passed on, these were sent in whichever secure method was most convenient (over the phone, email or in-person).

We printed simple trial reminder cards on brightly coloured paper and fixed these to the computer monitors (on suggestion of one of the clinical psychologists), and trial clinicians and Assistant Psychologists put e-reminders on the IAPT clinical record system for clinicians who had a client coming towards the end of treatment who may be eligible.

Informed consent

After receiving referrals from IAPT, a researcher contacted potential participants, and followed the screening call procedure (Appendix M). The researcher briefly asked some additional screening questions: if they were taking part in another research project, were not a recent IAPT client or did not feel they had had an issue with low mood or depression, they were not eligible.

If the person appeared eligible, they were then asked if they had any questions about participation, and whether they wanted to participate. The consent form (Appendix L) was reviewed verbally during the telephone call with the researcher, and was then sent to the participant to be signed (along with a stamped addressed envelope). After consent was provided, the researcher then went on to ask the IAPT Minimum Dataset questions (the PHQ-9, GAD7, and WSAS) and complete the depression section of the LIFE interview (Keller et al., 1987), and if they were not eligible (with a score above 10 on the PHQ-9, significant suicidal thoughts, or no depression on the LIFE interview), they were notified of this and thanked for their time. If experiencing suicidal thoughts, the risk protocol (Appendix O) was followed to ensure that they received appropriate support.

Any research procedures prior to informed consent should be kept to an absolute minimum, so informed consent was sought prior to the more detailed eligibility screening.

For those who were eligible and provided consent, the responses were used as baseline measures, and additional data collected on: the number of previous episodes of depression the person report in their lifetime, previous treatments, and whether they were currently taking antidepressant medication. All names and contact details of participants, and consent forms, were stored separately to symptom and LIFE information in order to comply with guidance on the conduct of clinical trials.

Following the screening/consent/baseline call, I sent an update email to the clinician or assistant psychologist who made the referral, in order to thank them for the referral and inform them of its outcome. All participants' GPs were informed by letter that their patient was participating in this research trial and that they may be informed of any suicide risk reported by the participant as part of the trial's risk reporting procedure.

Assignment of interventions

Immediately after screening and consent, the names and contact details of all eligible participants were sent to another member of UCL research staff who carried out the randomisation procedure (Appendix P). They independently administered the randomisation process using an online package (www.sealedenvelope.com) and then notified necessary parties (the trial therapist and the participant) of the results of the randomisation. The online package uses random permuted blocks to allocate all participants to treatment A or B (in this case the intervention or monitoring arm) in a ratio of 1:1. Data and randomisations made by the system cannot be changed or edited by users, providing some protection from selection bias.

To randomise, the staff member/randomiser logged-in to the website and entered the participant's unique identifier and a randomisation password. The system then allocated this participant to a study arm, and sent an email with this allocation to the randomiser.

This randomiser contacted the participants in the monitoring arm directly to let them know the result of the randomisation, and sent the names of intervention participants to the IAPT services. Lists were only accessible by the randomiser and trial clinicians in order to maintain blinding of the outcome assessor. In psychotherapy trials it is often not possible to have participants be blind to allocation, as they will be aware of the treatment they participate in, but given this, attempting to conduct blinded outcome assessment is important. There were no restrictions on participants seeking other treatments or medications throughout the trial period.

Participants in the control arm were discharged from their acute IAPT delivered treatment (this is routine) although they were free to seek treatment outside of the trial. It is expected that some participants would be receiving antidepressant medication on entry to the study, and this was measured on entry and follow-up. A researcher contacted them three months after enrolment for their first interview. As with the intervention arm participants, they were not restricted in seeking help or treatment outside of the trial.

Data collection, management and analysis

Data on recruitment and retention were collected in a 'Trial Management Log' throughout the study. Clinicians delivering the intervention completed logs, fidelity forms, and audio-recordings throughout intervention delivery. Participants completed follow-up research interviews with the researcher (blind to treatment allocation) at 3 and 6 months' post-randomisation where they completed the clinical measures planned for the main trial: the depression section of the LIFE (Keller et al., 1987), and IAPT minimum dataset measures (the PHQ-9, GAD7, and WSAS). At the end of their participation, all participants and trial clinicians were asked about their experience in brief semi-structured interviews, and the trial clinicians about their experience in the focus groups.

Trial monitoring data collection

The Trial Management Log of research delivery and processes included screening, baseline assessment and follow-up completion logs. In order to further explore feasibility

of follow-up interviews the Trial Management Log was reviewed to collect data on: uptake of evening and weekend time slots, and timeliness (in relation to the 'due' date), for 3- and 6- month interviews.

Data were collected on intervention delivery through records kept at site by the Intervention Delivery Coordinator (SA, who also delivered the intervention). These data were kept in the clinical site until after data collection was complete to avoid unblinding me as the outcome assessor. All trial PWPs completed adherence forms (which included recording completion of protocol components, notes on participant interaction and engagement, and the length of the call) for introductory and review calls. All intro calls were recorded but with only the practitioner's voice (and not the participants' voice) being captured. A sample of the workshops were audio-recorded where all participants consented to this.

Participant data collection

Measures taken during the screening call were used as baseline assessments. All participants were asked to complete 30-45-minute follow-up assessments with a researcher 3 and 6 months after their randomisation. Participants completed follow-up assessments over the phone, unless they requested otherwise, and were reimbursed for their time with £15 supermarket vouchers per completed assessment. The follow-up assessments included the IAPT minimum dataset (which includes the PHQ-9, GAD-7 and the WSAS), and the depression section of LIFE. It should be noted that within the constraints of this study there were no relevant changes from DSM-IV to DSM-V criteria, so adaptations to the LIFE evaluation were not necessary. A summary of participant data collection and time-points is provided in Table 6 below.

Table 6: Pilot trial participant data collection questionnaires/measures and timepoints

	Screening/ Baseline	3-month follow-up	6-month follow-up	After 6-month follow-up
Recent IAPT+ low mood/other research	X			
PHQ-9	X	X	X	
GAD-7	X	X	X	
WSAS	X	X	X	
Phobia scale	X	X	X	
Employment status	X	X	X	
Current ADM	X	X	X	
LIFE	X (prior 12 months)	X	X	
Dep and Tx history	X			
Action to protect MH		X	X	
Semi-structured interview				X

During the baseline interview, participants were also asked whether they were taking antidepressant medication, to estimate the number of lifetime episodes of depression they had experienced, and which treatments they had received. In the three and six month calls an additional question was asked about any current relapse prevention activities and antidepressant medication use. At the end of the final interview, all participants were asked about their experience, and participants who had been allocated to the intervention arm were asked about their use of the intervention. Questions on the use of intervention activities were reserved until after the final clinical measures had been collected in the 6-month interview, so that the outcome assessor could remain blind to treatment allocation where possible, and to allow participants the maximum number of chances to attend the workshop before answering these questions.

Participant clinical measures

Relapse of depression during follow-up, defined as an episode of depression that meets DSM-V criteria, was assessed according to the LIFE interview (Keller et al., 1987).

Clinically significant deteriorations in depression are also reported (5+ points to within the 'depressed' range of 10+) using the PHQ-9 (Kroenke, 2012), as well as depression and anxiety symptom scores and 'work and social functioning' at each follow-up point. Further details on these measures are provided below. For this pilot trial the aims were to collect the proposed measures after 3 and 6 months (but 12 months would likely be the minimum length of follow-up in for the larger effectiveness trial in order that it can contribute to the evidence base in Chapter 2).

Relapse (an episode of depression that meets DSM-V criteria) was assessed using the Depression Section of the LIFE (Longitudinal Interval Follow-up Evaluation, Keller et al., 1987). The LIFE has good inter-rater and long-term test retest reliability for depression and across diagnoses (Warshaw, Dyck, Allsworth, Stout, & Keller, 2001; Warshaw, Keller, & Stout, 1994). The LIFE (Warshaw, Dyck, Allsworth, Stout, & Keller, 2001; Warshaw, Keller, & Stout, 1994) was designed to provide reliable and valid data over the follow-up period during prospective longitudinal studies without the need for continuous measurements. The scale is validated to assess over a 6-month interval between interviews.

The use of this method of assessment of relapse provides a method and rationale to understand and characterise relapses within this thesis in Chapter 1. The LIFE in particular is useful if a study seeks to have a continuous picture of the course of depression over time, but without frequent measurement being needed. During the LIFE interview, the researcher initially asks the participant about how things are going at the moment, and then reflects back on how things were when the previous interview took place (or in a specified time period if first interview) and ask about any life events that have happened in the interval. Researchers interview participants about their level of symptomatology during the follow-up interval and identify 'change-points', anchoring these on events within the calendar e.g. 'So, was that around the summer time?' or within their own lives 'So coming up to your birthday you were starting to feel more low?'. This information is used to estimate a 'Psychiatric Status Rating' (PSR) for each week of

the follow-up period on either a 3- or 6-point scale. The PSR used in this study is a 6-point scale, where a score of 1 or 2 represents no or minimal depressive symptomatology, 3 or 4 represents some symptomatology, and a score of 5 or 6 indicates that the person meets full DSM-IV criteria for an episode of depression. This information was supplemented this with an assessment of relapse according using the PHQ-9.

To assess depression symptoms at follow-up the PHQ-9 (Kroenke, Spitzer, & Williams, 2001), the self-report measure of depression symptoms routinely used in IAPT services was selected. The questionnaire asks respondents how often they have been troubled by a range of symptoms over the past two weeks (derived from the DSM-IV symptoms of major depressive disorder). The nine items are scored between 0 and 3, giving a maximum total score of 27. A cut-off of ≥10 points is used to indicate probable major depression with a sensitivity of 88% and specificity of 88% (Kroenke et al., 2001). A score above the threshold for depression which was preceded by an increase of 5+ points can be used to indicate a 'clinically significant deterioration' (Ali et al., 2017). The measure has good internal reliability (Cronbach's α = 0.86-0.89), good test-retest reliability (intraclass correlation =0.84; Kroenke et al., 2001).

The second symptom assessment measure used, the Generalized Anxiety Disorder scale (GAD-7; Spitzer, Kroenke, Williams, & Löwe, 2006) is a self-report measure which focusses on anxiety symptoms. It asks respondents how often they have been troubled by symptoms of anxiety over the past two weeks. The seven items are scored between 0 and 3, giving a maximum total score of 21. A cut-off of ≥8 points is used to determine a probable anxiety disorder with a sensitivity of 89% and specificity of 82% (Spitzer et al., 2006). The GAD-7 also has excellent internal consistency (Cronbach's α =0.92), and good test-retest reliability (intraclass correlation =0.83; Spitzer et al., 2006).

The final measure, the Work and Social Adjustment Scale (WSAS; Mundt, Marks, Shear, & Greist, 2002), asks about any difficulties the person is experiencing in their ability to function in five domains: work, home management, personal leisure activities, social

leisure activities, and relationships with friends and family. Each of the five constructs is scored from 0 (not at all) to 8 (very severely), and cut-offs of 10 or more and 20 or more are used to indicate mild-moderate and moderate-severe impairment respectively. The WSAS has good internal consistency (Cronbach's α ranging from 0.70-0.94), acceptable test-retest reliability (intraclass correlation =0.73) and good external validity with clinician interviews (r=0.81-0.86; Mundt et al., 2002). Data collected at each time-point is summarised in the Data Collection section below.

Qualitative data collection of participant and staff experience

Participant and clinician experience were explored in brief semi-structured interviews with all trial participants after their final outcome measures were collected, and in a focus group with all of the trial clinicians after completion of their involvement in the study. The aim of participant interviews was to reflect their experience and identify any salient features of experience that could inform development of a future trial (rather than 'measure' behaviour change, or satisfaction as you might do in later studies, and for which you might use a standardised measure or formal feedback). The aim for the staff focus group was similar although the staff had more extensive experience in the study, completing training and delivering several interventions so were able to discuss their experiences and issues with feasibility in more-depth. The findings from this exploratory pilot qualitative data collection might inform the elements to be included in more in-depth qualitative work following a larger trial.

Participant experience

The experience of study participants was explored through qualitative interviews at the end of each 6-month outcome assessment call. For a description of the participant experience interview schedule see Appendix T. Given our feasibility aims, and to reduce selection bias, it was important to seek the views and experience of all recruited participants. The interviews were therefore conducted during the final call in order to ensure maximum completion, but after the completion of all clinical outcome measures so that blinding was not compromised during outcome assessment. For a conventional

qualitative research project, or qualitative work following a larger randomised controlled trial, a selection of the participants are likely to be interviewed (rather than everyone), and these interviews might be in more depth.

The primary aim of these interviews was to identify the elements of experience that were most salient, and so most important to participants. The semi-structured interviews began with open questions with only minimal prompts when needed, to avoid directing participants towards certain issues. The technique of 'bracketing', often part of phenomenological research (Fischer, 2009)' was used in order to encourage this free expression from the interviewee and for accurate elicitation of data around the participants experience, without my prior assumptions (Ahern, 1999; Tufford & Newman, 2012). The interview questions were broad and exploratory, and aimed to not to include prior assumptions, for example "Which study arm were you in? How did you feel about that?". The interviews had no fixed length: the time taken this was driven by the responses that participants chose or were able to provide. Non-directive encouragement was used to elicit further input from participants, for example picking up on certain words they used ("what do you mean by…"), using non-verbal cues (mmhmm), or leaving silences to give space for further comment. (Ahern, 1999; Fischer, 2009; Tufford & Newman, 2012).

This approach was used for several reasons: as this is the first time the PRotect intervention was being delivered it is not clear what were the key elements of experience that will might be deemed important to the participants, and so this questioning technique allows for the elicitation of rich data that directly reflect experience from the participants' perspectives. Open questions which are not led by researcher assumptions may provide a better insight into the breadth of issues which could be useful to inform any future definitive trial.

The participants were asked to reflect on their experience of trial participation in general, with prompts where necessary as detailed below, with a particular prompt about their experience of random allocation to be offered the intervention or not. Finally, questions

to those who reported being offered the intervention explored the experience of it: deciding whether to attend the workshop or not, and each intervention element.

Table 7: Participant experience interview schedule: summary of questions and prompts

Experience of the trial
Can you tell me a bit about your experience of being part of this trial? *Could you think back to when you first became part of this research study?* *Prompts: it was last December and we spoke on the phone…* *At the time we spoke I explained that there was a 50 50 chance that you would be offered a wellbeing intervention. Do you remember if you were offered it?* *Prompts- did someone called X at UCL get in touch after we spoke to let you know? Did someone at iCope get in touch over the phone or by email?* *How did you feel about (being offered it/not being offered it)? If offered, did you attend? Why/why not?*
Experience of the intervention (if offered)
What did you think of the intervention? *Prompts: Did someone from iCope have a ten-minute phone call with you before the workshop?* *How was that call?* *Did you attend the workshop? Why/why not?* *What was the workshop/review call like?* *Did you/do you use anything from the PRotect intervention in your everyday life? Do you use anything now?*

Given interviews were conducted with every participant, and due to resource and practical constraints, notes were transcribed live during the call, verbatim where possible,

rather than audio-recorded. Quotes may therefore have some inaccuracies but will still be used in the data reporting in order to provide the interesting, convincing or vivid reflection of experience that is deemed a key element of good reporting of qualitative analyses (Braun & Clarke, 2006)

Staff focus group

In order to explore the experience of those delivering the intervention a single focus group was conducted with the PWPs who delivered the PRotect intervention as part of the trial. A description of the focus group procedure and topics is included in Appendix U. A focus group was chosen rather than individual interviews to enable discussion, sharing of ideas, and group reflection on the future development of the intervention. Additionally, we sought to explore and represent the range of clinicians' experience in order to feed into any feasibility trial results or plans for a larger trial, so a free-flowing space for them to reflect was preferred to a more goal oriented group discussion such as used in nominal group technique (Powell & Single, 1996).

Clinicians were invited to attend my University offices after the completion of intervention delivery within their services, to reflect on their experiences in a two-hour focus group. In order to reduce demand characteristics, the focus group was facilitated by a University staff member and student and not be me, and attendees were assured that their names would be removed before the transcript was sent to the researchers. All participants gave consent to take part and to be audio-recorded. The focus group recording was transcribed and anonymised, and then analysed NVivo software.

A mixture of questions and tasks were used to elicit discussion and sharing. Given that the future implementation of this intervention would depend on how much it could be normalised within the therapies service, the focus group was structured around the four element of 'normalisation process theory' (Murray et al., 2010) as follows:

Coherence: Does the intervention make sense to clinicians?

Cognitive participation: Do they 'get behind' it?

Collective action: Do they act according to the aims of the intervention?

For the analysis of data however, an inductive thematic analysis was used: themes were drawn as far as possible from the data rather than from a theoretical perspective. In this way it was hoped to reflect the points which were most pertinent in the experience of the clinicians' themselves.

Analysis of feasibility

The nine feasibility outcomes were assessed against nine criteria using a traffic-light system (Avery et al., 2017). If the target was met then that criteria was rated green, if a target was under by 20% this was rated amber, and if under by 40% this was rated as red. Green indicates support for a full randomized controlled trial, amber indicates that this element may need adjustment, and red indicates this was not feasible and should either not proceed or be the subject of major change. Any amber or red ratings were further explored narratively through considering reports from the trial clinicians throughout the study period, fidelity forms completed for introduction and review phone calls, and assessment of a sample of audio-recordings. These were assessed in terms of adherence to protocol components, delivery style, and participant engagement.

Pilot analysis of clinical outcomes

The preferred primary outcome for the proposed full controlled trial: the total number of 'relapses' in the intervention arm compared to the control arm, along with the number who experienced a 'clinically significant deterioration' in depression symptoms is reported in each arm, and compared using the chi squared test. I report relative risk with 95% confidence intervals, and 'number needed to treat' (Cook & Sackett, 1995). For relapse of depression I also produce a Kaplan Meier survival curve and conduct and report a log-rank test of difference between curves.

The mean PHQ-9, GAD7 and WSAS scores at each time-point, along with 'change in scores' (the difference between 6 month and baseline), and the corrected effect sizes using Hedge's g (Borenstein et al., 2005) comparing baseline with 6-month follow up.

All pilot data analyses were on an intention-to-treat basis: all participants allocated to the intervention arm were analysed as such, regardless of whether they engaged with clinicians or attended a workshop. Similarly, follow-up points were taken from baseline and were not related to attendance at a workshop as the time between baseline and intervention receipt varied. Effect sizes and confidence intervals are reported (but no statistical significance tests as this is not recommended for outcomes within pilot trials; Eldridge et al., 2016). Analyses were performed using SPSS version 23. Analyses were conducted based on initial randomization to study arms and available data only, and missing data were not imputed.

Analysis of participant and staff experience

I analysed the interview and focus group transcripts using a three-stage analysis process, similar to that used in 'thematic synthesis' of qualitative research in systematic reviewing (Thomas and Harden, 2008) and drawing on 'thematic analysis' (Braun and Clarke, 2006). The table below describes my qualitative analysis plan in relation to the 3-stage thematic synthesis and 6-stage thematic analysis mentioned above:

Table 8: Three-stage qualitative analysis plan (alongside two established processes for comparison)

Qualitative analysis plan (3 stages)	Thomas and Harden's 3 stages of synthesis	Braun and Clarke's 6 stages of analysis
Stage 1: Reading and re-reading the transcripts whilst coding for 'importance' (completed for brief participant interviews and staff focus group)	Stage 1: coding text	Stage 1: Familiarizing yourself with your data
		Stage 2: generating initial codes

<table>
<tr><td>Stage two: Reviewing and revising codes, grouping into descriptive themes.

(completed for brief participant interviews and staff focus group)</td><td rowspan="2">Stage 2: developing descriptive themes</td><td>Stage 3: searching for themes</td></tr>
<tr><td rowspan="2">Stage three: generating analytical themes by interrogating the themes in relation to our definition of ‘importance’, and through presentation of the data in these themes with illustrative quotes

(completed only for staff focus group)</td><td>Stage 4: reviewing themes</td></tr>
<tr><td></td><td rowspan="2">Stage 3: generating analytical themes</td><td>Stage 5: defining and naming themes</td></tr>
<tr><td></td><td>Stage six: producing the report</td></tr>
<tr><td></td><td>(Thomas & Harden, 2008)</td><td>(Braun & Clarke, 2006)</td></tr>
</table>

Stage 1

Firstly, I read and re-read the transcripts, identifying and coding any ‘important’ pieces of information. Information was classed as more ‘important’ in the participant interviews if it was raised by the participant without prompt: there were no prompts initially and as such anything mentioned was assumed to be of particular salience in the experience of that participant, and also if it was endorsed by multiple participants. Information was classed as more important in the focus group if it a) occurred frequently; b) was an area of agreement within the group; c) was an area of disagreement within the group; or d) was mentioned ‘spontaneously’ unrelated to the question or topic of discussion at that point.

Stage 2

In the second stage, I reviewed and revised codes, and grouped similar codes to form descriptive themes. These themes were descriptive groupings and did not attempt to 'go too far' away from the source data. I aimed for the themes to be reflective of the entirety of the dataset(s). For the participant data this meant drawing out themes within each interview section, as each section was asked to a different set of participants. The first section on 'experience of the trial' applies to all participants, and the second on 'experience of the intervention' applies only to intervention arm participants, so data are analysed and reported within those sections. The interviews were relatively brief, so identifying themes across the two topics of focus was deemed not to be appropriate or valuable.

I largely sought to aggregate and summarise participant data, (drawing on content analysis methods rather than analytic themes), therefore analysis stopped at this stage for participants and descriptive themes were reported. Numbers of participants endorsing each theme, and numbers that were analysed (so could have endorsed) each theme are also reported. My primary focus in questions for each section and therefore the assumptions that I am aware I am bringing into the analysis (Fischer, 2009) are as follows:

'Experience of the trial',

- I identify themes with particular focus given to feasibility of trial methods, for the sample as a whole (not split by arm), and of the randomisation and allocation process.

'Experience of the intervention'

- Only participants in the intervention arm were included here, and I identify themes with a focus on feasibility of the intervention (e.g. attendance), and impact.

Stage 3

For the focus group data, I proceeded to step three and considered the descriptive themes in relation to the 'importance' codes, and produced analytic overarching themes, interrogating these themes whilst representing them narratively in text. Themes were analysed across the focus group as a whole rather than within each focus group question or topic of focus. The analytical themes are reported using direct quotes from the transcripts in order to further test the representativeness of these themes, and without a focus on number of staff endorsing each theme.

Finally, a second researcher (GP) reviewed all participant and staff experience themes and their relation to source data, and the themes and data presentation were revised.

Monitoring

Managing risk

Procedures were developed for managing risk to participants during the trial. During research calls, the "assessing and reporting risk in research settings" protocol was followed (included in Appendix O). This protocol gives instructions to conduct a risk assessment if an indicator of risk becomes apparent during the research call. Suggested indicators include a score of 1, 2, or 3 on the PHQ-9 question about suicidal ideation, and/or mention suicidal or self-harming behaviours or thoughts in the LIFE interview. The assessment then includes asking the participant about thoughts, plans, actions and anything preventing their suicide. There are three outcomes of the risk assessment: asking the person to go to, or calling them a taxi to A&E; contacting the person's GP or healthcare provider to tell them about the conversation and ask for an appointment to be arranged as soon as possible, or advising the participant that they could make an appointment to talk about these feelings. The CI trained the researcher conducting outcome assessments in this procedure, and reviewed any risk reporting forms within 24 hours of receiving them. In order to prepare for this risk procedure, a letter was sent to each participants' GP on recruitment explaining that they were participating in this

research trial and that if they told us that they were at risk of suicide during a research call we would follow our risk reporting procedure which may involve contacting the GP.

To comply with the requirements of the sponsor (UCL JRO), adverse events had to be assessed and, if 'serious', reported to the sponsor by the CI within 5 days of their occurrence.

Ethics and dissemination

Sponsorship was provided by the UCL Joint Research Office, who provide indemnity to projects within UCL and UCLH. The study protocol received independent internal UCL peer review on 20th January 2016, and external peer review on 31st January 2016. The study was reviewed and granted ethical approval by the Camden and King's Cross NHS Research Ethics Committee (14/06/2016, ref: 16/LO/0652). A study summary was then made available on the Health Research Authority website. I then proceeded to get site-specific confirmations to proceed. A study protocol was prospectively registered on a freely accessible and searchable online trials registry on 2nd August 2016 (ISRCTN17371456).

The dissemination plan was as follows:

- To participants: Produce a summary sheet of the findings for participants. In the final follow-up phone call participants were asked if and how they would like to receive this.
- Within IAPT: The results of the study to be presented to IAPT staff as soon as possible after completion of data collection. The intervention materials will be made available for use in any IAPT service which wishes to use them.
- To the scientific community: The results will be written up as one or more manuscripts and publication will be sought and results presented at academic meetings.

Discussion

This Chapter presents the design of a pilot randomised controlled trial of the PRotect intervention which pilot sought to test the method proposed for a hypothesis testing effectiveness trial. The design is pragmatic in that it focusses on assessing an intervention delivered in a routine clinical setting rather than an 'ideal' or lab setting (Schwartz & Lellouch, 1967). The pilot is therefore of an effectiveness trial that would estimate the effect of the intervention as routinely delivered, rather than an 'efficacy' trial which evaluates efficacy in ideal conditions (Roland & Torgerson, 1998). Pragmatic designs are well placed to answer questions around different care options, rather than to identify a specific mechanism behind a change, which fits with my approach of viewing the issue of relapse prevention at a whole-system level. Using random allocation to parallel groups means any bias between arms is minimised. A crossover design was considered but offering control arm participants the intervention would not be justified as we do not know whether the intervention will be helpful, and follow-up over time is necessary to identify any impact on relapse. Blinding of participants was not possible (as in most psychotherapy trials) but outcome assessment was conducted blind to allocation, and the process by which allocation is decided and communicated was independent (Page & Persch, 2013).

As such, random allocation to the intervention and control was deemed necessary in order to isolate the impact of the intervention from other factors that are known to be linked to relapse risk such as level of residual symptoms, length of recovery, or previous experience of depression (see Chapter 2). The intervention is intended to follow acute treatment, which may itself be protective against relapse, and may include some relapse-focussed work. Attributing any maintenance of wellbeing to the PRotect intervention rather than enduring effects of acute treatment would be impossible without randomising participants after acute treatment completion. Randomised controlled trials are the gold-standard in hierarchy of medical evidence (Craig et al., 2008) and are recommended in guidance for developing and evaluating complex interventions from the Medical

Research Council (Campbell et al., 2000; Craig et al., 2008; Skivington et al., 2021). Individual randomisation was chosen (using random permuted blocks), and allocation concealed from outcome assessors. Blocking randomisation reduces the risk of one study arm recruiting much larger numbers than the other (Schulz & Grimes, 2002) and individual rather than cluster randomisation means fewer participants would need to be recruited to a full randomised controlled trial to achieve adequate power to detect a difference between study arms (Lorenz et al., 2018).

In the control arm, participants were discharged from IAPT services as planned, and offered no further intervention (although they remain free to seek input outside of the trial). This inactive control condition was selected because this is the current 'usual care' in IAPT services generally, particularly for those who have not identified relapse as a specific concern. This design seeks to ask the question of whether the PRotect intervention is clinically effective compared with the current standard of care: acute treatment followed by discharge from services for the majority of people. Once this was established a trial comparing the PRotect intervention to an active or attentional control might then seek an answer to the question of whether the PRotect intervention specifically reduces relapse risk over alternatives.

It was important for the exclusion criteria of to be minimal so that the sample is more likely reflect the population that the intervention workshop is intended to serve. This was identified as important given the systematic review (Chapter 2) which highlighted that MBCT trials tended to have quite detailed inclusion criteria and so results may be less applicable to the broad range of people presenting to clinical services. In contrast, CBT trials included a range of experiences of depression and treatment, and the evidence they produce is then might be more likely to be generalizable to the population who are offered relapse prevention CBT. More broadly there are concerns that certain groups, such as older adults, are often excluded from research trials but are recipients of the care that has been tested (Herrera et al., 2010; He et al., 2020). Participants were eligible if they had experienced and recovered from depression based on indicators from the

LIFE (Keller et al., 1987) or the PHQ9 (Kroenke et al., 2001). Outcomes were also selected for applicability in applied health settings. The LIFE was used to apply diagnostic criteria in order that results for this could be compared with other studies, and the broader PHQ-9 from above to below the clinical cut-off was used as it is more likely to reflect how the intervention would offered in practice.

A key aim of this pilot was to assess the feasibility of intervention delivery, and as such we aimed to deliver five workshops, with the hope that this would allow for some variety in experience of intervention delivery, and perhaps to identify some issues or potential changes needed. The target sample size was then calculated to recruit sufficient people to fill these workshops and be part of the control arm, on the basis of a four-month recruitment period, and on the basis of expected numbers of people being discharged from the service with previous high PHQ-9 scores, with a 66% consent rate and then 30% drop-out. Rather than seeking to be an accurate estimate of the sample size needed, feasibility parameters are selected on the basis of the most likely numbers needed in order to fulfil the primary aim of assessing feasibility.

The target sample size was decided on the basis of adequate recruitment to assess feasibility of a larger trial: with the deciding factor being needing sufficient participants for five intervention groups to be delivered. Although fewer participants might give an indication of recruitment and retention rates, feasibility of delivering the intervention would be better tested with a variety of groups and practitioners. The sample size could not have been based on a percentage of those needed for a powered effectiveness trial (as is done in some studies, particularly internal pilots) as there is no estimate for the predicted size of effect of the intervention: prior to the study there had only been one, non-randomised study of a low-intensity intervention in a similar population (Rodgers et al., 2012). However, the clinical outcomes collected within this pilot might be used in a formal sample size calculation for a larger trial.

Existing data on the rate of discharge from services per month was used to estimate the rate of eligible participants that could be recruited and therefore the length of the

recruitment window needed. We aimed for a consent rate of 66% and expected sufficient referrals to be able to recruit and deliver these workshops with a four-month recruitment window (at least 49 per month) on the basis of previous service use data. A limited window was preferred, as group interventions require fast recruitment so that individual workshops have sufficient participants.

Data collection focused on outcomes relating to feasibility of trial methods such as consent and follow-up rates, feasibility of intervention delivery such as attendance at the intervention and follow-up calls. These a priori targets are set-out prior to the pilot trial in order to have an objective assessment of feasibility: what should proceed without change, what needs to be adapted, and what is not feasible (Avery et al., 2017). Although there is no hard and fast rule for what constitutes 'feasible', setting out specific criteria allows for an unbiased assessment and learning from a pilot trial. From a pragmatic perspective, if the consent rate is low from those we think are eligible, then selection bias is more likely to be an issue, hence it is important to identify a target consent rate.

This quantitative assessment of feasibility is important; but it should be supplemented with some qualitative exploration of experience to inform any changes that are needed, or explore methods which were or were not successful. The work conducted by PWPs and other IAPT clinicians on the ground was of vital importance, since PWPs would be delivering the intervention in a full trial and in services if subsequently implemented. Considering their perspectives, and understanding any difficulties in intervention delivery, can allow for modifications prior to this taking place, and inform whether and how the intervention could be integrated into IAPT services more widely going forward. The extent that healthcare staff understand, feel connected to, deliver, and are able to reflect on their intervention delivery is fundamental to a change in practice according to normalisation process theory (Murray et al., 2010). Any change in healthcare will only become 'normalised' if staff are able to understand, to be fully involved, on board, and to work towards making an innovation 'routine'. The questions therefore focused around

these areas of work: coherence, cognitive participation, collective action, and reflexive monitoring.

Participant and clinician experiences and views are also of vital importance to incorporate into future work. In this study the PWPs may be able to contribute a more in-depth examination of their experiences given their involvement in recruitment of participants and speaking with other clinicians about the trial within their service, and training and delivery of several workshops. As such an in-depth focus group was arranged for PWPs to discuss and reflect on their experiences. On the other hand, each individual participant might only be able to provide relatively brief thoughts given their relatively brief involvement. Given this, brief bracketed interviews were sought from all participants. If a more in-depth view of participant experience is needed further development workshops may be a helpful supplement to this initial qualitative work.

Strengths and limitations

Design decisions were informed by detailed consultation and development work with the IAPT services who would be delivering the intervention, which is likely to increase feasibility. It used measures that are already used by the services. The decision to use current IAPT staff to deliver the intervention largely within the systems used by the service for other workshops addressed feasibility concerns raised by the service such as the difficulties experienced by IAPT clinicians in understanding complex eligibility criteria, or the gaps between expectations of research and what is practical to deliver. It also means in future that the likelihood that any clinical effect would be reduced when applying the intervention within the ‘real world’ was less likely.

However, the pragmatic focus means that whilst efforts were made to make the intervention feasible for these two IAPT services, further feasibility work would be needed prior to a larger trial to consider regional variation in delivery of workshops, structures of different services, or even differences in client groups (which the conceptual framework presented in Chapter 2 could structure). Additionally, if this intervention were to be

delivered online or within a workplace or community centre, specific adaptations to those contexts might be needed. There is a balance between adapting the trial design for optimum feasibility, and ensuring that the evidence provided within a larger trial sits within the broader field of research and can advance knowledge of relapse prevention.

Using individual rather than cluster randomisation has two key risks: delivery of the intervention to suitably sized groups, and contamination. Using 1:1 randomisation for a group intervention means that only half of those who may be eligible in future are actually offered the intervention within the trial, and so may be more likely to deliver to small groups or have people drop-out due to being unavailable at the specific workshop time (Egan & Kenny, 2005). In order to protect against this risk, workshops were delivered across the two recruiting IAPT services. The PRotect intervention is offered as a standalone intervention after completion of acute treatment, and so there may be potential contamination and dilution of treatment effect through trial clinicians bringing elements of PRotect into acute treatment (although this should be balanced between arms as participants are randomised after completing acute treatment).

At this stage I have not included a consideration of cost effectiveness as this is inextricably linked to feasibility and aspects of intervention delivery such as group size within a workshop. As such these further measures would be usefully added if it is found that the more limited pilot trial plans are indeed feasible. Additionally, there would be some statistical considerations and further development of the analysis for a larger trial. For example, an assumption of independence of observations may not be correct in the intervention group: group membership and therapist may impact outcomes, which could perhaps be explored through calculating the intra-class correlation coefficient (ICC) for intervention group and for therapist.

Conclusion

The PRotect intervention is a standalone relapse prevention intervention designed to be offered to people who have completed treatment in an IAPT service. In the pragmatic

pilot trial presented here, participants inclusion criteria were broad in order that the participant group matched those who might be offered the intervention in future, but with further data collection in order that this group could be compared to those within the existing psychiatric evidence base. The pilot aims to test whether a full randomised controlled trial would be feasible and which adjustments that would be needed.

Chapter 6 Results of the pilot trial: Feasibility and clinical outcomes, and experience of participants and clinicians

Abstract

Background: The PRotect intervention, which aims to help people maintain their recovery after depression, was tested in a pilot randomised controlled trial.

Feasibility: 91 participants were eligible and 83 agreed to participate in this study. Follow-up assessments at 3- and 6- months were well completed (87% and 88%), and nine intervention workshops were delivered. The rate of referrals was slower than expected so recruitment was extended and group sizes in workshops small. The introductory calls were shorter than planned, but workshop delivery was feasible with components well completed, and review calls had good attendance and good fidelity.

Clinical outcomes: Risk of relapse was lower in the intervention than control arm (RR= 0.52, 95% CI 0.12 to 1.89). Recovery was well preserved in both arms (but favoured the intervention: Hedge's g= -0.17 for depression symptoms [95% CI=-0.64-0.029], -0.08 for anxiety symptoms [95% CI=-0.52-0.39], and -0.05 for functioning [95% CI=-0.52-0.42].

Participant and clinician experience: Participants' experiences tended to be positive, and in particular they felt expecting the research interviews and reflecting on progress was important in maintaining their mental health. Clinicians spoke of their investment in clients and the research, and how this intervention felt different to usual ways of working.

Conclusions: A larger randomised controlled trial to examine the clinical and cost-effectiveness of the PRotect intervention with some adaptations to intervention delivery is warranted.

Protocol prospectively registered with the ISRCTN Registry: https://doi.org/10.1186/ISRCTN17371456

Introduction

The PRotect after depression intervention was designed to be offered to people who have experienced depression and whose symptoms have reduced to the point that they are within the 'normal' (non-depressed) range. It focuses on wellbeing and habit formation, with the aim that if people have fewer residual symptoms, and stay well for longer, they may be protected from the risk of relapse. The intervention is intended to be feasible to offer people who have recovered from depression under the care of IAPT services (see Chapter 4), and an appropriately powered effectiveness trial would give evidence as to whether it reduces relapse risk.

In order to prepare for this and to answer questions and uncertainties around feasibility and participant and clinician experience, a pilot randomised controlled trial was conducted. It is important that interventions should be pilot tested with the primary focus of assessing and evaluating the feasibility of conducting a larger trial (Avery et al., 2017). This allows for researchers to adjust trial methods, and to prevent time and money being wasted on research that is unlikely to influence healthcare (Skivington et al., 2021). In particular, the feasibility of trial methods, feasibility of intervention delivery, the potential for efficacy, and participant experience should be considered when designing a larger trial, hence the pilot design in the last chapter.

The first feasibility outcomes assessed trial methods: recruitment and retention of participants, and completion of follow-up research interviews. Outcomes assessing intervention delivery were attendance at intervention calls and workshops, and the lengths of calls. If the nine outcomes are met this suggests this element of trial methods or intervention delivery is feasible without changes, if almost met changes are warranted, and if not met this element is not feasible and should be majorly changed or stopped. Given this is a feasibility study rather than internal pilot and it is not likely that all feasibility criteria will be met from the outset, additional trial monitoring was conducted that might suggest the direction of any changes needed: fidelity forms for clinicians to complete in intervention calls, audio-recordings of calls and workshops, and records of

correspondence during the trial including reports from trial clinicians. This is as advised for trials with an internal pilot (Avery et al., 2017), but which also could be useful here.

The potential for efficacy of the PRotect intervention which might inform a power calculation was examined by collecting the clinical outcome measures and running pilot analyses that could be used in a larger trial. The primary clinical outcome proposed for the main trial was a relapse of depression according to DSM-IV criteria, as assessed using the Longitudinal Interval Follow-up Evaluation (Keller et al., 1987). For the pilot, this was assessed up to 6-months following entry to the trial. Depression and anxiety symptoms, and work and social functioning were also monitored, using the measures that are routinely collected within IAPT services (Kroenke et al., 2001; Mundt et al., 2002; Spitzer et al., 2006). These outcomes were selected on the basis of producing evidence that could sit within the wider body of evidence reviewed in Chapter 2, and also that would be useful within an IAPT service context (as explored in Chapter 4).

Collecting qualitative data on experience to supplement the information on feasibility and potential for clinical efficacy was deemed important in order to explore any feasibility results, and in order to guide any changes to the trial design needed for a larger trial. To this end, all participants were asked questions about their experience on completion of participation, and the clinicians delivering the intervention attended a focus group discussion following the final intervention delivery. Of course, the experience of participants and particularly whether the intervention had an impact within their lives is of fundamental importance to the point of this work. The level to which the clinicians understand and can explain, deliver, and reflect on this work are all fundamental to the viability of any intervention which constitutes a change to normal practice (Murray et al., 2010).

In the previous chapter the trial design was described in detail. This chapter reports an analysis of whether the trial methods and intervention were feasible to deliver, the clinical outcomes collected from participants, and whether they would be useful in a larger trial

to indicate the effectiveness of the PRotect intervention. Finally, I report key themes in staff and participant experience which emerged from focus groups and interviews.

Objectives

The primary aim of this pilot trial was to establish whether a large scale randomized controlled trial could be feasible, in terms of both trial methods and intervention delivery. Secondary aims were to give an indication of the potential effectiveness of the PRotect intervention in maintaining wellness and reducing the risk of relapse to depression, and to explore staff and participant experience of the trial.

Our hypotheses were as follows: (a) that the methods of recruitment and intervention delivery will be feasible, (b) that the study could be used to estimate of effect-size that could be used in a sample size calculation for a definitive trial of the PRotect intervention, (c) that the experiences of trial clinicians and participants could be used to inform a future trial of this intervention.

Results

Changes to protocol

A study protocol was prospectively registered on the ISRCTN registry on the 2nd August 2016 (https://doi.org/10.1186/ISRCTN17371456). The only significant change from protocol was an extension to the recruitment period in order to recruit to sufficient workshops to meet the feasibility aims. The predicted referral rate was based on service-use data from earlier that year and seasonal variation, as well as the trial recruitment spanning the Christmas break, may have contributed to these longer timelines.

Participant flow

There were 115 referrals to the study during the 6.5-month recruitment period. 13 of those either did not respond to any contact (n=8), or made some contact but were unable to arrange the screening call (n=5) and so were excluded, and the remaining 102 people spoke with the researcher. Seven of these were not eligible according to the brief pre-

consent checks, one was not a recent client of IAPT (their care had finished several months earlier), four did not have prior depression or low mood as their primary problem (1 had anxiety, 1 stress, 1 panic attacks, and 1 person had current low mood), and 1 person did not have sufficient levels of spoken English to complete the call. Further to this, seven people declined to participate: 1 was busy with exams, 1 didn't want to be randomised if might be a group intervention (didn't like groups), 2 didn't want to do this trial but wanted to be asked of others, 2 did not provide a reason.

Following this, the remaining 88 people provided informed consent to participate prior to formal eligibility assessment and baseline data collection. Of these, 5 were subsequently excluded on formal eligibility assessment: four because their PHQ-9 scores were above threshold, and one because they had not recovered from an episode of depression according to the LIFE. The remaining 83 people were allocated a participant ID and those were sent for random allocation. Full details of participant flow are displayed in Figure 14.

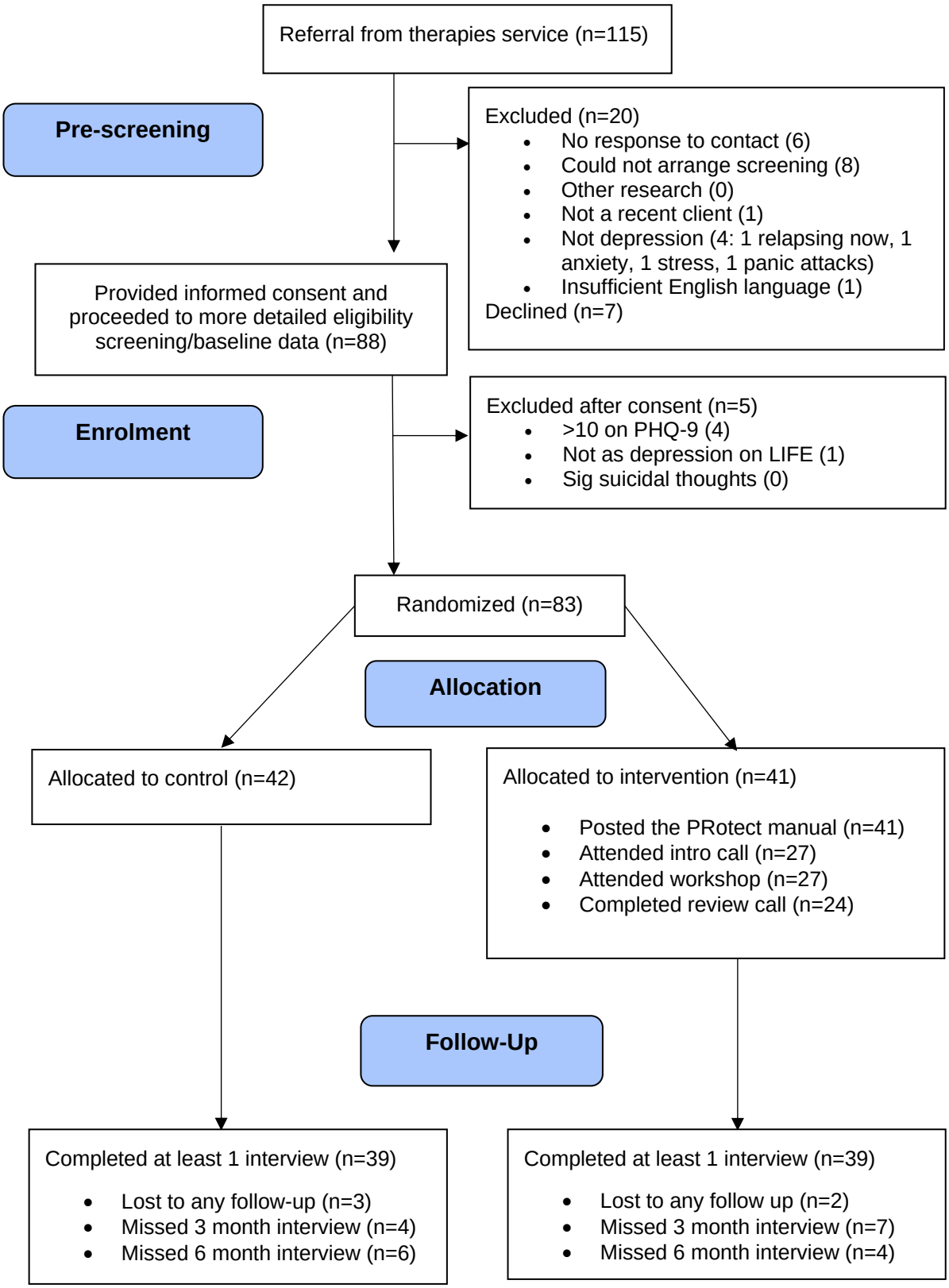


Figure 14: CONSORT 2010 Participant Flow Diagram completed for PRotect pilot trial

At baseline the 83 trial participants were aged 18 to 86 (Mean=37.15, SD= 14.36), they were more often female (n= 55, 66%), British (n=52, 63%), white (n=57, 68%), heterosexual (n=69, 83%), and not religious (n=45, 54%). Less than half of participants

reported having a long-term health condition (n=33, 40%), and few reported having a disability (n=4, 5%). At the time of entry to the trial 43 participants were single/separated/widowed (52%) and 34 were in a relationship/married (41%). Most were employed full-time (n=42, 51%) or part-time (n=14, 17%). Baseline demographic and clinical characteristics split by trial arm are presented in Table 9 (below).

Table 9: Baseline demographic and clinical characteristics for 83 pilot trial participants

Baseline characteristics	Intervention arm (n=41)		Control arm (n=42)	
	participants	%	participants	%
Demographics				
Age in years, Range	18-72		23-86	
Age in years, *M* ±*SD*	37.0 ±13.2		37.3 ±15.4	
Sex, female	26	63	28	67
Nationality, British (including dual)	24	67	28	78
Ethnic group, White British	13	32	23	55
Religion, not religious	23	68	23	64
Sexuality, heterosexual	32	78	37	88
Relationship status, single	21	57	22	55
Employment status, full-time employed	25	61	17	40
Clinical characteristics				
PSR, *M* ±*SD*	1.65 ±0.75		2.08 ±0.81	
PHQ-9 *M* ±*SD*	4.1 ±2.4		4.8 ±2.3	
GAD-7 *M* ±*SD*	3.9 ±2.7		4.4 ±2.7	
WSAS *M* ±*SD*	6.8 ±6.2		9.0 ±6.9	
ADM use	18	44	12	29
Lifetime ADM use	25	61	26	62

Note: PSR= Psychiatric Status Rating (0-6), PHQ-9 = depression symptoms (0-27), GAD-7= anxiety symptoms (0-21), WSAS= work and social functioning (0-40), (for all 0 is fewer symptoms/better functioning), ADM= antidepressant medication, Lifetime= self-reported (ADM use) ever

It appears that people in the control arm were more likely to be White British and to have higher Psychiatric Status Ratings, to be full-time employed. Intervention arm participants had slightly lower levels of symptomatology on most measures. These differences may not be clinically significant (Button et al., 2015): symptoms of depression where present, were below threshold in all participants, and anxiety symptoms below threshold for 38/41 intervention arm and 27/42 control arm participants.

Feasibility outcomes

The majority of feasibility criteria were met: five were rated as green, two as amber, and two as red. Assessment of the nine criteria is in the Table below and then described in more detail, drawing on trial monitoring data including the trial management log, clinician reports, and audio-recordings and fidelity forms completed during intervention delivery.

Table 10: Nine a priori feasibility criteria with outcomes and red/amber/green rating

	Feasibility progression criteria	Target	Actual	Rating
Recruitment and retention	The rate of referrals (number/month)	49	15	Red
	Consent rate (consented/eligible)	66%	93% (88/95)	Green
	3-month interviews	80%	87% (72/83)	Green
	6-month interviews	80%	88% (73/83)	Green
Intervention delivery and receipt	Introductory calls[a]	80%	66% (27/41)	Amber
	Workshop attendance	80%	66% (27/41)	Amber
	Review call	80%	86% (24/28)	Green
	Length of intro calls[a]	8-12 min	*M*= 5min 49s, *SD*= 1min 41s	Red
	Length of review calls	16-24 min	*M*= 17min 22s, *SD*=4m, 37s	Green

[a]*These calls were modified after one month, and so 16/27 calls reported in this table were delivered by an Assistant Psychologist*

Recruitment and retention

The referrals to the trial were slower (15 rather than the 24.5 needed per month) than needed to recruit within the proposed recruitment period (4 months), so this was extended to 6.5 months. The trial was stopped as we had achieved our lower target in terms of participant recruitment and had sufficiently tested workshop delivery to meet feasibility objectives. Referral rates ranged from 2 to 11 per fortnight (mean= 7.2), with no obvious pattern to referral rates through the trial period.

Of the 115 referrals to the trial, 69 of these (60%) were from Camden, and 46 (40%) from Islington. The two planned sources of referrals were: clinicians who were finishing treatment with a potential participant, and directly from Assistant Psychologists if they had contacted someone who had been missed by their clinician (and had consented to be contacted about research).

Table 11: Source of participant referrals to the trial: staff group, number and percentage

Source of referral	**Number**	**Percentage**
Clinician	25	21.7
Trial Clinician	20	17.4
Clinician via the AP	11	9.6
Assistant Psychologists	57	49.6
Not recorded	2	1.7
Total	115	100

As Table 11 (above) shows, the Assistant Psychologists searching of the clinical records system (IAPTUS) were an important supplement to the direct referral route, providing 57

referrals. 56 referrals came from clinicians, either directly or passed on via the AP. Interestingly clinicians also used the AP to pass on referrals to me, perhaps due to the availability of the Assistant Psychologist in the offices rather than seeing clients, and also the fact they flagged potential participants to clinicians made them also ambassadors for the trial. There was no difference in the suitability of referrals from any of these staff sources.

A two-stage referral process was conducted, where clinicians gave clients information sheets and asked if they would like to be contacted by a researcher (rather than providing any detailed information themselves, answering questions, or being responsible for assessing eligibility). This process was used without issue during the pilot, and as such seemed to be well understood and minimised responsibility and time for clinicians.

Paper referral forms were provided to clinicians to complete in a final session with a client (Appendix L) but the form itself was not a requirement: the fundamental principle was to have permission to pass someone's details on to me. The paper referral forms were not well used: around five referrals came to me directly through the paper referral form. Some clinicians emailed me an electronic version of the form or simply wrote the referral in the body of an email to me. Most referrals were emailed via a spreadsheet managed by APs.

Of the referrals received, we had a high consent rate: 93% of those who were eligible consented to participate in the study. Even taking a broader feasibility measure such as percentage of total people referred who then enrolled would exceed the consent rate target of 66% at 72% (83 of a possible 115).

Outcome assessments were attempted with all participants at three and six months (+/- 1 month) after their baseline assessment. For three- and six- month time points 72 and 73 out of 83 participants completed the outcome assessments. 67 participants completed both assessments, and 16 participants missed either one or both follow-ups. Overall, 145 of the possible 166 outcome assessments were completed (87%). 94 of these

(66.20%) were within a week of the target date and 58 (40.85%) were conducted outside of office hours.

Intervention delivery and receipt

There were 41 people allocated to the intervention arm and with whom intervention delivery was attempted. 22 people completed the introductory call and then attended the workshop, 5 people completed just the introductory call and another 5 just the workshop, and 9 people completed neither. 23 of the 27 workshop attenders completed the review call, plus one additional person who didn't attend workshop but reviewed materials alone.

Attendance at the intervention introductory call and workshop were lower than target, with 65% of people in the intervention arm actually attending at each point. I was aware that attendance at group interventions can be difficult due to the fact they must run on a fixed date and not everyone will be available then. Two additional factors contributed to this difficulty with attendance: the slower rate of referrals to the trial then expected meaning workshop dates were more spread-out, and also the introductory calls not being as successful at encouraging attendance as hoped due to difficulty getting hold of people for these calls. However, most who attended the workshop then completed their review call (85%) suggesting those who attended were engaged and found the workshop acceptable. In order to examine the feasibility of intervention delivery further, I considered clinician report, audio-recordings and fidelity forms. These findings are summarised in Table 12 below.

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Table 12: Summary of feasibility of intervention delivery from clinician report, audio-recordings, and fidelity forms

	Reports from staff	Audio-recordings	Fidelity forms	Details
Introductory calls	Significant difficulties	Mixed adherence	Mixed adherence	• Having a combination of a longer call but with no appointment time was difficult to arrange and for participants to understand the point of • Administrative components more often completed than the motivational interviewing components • Calls were often shorter than the target 10 minutes (mean= 5 minutes 49 seconds, SD= 1 minute 41 seconds)
Workshops	No difficulties	Good adherence	N/A	• Participants appeared to be engaged and workshops were highly interactive • Main intervention components covered in all cases • The workshop facilitators personalised the wellbeing routes with their own examples
Review calls	Minor difficulties	N/A	Good adherence	• Participants were engaged in the calls and actively reflected on their wellbeing • Call components completed and call length around the target 20 minutes (mean= 17 minutes 22 seconds, SD= 4 minutes 37 seconds) • Some calls had to be rescheduled and four were not completed

All intervention arm participants were posted the PRotect self-help workbook, and some were emailed an e-version (this was offered during introductory calls). Use of these materials was not monitored.

PWPs reported significant challenges in delivering introductory calls due to scheduling issues: to successfully complete a call sometimes took several attempts and this was difficult to fit around their full schedules of appointments for treatment delivery. In the first month of the trial completion rates were minimal (three calls in total) so after another month some calls were re-allocated to an Assistant Psychologist working within the therapies service, who, under the supervision of the lead PWP and alongside the trial clinicians, was then able to complete more calls. They were able to set-aside a whole morning to complete calls alongside other tasks such as manning reception. In total 16 calls were completed by Assistant Psychologists and 11 by trial clinicians. The calls were on average shorter than the target 10 minutes (mean= 5 minutes 49 seconds, SD= 1 minute 41 seconds). Fidelity forms and audio-recordings show continued lack of engagement in these calls from participants: it did not seem clear to participants what the 'point' of the call was, and administrative components of the call were more often completed than the motivational interviewing components. It is not clear what impact this had on recruitment (if any).

A total of 27 participants attended one of 9 PRotect workshops. If a person could not attend the first available workshop, there were offered further dates. Those who entered the trial later where there were three (or fewer) workshop dates remaining were much less likely to attend (45% attendance compared to 73% for the first phases), and self-reported reasons for non-attendance for most were being busy or unavailable on workshop dates. Two people reported not wanting to attend a group. Audio-recordings of workshops showed all intervention components were covered, delivery style was per protocol, and participants showed high levels of engagement and interaction. Most participants that attended a workshop found it helpful (19 of the 24 people who attended and completed their 6- month interview) and gave examples of how the workshop had impacted their everyday lives. For further details about the self-reported experience of participants, see the Participant Experience section later in this chapter.

Most workshop attendees completed their review calls (23 of 27), and one person completed a review call after reviewing the PRotect manual at home. These calls were around the intended 20-minute length (mean=17 min 22s, SD= 4m 37s), although there was variance in call duration due to two calls being short (1 minute 0 seconds and 8 minutes 20 seconds). Fidelity forms indicate all protocol elements were completed and participants were engaged in the calls, and actively reflected on their wellbeing. These calls were scheduled with the PWPs at the end of the workshop, and this seems to have worked well.

Feasibility summary: trial methods appeared acceptable, with high consent and retention rates. However, recruiting from a larger participant pool would be recommended for a future study, in particular so that there would be sufficient numbers of people allocated to the intervention arm to allow for good attendance at workshops and flexibility in workshop dates. The plans for introductory calls require modification.

Pilot analyses of clinical outcomes

There were three episodes of depression meeting DSM-IV criteria in the intervention arm and six in the control arm (RR 0.52, 95% CI 0.12 to 1.89, NNT=14). The episodes started in weeks 8, 10 and 10 in the intervention group, and weeks 8, 9, 10, 18, 19, 21 in the control group. Figure 15: Survival curve of percentage of participants remaining out of a depressive episode shows the Kaplan-Meier Curves for relapse of depression according to DSM-IV criteria in intervention and control arms.

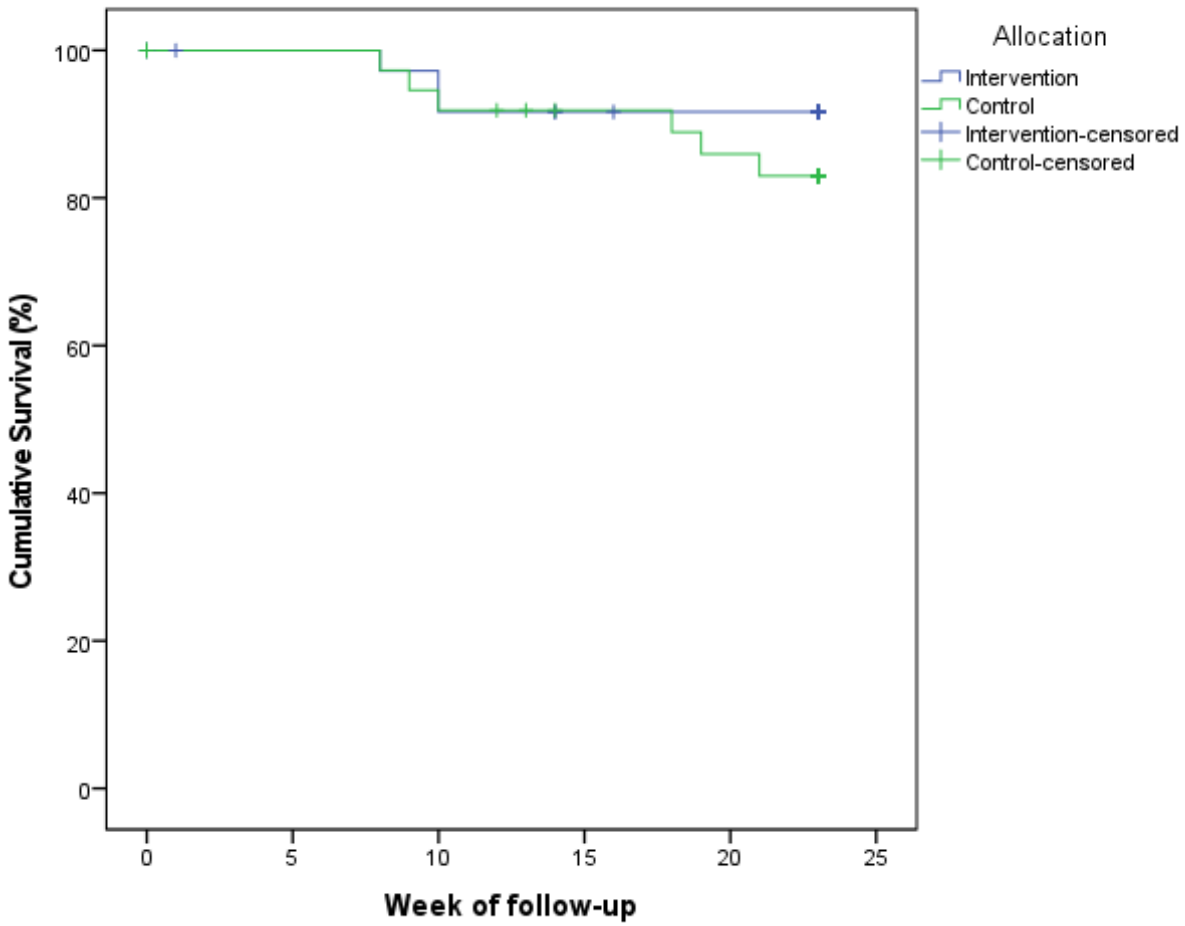

Figure 15: Survival curve of percentage of participants remaining out of a depressive episode during PRotect pilot trial 24-weeks of follow-up

The log-rank test found no significant differences between the two curves. Censoring occurred when a participant was lost to follow-up, and censoring appeared to be balanced between the two groups, with 8 in the intervention (5 in week 0, 2 in week 14, 1 in week 16), and 8 in the control arm (5 in week 0 and 1 each in weeks 12, 13 and 14). There were four clinically significant deteriorations (PHQ9 score which rose to 10+ and changed by 5+ points) in the intervention arm, and seven in the control arm, which is a relative risk of 0.59 (95% CI 0.19 to 1.85) or NNT of 15.

The clinical symptom scores for baseline, 3- and 6-month follow-up are reported below in Table 13. The difference in score between baseline and endpoint (6 month) are also provided, and compared statistically between groups. For these, 0 indicates no change, and a positive value indicates that symptoms increased (i.e. there was a deterioration).

Table 13: Clinical scores for pilot trial participants at baseline, 3 and 6 months, and change in clinical scores

Study arm	Measure	Baseline n=83 (41 and 42)	3 months n=71 (33* and 38)	6 months n=66 (34* and 36)	Change from baseline to 6 months	Hedge's g
		M (SD)	*M (SD)*	*M (SD)*	*M (SD)*	g (95% CI)
PRotect	PHQ9	4.17 (2.45)	4.91 (2.99)	4.59 (3.31)	0.24 (3.46)	---
	GAD7	3.93 (2.67)	3.76 (3.56)	4.41 (3.36)	0.29 (4.02)	---
	WSAS	6.80 (6.16)	7.79 (6.91)	7.93 (6.10)	0.51 (8.32)	---
Monitoring arm	PHQ9	4.76 (2.28)	5.16 (5.33)	5.81 (4.94)	1.03 (5.42)	-0.17 (-0.64 to 0.29)
	GAD7	4.38 (2.75)	4.87 (4.23)	5.03 (4.04)	0.64 (4.92)	-0.08 (-0.54 to 0.39)
	WSAS	9.00 (6.93)	9.24 (9.74)	10.50 (9.35)	0.94 (9.27)	-0.05 (-0.52 to 0.42)

**participant scheduled follow-up but chose not to answer questionnaires so this number is lower than participant flow diagram*

In both arms mental health was largely maintained with limited change in measures noted, however the direction was for there to be a larger deterioration in all measures in the control arm).

Clinical outcomes summary: Each participants' depression symptoms were tracked through follow-up using the LIFE measure, and depression, anxiety and functioning at follow-up time points using the measures that are routinely used by IAPT services. There were double the number of relapses in the intervention arm participants, although overall most participants seemed to maintain their recovery. The data presented here could be used in a sample size calculation for a full randomised controlled trial.

Participant and staff experience

Participant and clinician experience were explored in brief semi-structured interviews with all trial participants at the end of their final follow-up phone call after their final outcome measures were

collected, and in one 2.5-hour focus group with the trial clinicians after completion of their involvement in the study. I analysed the verbatim notes from participant interviews and the focus group transcripts qualitatively as described in the analysis plan in Chapter 5, and report the themes and summaries below.

Participant experience

Overall 73 of 83 participants completed their 6-month follow-up call and 72 answered at least some of the questions on participant experience. Participants were asked initially a bracketed open question asking about their experience of participating in this trial. Almost all indicated having a positive experience, using phrases like '*100% happy', 'good'* or '*Oh, in terms of the experience it's been really good, can't think of anything bad at all*'. A few people (4) didn't want to comment on their experience: *"No, it's been alright. I mean, nothing...I don't know what to say to be honest"*, and *"Not to be unhelpful at all, but no, not really. I don't have anything to say",* and for the remainder of this section I focus more on the comments of the 68 people who wished to provide more detailed responses to the qualitative questions.

The most common experience brought up initially was the research interview phone calls being somehow beneficial to their own mental health, which 36 people brought up straight away and a further 8 brought up prior to any prompts. In addition, 10 people immediately commented on the flexibility and ease of organising the research phone calls. As such, two of the overarching themes which emerged and are reported below are about these research calls. Another theme that emerged in terms of overall experience was that participants tended to speak about their motivation to participate in the study originally, and the importance of mental health as a topic. The experience of the intervention was what came to mind first for a large group of those in the intervention arm, but less often the experience of being allocated to the control arm, which often required prompts to elicit comments. For those who experienced the intervention I provided prompts to elicit responses/data on all aspects of the intervention and its impact, which are reported below. I noted that some other aspects of the experience of the trial such as receiving vouchers was only mentioned twice at all: both times as 'nice' but with one person noting "I would have done it anyway", and as such do not form part of the themes identified.

The four major themes are described here narratively and supported by illustrative quotes, with further detail provided about the experience of and impact of the intervention for that sub-group of participants.

Theme 1: Expecting a call from someone, and reflecting, was beneficial

The overwhelmingly clear theme within the mentions of research calls, endorsed by 44 people, was that they in some way experienced a benefit from the research interview phone calls. This was often described as being due to the impact of thinking through their progress when expecting someone will be *'checking in'* with them, for example: "*I think just having someone else you can run it through and hear yourself saying it has been helpful. The questionnaires and the interview. Knowing there's someone checking in once in a while."* Both the expectation, and the calls themselves seemed to encourage self-evaluation and reflection: "*It's been interesting to have these moments of self-reflection and weighing things up, as it's not something I tend to do very often"*, and "*I like this format where you think about 'what have these last 3 months been like?'".* One participant commented: "*I think having, remembering you would be contacting me has been a helpful sort of goal. Like a target in the future. I'll be talking in 3 months make sure you're looking after yourself."*

The participants seemed aware that the purpose of the interviews was for research rather than to be therapeutic but nevertheless found them helpful: "*It feels a bit like follow-up care even though I know it's just a trial".* Another describes this dual function/benefit:

> *I think it's excellent to have the follow-ups. Obviously it helps **you** to evaluate whether it's been a success, and it's good for **me** to take stock. And I can plot how far I've come because I imagine my scores on (the questionnaires) will be better than they were.*

Theme 2: Ease of organising calls and flexible timings is important

For 10 people their immediate thought when asked about their experience of the trial was that the research calls felt easy to organise, with flexible timings and persistence from the researcher being needed or appreciated. One commented that the experience has) *"been completely positive from my perspective, it's been… a couple of phone calls. And you were really amenable in terms*

of times, that's appreciated as well". Another said: "*You're very good at following people up when they don't reply, which is good because that's necessary"* and another: "*You've been good at making the effort to find a time that's suitable. I think it's been great, not taken too much time out of my day."*

Two people felt that face-to-face would be better and should be offered, and three people felt further flexibility could have been helpful in terms of booking the calls, for example:.

> *I think it's been a really good trial and I hope you get some good feedback. I have felt bad as I haven't been very available to me when you've tried to call me. Would you consider emailing out the questions? Would there be flexibility in the approach?*

Theme 3: Hoping to help, and importance of mental health

For several people their motivation to participate and to 'help' was the most salient experience of being part of the trial, and their comments were around the importance of mental health: "*my only thought towards this was I wanted to partake to, for my own benefit and to contribute to better understanding of mental health generally", "I've been very pleased and grateful that I was able to contribute.",* and *"Generally it's been a good experience. I'm happy to help…If it can help in a positive way to give people a broader spectrum of support…I hope that it's going to be used for health".* One participant commented on the importance mental health support and inclusion of older adults:

> *It's good that they are taking old people seriously, because I can remember my mother being given no help at all, mentally or physically. It's a big improvement now but, a big problem is not including people over 70 in trials. It's great to feel that I'm old but still part of the human race.*

Theme 4: Aspects of the intervention or lack of intervention

Aspects of the intervention were what came to mind first for 10 people when asked about their experience of participating in the trial. It should be noted that this could only have been mentioned by the intervention arm participants who experienced the intervention, and two people described

their experience of being in the control arm without prompting, suggesting for most people being in the control groups did not feature as prominently in their experience.

I explore the experience of the intervention and its impact in more detail below as prompts were provided to ensure I collected responses to inform feasibility assessment and any changes needed, but some initial unprompted thoughts participants expressed were around the workshop itself, "*I found it very helpful to sit in a room and talk to people who had experienced the same thing, and be able to sit and quite openly talk about things",* and on the ideas in the intervention being interesting and adding to what was already felt to be progress. For example:

> *I haven't consulted my notes that much, but just going to the session and looking at different areas where you can have options to kick start your mental health again made me realise I was quite well on track, especially with mindfulness and trying different things*

One person mentioned being in the control arm:

> *I have to say that when I signed up for the trial, if I remember rightly you were trialling a course. I am in the control group. Inevitably I felt a bit disappointed I drew the control arm. It didn't put me off…I wouldn't drop out for that because control arms necessary.*

Summaries of further data on experience of the intervention and impact, non-attendance, and control arm participation

Prompts were used to ensure fuller coverage of data for 3 key areas for feasibility:

- Experience of attending the intervention and any impact (self-reported use of intervention activities)
- Reasons for non-attendance
- Experience of being a control arm participant

For those who were allocated to the intervention (41), prompts were provided asking for their experiences of the intervention for those who attended (27), including how the intro call, workshop, booklet, and review call were experienced, or for those who didn't attend (14), their reasons for non-attendance.

Experience of attending the intervention and any self-reported impact

27 of the 41 offered the intervention did attend the workshop, of which 25 completed their participant experience interview (2 attenders didn't complete their interview). Of the 25 people who attended and also completed their 6-month interview, 19 found it useful, 4 did not, and 2 were unsure or undecided. Of the initial 19, most (16) gave examples of specific behaviour changes following the workshop, some of which were ongoing at 6-month follow-up. The 6 people who did not like the workshop or were undecided often did not report any significant impact on their everyday lives attributed to the intervention.

The majority of participants (19) reported finding the workshop useful. They talked about elements of the intervention and impact, for example "*I've found it really helpful.", "I thought it was fundamental for me to be able to at least maintain or improve my mental health", and "I thought it was fantastic definitely. Especially the workshop: giving us leaflets, ideas that I probably never would have had".* Some people commented on specific elements such as the four routes to wellbeing "*I quite enjoyed the kind of training thing and describing different strategies. I think it's good to see the different options that are available".* Several people mentioned sharing with and interacting with the group, and facilitators sharing their own experience: "*It was nice to meet other people having the same problem*", and *"the workshops was really useful as it was much more interactive…the pitch that they gave us, showing [their own] experience. It was very good, it helps*".

Of those participants, 16 gave specific examples of well-being activities they started because of the workshop. Some were repeated and habitual behaviours, for example *"Actually yes I put the Wi-Fi off before going to bed",* and *"I've added the affirmations, doing daily affirmations".* In some cases, the workshop was a catalyst for participants to start activities that they had previously found useful. One person reported: *"After the workshop I joined the gym 1 or 2 days later…That was a surprise to me as I've always lied to myself saying I'll start going next week or next month".* Another participant explained they had been able *"to get back into listening to music again. I had stopped before the trial"*. For some, impact seemed to be wide-ranging, e.g. *"yes so I did lots of (the activities) in the pamphlet. I put plans in place, some of which I did straight away, some I put*

off for a month or two and came back to it.", or "In many situations during my day…I would either take an action or decide something based on something that was talked about in the workshop. Wasn't just one thing". One participant described passing tips on to colleagues and that he felt impact had gone beyond people that attended the workshop. For others the impact was more limited, for example *"That's it- just cooking and going to the gym".*

Participants often reported continuing activities at the 6- month time point. Examples of this, *"I still do that now", "It's because of the trial I ended up going to yoga, I go every week.", and "I reflect on (the intervention) periodically. I had implemented some actions straight away. There are still some things I want to do…It's alive in my mind-set."*

However, the remaining 3 of the 19 participants who liked the workshop reported minimal impact on their everyday behaviour: it did not add anything to what they already knew, or perhaps that they made changes but did not continue or remember them: "*At that time I did take a couple of notes and goals that I did do, but I must say I haven't carried that on"*.

A minority did not like the workshop or didn't feel it added anything (4), or were unsure or undecided (2). These 6 people tended to report minimal or no changes to their behaviour following the workshop. Several reported that this was because the workshop didn't add anything to their existing routine, for example *"No I didn't actually. Felt like I was already doing those things already." Or "it does sometimes prompt me to think about how things are going in my mental health, but not a profound change in my behaviour".*

Reasons for non-attendance

14 of 41 people offered the workshop then did not attend, of which 12 reported the following experiences/reasons for non-attendance (2 non-attenders didn't complete interview). There were five response types: unsure whether offered/why they didn't attend (endorsed by 4 people), too busy, in particular with work commitments (endorsed by 6 people), not seeing the point or need to attend (endorsed by 4 people), that the group delivery was off-putting (3 people) and that flexibility in offering timing or location would have been helpful (3 people). In order to illustrate the overlap in reasons in this small sample I have provided the Table below.

Table 14: Matrix of 22 reasons for non-attendance at PRotect workshop provided by 12 participants

	1	2	3	4	5	6	7	8	9	10	11	12
Unsure	X	X	X	X								
Busy/work commitments					X	X		X	X	X	X	X
Didn't see the point/don't need it				X		X	X			X		
Group setting off-putting								X		X		X
Flexibility of time/location would have helped					X					X	X	X

Experience of being a control arm participant

When asked how people had felt about being in the control arm of the study, responses ranged from slight disappointment: "*I wasn't offered the workshop. I didn't know what to feel, there must be an element of disappointment."*, to indifference, to an understanding of the importance of control groups and feeling less time burden than if they were offered the intervention. (see also previous quote about the control arm in theme 4 above).

Participant experience summary: Participants tended to report that review calls were the most salient element of their experience, and this was mostly that they were beneficial to their mental health, and they were easy to organise. They also reported their motivations to participate being to help, and that mental health is an important topic. Overall most people who attended the workshop found it useful and impactful, sometimes with wide-ranging impacts over the 6-month follow-up. A few people reported that it didn't add much to what they were already doing. Those who did not attend generally described being busy or not available at the workshop date.

Clinician experience

All of the trial clinicians delivering the PRotect intervention attended a focus group where two researchers (KV and AW) asked about their experience of the trial following completion of their participation. The sense from this focus group was of enthusiasm for and engagement with the trial and the intervention. The overarching themes which emerged were: 'personal investment',

‘this different PRotect way of working’, and ‘prevention not treatment?’ Each theme has sub-themes which are illustrated by quotes.

Overarching Theme 1: Personal investment

This theme centred around the PWPs investment in their clients’ futures, and their own personal development, which motivated their participation. They spoke about the personal investment needed to participate in research within an already busy schedule of work, and specific aspects of this trial that reduced burden.

Sub-theme: What’s next for clients? “I just want to find out … how things are for people”

The PWPs were often driven by concern for clients, and curiosity as to what happens after they leave treatment and what the follow-up calls after the workshop would show. They were concerned about how it feels to complete therapy *“it can feel so scary and it can feel like you’re on your own”*, and also felt that the end of acute treatment could sometimes feel rushed, *“often the final session can feel a bit rushed because we’re trying to recap (everything)”* as well as create a prevention plan.

There was also a feeling of personal responsibility for their clients’ continued mental health. The PWPs generally enjoyed conducting the review phone calls with clients who were well but found them more difficult when they weren’t. One practitioner described how it was ‘*really nice to hear’* from a client that they had ‘*benefitted so much from the workshop’*. On the other hand, when during a review call, a client said that the workshop had not been helpful as ‘*it was all quite common sense or stuff I was doing already*’, one practitioner commented that *‘I wasn’t quite sure how to deal with that’*.

People felt that the intervention could reduce the need for people to return to the service. This was seen to be important, not only for the individual *“empowering them to continue the progress that they’ve made*” but also for *“the knock-on effect it has on costs as well”,* to *“prevent*

them from accessing the service again", specifically freeing up more time to see people who are having their first episode.

Sub-theme: Personal development was a motivator and reward: "it was really nice to learn a little bit more"

Professional development was a frequent focus of the conversation: both as a motivator for becoming involved in delivering the PRotect intervention, and an outcome of participating. One person noted that *'it made me think about some of the things that I do, or I don't do, or I could do, so that was really helpful.'* Another found that there were certain resources from the PRotect intervention that they wanted to incorporate into their wider work, saying that '*some of the material is stuff that I sometimes use with my one-to-one work, so bits about habit formation and neuroplasticity*'. They also reflected that they had learnt from client's describing what worked for them and the review calls had been a way to receive '*helpful tips or suggestions'* from the clients**,** *"they always had really amazing ideas and I think it would be really interesting for the service to use that a bit more".*

Sub-theme:The burden of this particular trial was low "it seemed there was a natural flow to it"

Research is a service priority but the group described clinicians often feeling a burden to remember trials; *"we have a lot of different research trials running and it can be quite hard to keep them all in mind".* There was good agreement that this intervention fit well into the existing systems and the level of investment needed to deliver this intervention was therefore easier: *"I felt like we were able to …pick up appropriate referrals into the trial quite easily and quite quickly, and for us, as practitioners, it was quite easy to remember",* and that *"it wasn't interrupting what we'd usually do".*

Reasons for this were often mentioned when not directly asked about by the focus group facilitator, and related to specific practicalities within this trial: *"it helps to have Assistant Psychologist searches on our case notes…picking out who might be suitable", "this was the only*

trial…for picking people up at the end of therapy", "there was just one focus" for therapists recruiting; "we didn't have to bear in mind numerous and multiple different criteria", "we were all quite invested in it and that encouraged our colleagues", and "people knew they were going to be followed up in some capacity".

Overarching Theme 2: This different 'PRotect' way of working

This theme centred around the experience of delivering an intervention after treatment discharge, and the differences people felt between this role and 'normal' practice. The intervention was felt to emphasize individual choice and be flexible, and the group setting seemed to support collaboration and a 'level playing field' between facilitators and attenders of the workshop.

Sub-theme: It was a new style of working: "it felt very different to … the work we usually do."

Delivering the PRotect intervention felt to the PWPs different to their usual work and role. This was often related by them to the workshop being more interactive and collaborative "a different format for the workshop where it is more interactive", and the PWPs role as an active participant and collaborator, rather than workshop lead: "*the facilitators getting involved is less 'us and them', and it's something that everyone can do"*. Another person explained that '*often we're asking people to go away and do something on their own, whereas in the [PRotect] workshop, you've got the chance to join in'*. Several PWPs commented that delivering the intervention '*involved a lot more personal disclosure but it felt comfortable*'. One person commented "the facilitator's getting involved is less 'us and them'" and another agreed "That's exactly the feedback I had (from a client), that it was really normalising". This different way of working could be challenging: one practitioner felt a tension between their two roles, saying '*you felt a pull to start being a PWP rather than a relapse prevention workshop facilitator'*. They reminded themselves within workshops *'we're here to talk about wellbeing rather than behavioural activation or things like that*'.

Sub-theme: It felt empowering: "a nice experience of actually really engaging people's strengths and resources"

PWPs described, in various ways, a feeling that within the intervention people made genuinely personal contributions and plans, and that the focus on individual difference and choice seemed to be enacted by the group, allowing the patients to be *"experts in their recovery".* One person mentioned how everyone in the group *"had their different opinions and we were standing by … what we felt was most helpful and what we were most interested in, so I think there was something about the choice and a discussion and the differences that came out".* There was a feeling that the intervention's emphasis on activities that might benefit everyone was somewhat normalising and may have been beneficial: *"we're saying … it can benefit everyone, and maybe that does help people to feel included and less isolated because they're thinking about things that everyone can do day-to-day".* Overall, upon conducting patient review calls afterwards, many had continued to benefit from the intervention. One PWP mentioned how a patient had *"benefitted so much from the workshop and he had put changes into place pretty much immediately and … was still enjoying the benefits".* Another PWP believed that everyone they had spoken to *"got some benefit out of it"*, concluding, *"I wouldn't say that it didn't work for anybody".*

Sub-theme: The group format enabled collaboration and sharing of ideas: "it was quite beneficial for people to be able to think and share ideas and bounce off each other"

There was a consensus amongst the PWPs that conducting the workshop as part of a group was beneficial and an "*effective way of delivering the information and engaging people*". The overall view was that the group setting provided an "external focus" where ideas could be explored*: "I think in terms of generating ideas, it was really good at doing that"*. The group setting also provided comfort for people to be around others similar to themselves, with a PWP recalling an instance with one patient where "*it made her feel more comfortable in a group setting, and so that was quite a good benefit to have somebody that … you can identify with or somebody who's in a similar situation to you".*

Despite the consensus that the group setting was ideal, there were some instances where this did not work so well. For example, another PWP described having to manage group dynamics differently to their normal ways of working to enable the group to be open, for example, "*if someone else starts giving ideas or advice to another participant, that's something that we counter-manage in our IAPT workshops and groups".* Smaller groups *"had its positives and negatives, we were able to do it a bit more like a discussion".* Concerns were raised over perhaps having a dominant character and the impact of small groups. However, the group strongly disagreed with the statement that the intervention would be better as an individual session, but that it could be delivered as an individual if needed, *"There are things you could pull out and do in one-to-one work".* Additionally, the group recognised that depending on the patient population, there might be some instances where a group dynamic might not work, such as when there are language barriers as *"it doesn't take into account those who might be speaking a different language".*

Overarching Theme 3: Prevention not treatment? The workshop in context

This theme was largely drawn from comments and questions the group raised about the intervention within the normal operation of the IAPT service. The focus was on the context for the intervention within IAPT service operations and particularly questions around a potential future for the intervention.

Sub-theme: Who should the intervention be for? *"Would they still benefit from the workshop?"*

The group questioned on several occasions who the intervention should be for. For example, one suggestion was *"I think it could be helpful for people who haven't engaged with CBT that well, because it's a slightly different approach",* and *"if working on anxiety can reduce depression, then maybe a wellbeing workshop can help depression and anxiety*". There was general agreement that the content of the intervention did not necessarily feel depression specific: *"it seems like the workshop was fairly universal in terms of the content and the choice and the*

information available". This raised questions like *"if people have got anxiety as their main problem, should we encourage them to attend this workshop?"*

Several times the question was raised as to whether people who had not yet recovered could be offered the workshop. One questioned: *"I wonder if it would be helpful if we did it, even if somebody hadn't come into recovery"; "It would be interesting to know from people who don't reach recovery in IAPT, would they still feel a benefit from the workshop?",* and also whether the workshop could be offered before any intervention. Furthermore, one of the PWPs found the cut-off point score based on recovery for patients to be able to take part in the intervention as almost futile, *"I don't know if there's still some idea there that they [those below the cut-off] could benefit from, but it's not necessarily targeted at them"*, commenting that the workshop was *"fairly universal".* Another PWP felt that *"there might have been someone who really benefited from the group and they might have just been one or two points out".*

However, there was a fairly strong and consistent disagreement to this by several group members who had facilitated workshops were people appeared to be currently not recovered: *"I think having a room of people where some people have really benefitted from treatment and are in a really good place, it almost made those differences a bit more obvious",* and, "*I think they were still maybe struggling at the time. And I'm not sure they engaged as well with the concept of the materials because actually they probably had a bit further to go before they were at that same stage of wellbeing… having a room of people who... are in a really good place, it almost made those differences a bit more obvious as well.*

Sub-theme: The role of IAPT services "it raises the question of when and how therapy end(s)"

There was uncertainty and discussion in the group around how delivering relapse prevention work fits in IAPT services following treatment completion. This was partly to do with confusion about caseloads: "people are discharged and then they're kind of re-opened". The question was raised as to whether therapy includes the workshop or "actually they've ended contact with the service

but there's something additional that's external to it". The implication of this for PWPs was on caseloads, "it will increase our caseload a little bit, whether it was an active case (or not)". Costs and cost savings were seen as a challenge for the future of the intervention in IAPT services.

Summary of clinician experience: It appeared from the clinician's discussion in the focus group that they were clear about the intervention and its difference to usual practice, and embodied this in their delivery and reflections. They raised important questions around the role of a relapse preventive intervention within a service focused around acute treatment, which may be worth exploring further.

Discussion

In this chapter I present the results of the feasibility randomised controlled trial of the novel 'PRotect' intervention which was delivered in an IAPT service to people who had received acute treatment from that service and been discharged. In total 83 participants were recruited and randomly allocated to the intervention or control arms of the study, and 87% of outcomes research calls were conducted. Those participants in the intervention arm were offered to attend one of the nine workshops which were delivered. Following participation nearly all the participants and all of the trial clinicians shared information about their experience during the research. The primary aim of this pilot trial was to establish whether a large scale randomized controlled trial would be feasible, in terms of both trial methods and intervention delivery, and the pilot trial results suggested that similar trial methods and adapted intervention delivery would be feasible in a larger study. I will now report the feasibility results, clinical outcomes and experience of those who were part of delivering this trial, the strengths and limitations, and future directions for this work.

Feasibility

The recruitment methods were largely feasible: 89% of referrals participated in the telephone screening, and 91% of those screened as eligible decided to participate. This consent rate is very high in comparison with targets in similar studies (Avery et al., 2017). Outcome assessments

were 87% completed which is within the range recommended to minimise bias (Page & Persch, 2013). Interviews outside of normal office hours were chosen for at least four of every ten assessments, which may have enabled me to minimise attrition. Indeed, several participants commented that researcher persistence in contacting and flexibility with dates was useful and/or needed for the follow-up research interviews. It also suggests that the outcome measures were acceptable to clients. The rate of referrals to the trial however, was lower than expected and so the recruitment period was extended. Expanding to further sources of referrals such as people discharged from another service could also have mitigated this issue.

The intervention delivery was also largely feasible with some potential modifications. The workshops that were delivered went well and were delivered according to the model. Participants who did not attend reported they were not available on the workshop date, and the fact that people who enrolled towards the end of the trial were much less likely to attend than those who had a greater choice of workshop dates provides support for this. Group interventions must have fixed and limited dates and therefore may result in higher rates of non-attendance when compared with individually delivered interventions. Review calls were very well attended, of the planned length and meeting key intervention components. An Assistant Psychologist stepped in to conduct the majority of the introductory calls which tended to be shorter than planned: it might be that unscheduled calls are expected to be brief and administrative.

Clinical outcomes

The clinical outcomes collected could give an indication of the potential effectiveness of the PRotect intervention that could be used to estimate of effect-size that could be used in a sample size calculation for a definitive trial of the PRotect intervention. Sample size estimates from small pilot studies are limited and can be misleading (Thabane et al., 2010). For example, it is possible that at baseline the intervention arm participants had a lower risk of relapse than the control arm participants. I therefore suggest considering the range of possible effect sizes along with a consideration of what effect would be clinically important going forward.

Three people in the intervention and six people in the control arm had a relapse of depression during the study which, if replicated in a larger sample would translate as a 'number needed to treat' of 15. It was broadly comparable to the risk reduction reported in more intensive relapse prevention interventions. This was a relatively severe clinical event: an episode of depression meeting full diagnostic criteria, and most people did not experience this. In the intervention arm, symptoms scores remained consistently low. In the control arm there was a deterioration in depression symptoms (with a medium effect size), and anxiety symptoms, and work and social functioning (with a small to medium effect size). Taken together these results suggest that the PRotect intervention merits further investigation.

I assessed relapse using episodes of depression that met full diagnostic criteria, which reflects a distressing, relatively severe, and costly clinical event. Even small reductions in the risk of this outcome, particularly from a brief intervention, could be of clinical and practical importance. The LIFE evaluation (Keller et al., 1987) used to assess this is a method with established reliability and validity (Warshaw et al., 2001, 1994). However, only 11% of our sample met this strict criteria, and further participants had significant issues with depression during the follow-up but did not meet full diagnostic criteria. For example 17% of the sample had a change of 5 or more points on the PHQ9, ending above threshold, which is sometimes used as an indicator of relapse (Ali et al., 2017). Preventing a full episode of depression, a relatively severe clinical event is highly valuable to individuals and could reduce long-term mental and physical healthcare costs.

Scores on our secondary continuous outcomes also favoured the intervention arm for all measures, but importantly people in the control arm were more likely to *deteriorate* in terms of their depression and anxiety symptoms as well as their personal functioning when comparing their 6-month scores with their own baseline scores. The effect sizes for these measures are not dissimilar to those reported in trials of intensive and lengthy depression acute treatment (e.g. 0.3; Coventry et al., 2015).

Participant and staff experience

Participants reported that the trial had been a positive experience, and in particular that having research phone calls at pre-specified time-points enabled them to reflect on their mental health and on their progress over time. There was convincing and rich qualitative data supporting this link from several participants prior to any prompts: the research calls appeared to be helpful because of the expectation of them, knowing that someone would be checking on your mental health at certain time points, reviewing time periods over the phone enabled people to maintain a long-term focus on their mental health. Participants in both arms of the trial reported the research interviews had been mutative and beneficial, which is perhaps reflected in the maintained wellness that the majority of our participants experienced. There is some weak evidence that participating in trials may improve outcomes in general (Braunholtz et al., 2001), although this may be particularly strong in this trial where people were expecting the calls, and where the calls involved a detailed reflection on their life, life events, mental health, and actions they were taking to protect their mental health.

The experience of the intervention was also important for several people: the workshop being experienced as a space to share ideas with people who have had similar experiences. The clinician echoed this, with a consensus that the group setting was beneficial and allowed interaction and for the normalising aim of the workshop to be enacted by the participants. The group setting itself was reported to be a barrier by two participants which is important when considering the accessibility of interventions, however most of the people who did attend the workshop reported that they found it useful, and that they changed behaviour following attendance and even at six-month follow-up.

Where there were criticisms or people did not feel benefit from the intervention it was usually because it didn't add to what they were already doing, or it felt too simple or obvious. The reading age was kept low and text to a minimum in order to ensure the workbook was accessible, on the basis of surveys of the adult population indicating an average reading age of perhaps 11 (Great Britain. Department for Business & Skills (BIS), 2013), and given guidance from several authorities on improving the accessibility of health information. However this simplicity was perhaps in conflict with 'education' as one of the key behaviour change functions of the

intervention (Michie et al., 2011). Perhaps the simpler intervention messages could be supplemented with optional in-depth content with more research evidence for those who would benefit from it in order to meet this aim of the intervention which some participants seem to report was not met for them.

The PWPs were highly motivated to undertake additional relapse prevention work with clients, and felt there was a need for it. Having trial processes that were centred on IAPT clinical time points improved the clinicians experience and the flow of research within their practice, compared to other trials which do not do this. There were questions raised around the role of IAPT and whether continuing to provide intervention after 'recovery' fit within an IAPT service or would be better placed in a non-clinical setting.

Strengths and limitations

This pilot trial had several methodological strengths, the first being its pragmatic design. The setting was naturalistic: an existing psychological therapies service that would be well placed to provide this intervention to the large numbers of people who complete treatment for depression within their service. Using an ecologically valid setting increases the chances the intervention effects would hold in normal practice. I sought to recruit a participant group that was representative of people that could be offered the intervention in future, as recommended in Medical Research Council Guidance (Craig et al., 2008) through using a routine clinical time-point (discharge) and routinely collected measures to identify potential participants, and by keeping exclusion criteria to a minimum. I used consecutive recruitment and had a high consent rate which minimises selection bias. Our participant group included adults over 65 (n=4), and people with anxiety, who are often excluded from studies and therefore the evidence base for interventions. In fact, most of our participants (86%) had a score above threshold on the GAD-7 during the treatment episode prior to participating in this study. However, the pragmatic design also means less control over elements including monitoring of intervention receipt and uptake. For example, I posted the PRotect booklet to all intervention arm participants but it is not known how or whether they used the material unsupported.

A limitation inherent in any pilot is that it cannot show clinical effectiveness, however there was a trend towards a positive effect. Within the healthcare domain, relapse prevention interventions are generally considered effective if they help people to avoid any significant deterioration or relapse, or to maintain their post-treatment level of depressive symptoms (low to none) rather than the extent to which they 'build' recovery (Leamy, Bird, Boutillier, Williams, & Slade, 2011). We used clinical trials methodology, selecting our participants based on a history of mental ill-health, and assessing effectiveness based on avoidance of mental ill health. This may be a necessary step when testing whether acute treatment should be augmented within mental health services, which are structured around responding to distress, disorder or illness, however it is not as positively focused as it could have been. Expanding the analysis away from looking at the binary outcome of 'relapse' and looking at the whole trajectory of wellbeing could be worthwhile and more in line with the complex systems theoretical framework which is the basis of this intervention.

The LIFE measure gives a 'Psychiatric Status Rating' for each participant for each week of follow-up, so could be used to look at the shape of individual participants' trajectory during the follow-up period. This kind of representation could be used to identify further important outcomes for people, such as weeks well (PSR 1) or weeks with significant symptoms (PSRs 4 or 5), which simply looking at relapses (scores of 5 for 4 weeks in a row) does not incorporate. However perhaps more interesting in relation to complex systems theory would be to use the weekly Psychiatric Status Rating scores for participants throughout follow-up, so for example more differences in trajectory could be explored. As explained in Chapter 3, the whole trajectory of the emergent phenomenon of depression could be worth looking at and there could be multiple different aims of an intervention in relation to trajectory. It might be most important to increase the level of recovery (so for example seeking a PSR score of 1 rather than 2, or reducing 'residual symptoms), if there are depressive episodes for them to be less severe (PSR of 5 rather than 6), of shorter duration (fewer weeks), or even to prevent increases in symptoms that would not constitute a full depressive episode (for example if the PSR was 4). This opens up further avenues of analysis looking at whole trajectories of biopsychosocial resilience (Pincus & Metten, 2010)

This pilot was limited to one geographical location, and selected therapists and clients in only two areas in central London. It is likely that there were aspects of the specific area that influenced feasibility. For example the clinics were close to the University, and this enabled the researcher to be physically present in the offices, identified as important in the recruitment strategy but would be more difficult if the site were a long distance away. There is an existing relationship between the research group at UCL and those services. The implication is that we can conclude feasibility here but not everywhere. In a way this is inherent in all pilots, and here I have tried to properly note characteristics of the sites in study setting (chapter 5) and describe the recruitment strategies in detail so that this can contextualise future work. Indeed even within this small area, participants who had insufficient English language ability to participate in the intervention were excluded. Additional work would have to be conducted with other IAPT services within England if planning a larger multi-site trial Future pilots could consider randomly selecting a service in which to test feasibility.

Clinical and Research Implications

The brevity of the intervention, and the fact that it is facilitated by psychological wellbeing practitioners, means it has the potential to be widely available to the large numbers of people who experience and recover from an episode of depression in IAPT. Workshop sizes in this trial were smaller than they are likely to be in routine practice, yet contact time did not exceed 70 minutes per participant. If there were a minimum of 6 people per workshop contact time would not exceed 30 minutes. Regardless, participants would participate in the intervention for 2 hours and 20 minutes. This is relatively high compared to other brief interventions, which may be important as having some contact time with a paraprofessional has been suggested as a key difference between effective and non-effective guided self-help (Holländare et al., 2011; Klein et al., 2018). However, the rate of referrals to the trial was lower than anticipated, and so any future trial would have to recruit from a larger participant pool, extend recruitment, or consider alternative methods of recruitment.

It could be argued that brief interventions are insufficient to deal with what is a complex mental health disorder, but it is worth noting that this intervention is designed to be offered after recovery

from depression, so the participants will not have a mental health disorder at the time of the intervention. Their episode of depression will have resolved and any remaining symptoms will be within the non-clinical range. As such, the intervention is non-prescriptive, and has the underlying assumption that the intervention participants are best placed to decide realistic long-term strategies for themselves. The level of choice within the intervention means we will not be able to explore which strategies were 'best', and there may be some strategies that are more suited to certain groups (for example there is a suggestion that positive psychology interventions work better for people who come from individualistic cultures, Lyubomirsky et al., 2011). I hypothesize that there are several different strategies that may be effective, perhaps differentially for certain individuals, and which interact over time.

The PRotect intervention as tested in this thesis was well suited to IAPT delivery. The feasibility of delivery within the pilot reported here of the PRotect intervention within IAPT, the largest psychological therapies provider in the world, does mean that *if effective* it has the potential to be accessible by a very large number of people who might be at risk of relapse. Considering some of the participant experience findings, for example the fact that almost all trial participants reported finding the follow-up research interviews as mutative, services may wish to explore this in a service evaluation. There were also several questions raised about who the PRotect intervention might be best suited for. I think it would be interesting in future to explore this further, perhaps using an individual patient analysis of effectiveness, or even expanding the inclusion criteria for future research to all those who self-identify as having recovered from depression whether using IAPT acute treatment, medication, or other routes to recovery. PWPs also raised the question of whether 'peer workers': IAPT staff who have expertise in mental health through their own experience of mental health problems which they bring in to their role.

However, accessibility of the intervention however is not as simple as therapist time per participant and other elements must be considered, such as attendance rates. For this trial there was lower attendance due to it being a group intervention on a fixed day although even increasing the rate of recruitment and putting on more workshops there would still be a minority of people who were put-off by a group intervention or could not fit the workshop into their schedule.

Flexibility in delivery, or online delivery might be considered. Indeed, the participants' experience was line with this: most people were keen to attend the workshop but more options might have helped them to attend. However, the trial clinicians and several participants expressed that the workshop was useful as people shared ideas, and so perhaps removing the group element might remove the element of the intervention which aims to model empowerment and the people who have recovered from depression as the experts. This feeling that the intervention was empowerment was expressed by staff who delivered it in their focus group, which goes some way to allay concerns raised in the Discussion of Chapter 3 that focussing in the intervention only on aspects within a person's control could either be empowering or experienced as blaming.

All this being said, prior to these potential clinical implications some further development work and testing of the intervention in a randomised controlled trial would enable an assessment of whether the intervention can be clinically and cost-effective. A future trial could augment the symptom-focussed measures, with a measure of subjective wellbeing (e.g. Tennant et al., 2007). The interview for the longitudinal interval follow-up evaluation (LIFE) could be expanded to assess states of wellbeing as well as other psychiatric diagnoses. There are existing parts of the interview, such as asking respondents if they feel back to their 'usual self', which elicited detailed reflections on respondents' experience of wellbeing. Perhaps further constructs could be measures such as self-efficacy (e.g. Sherer et al., 1982), which has been associated with better health outcomes and is a potential mechanism by which an intervention may exert it's effects (Gallagher et al., 2013; Strecher, McEvoy DeVellis, Becker, & Rosenstock, 1986). Given our high outcome completion rate, we suspect the addition of limited further questionnaires would not dramatically affect the feasibility of follow-up interviews. Personal choice was emphasized and the plans people made varied. Measuring uptake of the four routes could be an interesting avenue for future research, as well as whether and how people were able to introduce new habits. Future trials could investigate how this intervention may be carried out within other services, or explore further who the intervention is most suited for, a key theme which came from the clinician's focus group. However, the hope is that the intervention is personalised to each individual, making it suitable for any population.

A larger trial could also look at potential mechanisms of effect: perhaps initially whether the intervention appears to 'educate, model and train', the key aims in terms of behaviour change (see Chapter 4 and Michie et al., 2011). If the intervention increases empowerment then you might see an increase on a self-efficacy questionnaire such as the General Self-efficacy Scale (Chen et al., 2001). A decline may suggest that the intervention has the opposite effect and leads people to self-blame where their depression is actually more determined by factors outside of their control, as described in the limitations section of Chapter 4. Uptake of the four routes could be monitored and consider choice and the extent to which people choose different activities. specific measures of behaviour change could be used and compare with the control arm (or arms). Some potentially important clinical characteristics, such as use of antidepressant medication at baseline, were not adequately balanced by the randomisation procedure, which although a more significant risk in smaller studies may be considered a risk for a future trial, and a stratified randomisation procedure may be preferred.

Conclusion

A brief wellbeing intervention was in the most part feasible to deliver in an ecologically valid setting. Mental health outcomes were better in the intervention than the inactive control arm of this pilot. If replicated, this could represent an important effect given the brief clinical contact time needed for the intervention, the high numbers of people leaving IAPT treatment each year, and the severity and clinical importance of a relapse of depression. This intervention could be routinely offered after acute treatment, has the potential to prevent relapses and improve wellbeing and should be tested in a fully powered trial. Taken together, these results suggest the PRotect intervention merits further investigation following some adjustments to the process of generating referrals, and the availability and engagement with the introductory calls and workshops.

Chapter 7 Discussion and Conclusion

This thesis explores the maintenance of recovery after an episode of depression by considering two issues: firstly, how best to characterise and understand relapses of depression, and secondly how relapses might be prevented from a theoretical and an interventional perspective. The problem statement set out that while the majority of people recover from an episode of depression, relapses are common, and approaches which move beyond (even optimal) episode treatment will be a necessary part of reducing the impact of depression at a population level (Vos et al., 2004).

There are various approaches and timepoints for potential relapse prevention in the healthcare domain. Psychological therapies such as Cognitive Behavioural Therapy (Beck, 2005) delivered in the acute phase of illness are known to have enduring effects after treatment completion at the point a person has recovered (Hollon et al., 2006). This enduring effect is not seen after stopping antidepressant medication, but continuing to take medication after recovery does reduce relapse risk whilst being taken (Geddes et al., 2003; Thase, 2012). Non-pharmacological interventions such as Mindfulness-Based Cognitive Therapy (Teasdale et al., 2000) may also be useful as standalone relapse prevention interventions delivered after recovery: and may work in addition to any enduring effect of acute treatment, or for those who didn't use or wish to stop medication. For all of these options, accessibility remains a priority if the burden of disease is to be reduced (Holmes et al., 2018).

A mixed-methods approach largely located within the 'applied' health research domain was used in this thesis. The focus was on non-pharmacological strategies for people who have recovered from an episode of depression, separating out the issue of relapse prevention from that of acute treatment. Here I will summarise the thesis and then integrate and discuss the key findings.

Summary of key findings

There is evidence that the prevalence of depression may in reality be higher than estimates from research studies due to several specific methodological constraints (as presented in Chapter 1), and, as such, lifetime prevalence may be as high as 40+% (Kruijshaar et al., 2005; Moffitt et al.,

2010). Following recovery from an episode, relapse risk is higher for those who have residual symptoms, comorbid problems such as an anxiety disorder, shorter length of time in recovery, and who had experienced childhood maltreatment (Buckman et al., 2018). There is also some tentative evidence presented in Chapter 1 from studies beyond the scope of, or not measured within the cohort studies within that review, that there are differences between first and subsequent depressive episodes in terms of their predictors, their clinical characteristics, and their response to treatment. However, this picture is not entirely clear, perhaps partly because most models of depression treat all episodes of depression as equal and do not differentiate between episodes. The evidence from studies which do identify differences are explored in order to examine whether relapse prevention in those who have recovered from depression could usefully be addressed as its own clinical issue separate to and to an extent independent of acute treatment or primary prevention.

The systematic review presented in Chapter 2 identified several non-pharmacological interventions which reduce risk of relapse independently of any enduring effects of their acute treatment. Adapted versions of Cognitive Behavioral Therapy (cCBT), Mindfulness-Based Cognitive Therapy (MBCT) and Continuation Inter-Personal Psychotherapy (IPT) all reduce relative risk of relapse by around 22% in the year after recovery, with more limited evidence at 2 years (Clarke et al., 2015). IPT was only tested in those who had received IPT acutely, whereas MBCT and CBT were tested as standalone relapse prevention interventions after a variety of acute interventions. The review's conceptual framework hypothesized that effectiveness would vary by intervention content, however this was not clear in the results: there was no apparent difference in effectiveness at a study-level between the three main types of therapy despite their different purported mechanisms of action. If residual symptoms and shorter recovery are linked to relapse risk, it is possible these interventions work by simply increasing treatment duration to reduce any remaining symptoms and extend the benefit over a longer time period.

Chapter 3 addressed the question as to *why* lower residual symptoms over a longer time-period could protect against relapse, and in addition why interventions with different targets all appear to work to a similar extent, by examining relapse prevention from a 'complex systems'

perspective. ‘Open’ systems learn and adapt and so would be expected to adapt over time to a depressed state (Chapter 3). This could explain the higher risk of episodes of depression in those who have previously experienced it, as compared with those who have not. If depression is an ‘attractor state’ which complex systems tend towards, the period soon after relatively brief or ‘incomplete’ recovery may therefore be a vulnerable time-point and limited stressors on the system may be likely to be sufficient to push a person back into depression. The framework suggests that there are several areas or ‘nodes’ in the complex system of interactions that sometimes results in depression, such as described in the cognitive neuropsychological model of depression (Roiser et al., 2011) which draws together evidence for mechanisms at several different levels of explanation (Marr et al., 1982). The complex systems relapse prevention approach presented in Chapter 3 is that an intervention focusing on repeating actions that may reinforce wellbeing may help an individual to achieve or maintain a wellness equilibrium state that is then resistant to change, and that those actions could be drawn from four key ‘nodes’ derived from a cognitive neuropsychological model: environmental stressors or impacts, negative schemata, imbalance between cognitive control and attentional biases, and physical health of the system as a whole.

This approach was translated into key intervention components of a wellbeing focused intervention (Phase I in Chapter 4) and further developed into the PRotect intervention for delivery in IAPT services (Phase II Chapter 4). The intervention principles were that they should be targeted towards a population that is currently well, and to aim for people to ‘practice’ wellbeing, with target ‘nodes’ which have evidence linking them with relapse risk. The intervention materials were developed to be delivered by an IAPT service with input from clinicians, a depression peer support group, and members of the public with and without prior depression. The intervention included an introductory phone call, a workshop, and a review call, all based around the intervention principles presented in a workbook.

The design of a pilot randomized controlled trial that could test the feasibility of a larger trial was developed on the basis of early feasibility work and discussions with the study site (Chapter 5). Key elements of this design were: it incorporated clear pre-determined objective feasibility

outcomes, was as close as possible to that which would be conducted at a larger scale, and included qualitative data collection for trial monitoring and exploration of participant and staff experience. This pilot trial established that the intervention could be delivered within IAPT services and within a randomized controlled research study. A few changes were suggested: limiting the length and content of introductory calls, exploring online delivery of the workshop and 'peer' facilitation, and additional wellbeing and behavior change outcomes.

Specifically, the pilot randomized controlled trial (as reported in Chapter 6) showed it was feasible to recruit, and retain participants, and to deliver the PRotect intervention in an IAPT service. Results were promising: 83 IAPT clients who had recovered from depression and reached the end of their acute treatment were recruited, and retention in the study and completion of outcome measures was high. Rates of consent and retention were very high, and workshops and follow-up calls were largely completed and adherent. The clinical outcomes collected were feasible for use in a larger randomised controlled trial. Participants and clinicians reported experiencing the intervention as worthwhile and to a large extent 'different' to acute treatment. Interestingly participants felt that research interviews also had a positive impact on their mental health, which may be worth exploring further. The PRotect wellbeing-based intervention was therefore seen as feasible to deliver within existing services, and a larger randomised controlled trial is warranted, with some further development.

The thesis in context

The thesis goes some way to suggesting a novel approach to characterising and preventing relapse through focusing on relapse prevention as separate from primary prevention or acute treatment. It brings together an applied health focus with a view that long-term change outside of a healthcare or 'treatment' setting may be useful in preventing relapse. It also brings together a focus on models of depression and the possible mechanisms linked with depression, with a positive or recovery or wellbeing focus: on pleasant or meaningful activities. This work does not investigate mechanisms of action, but does draw on a model of depression which brings together evidence from mechanistic studies as well as treatment studies (Roiser et al., 2011). It also draws on overarching view of how systems and how long-term processes work (Bar-Yam, 2002;

Boulding, 1956), the potential need for a positive psychology focus (Aspinwall & Tedeschi, 2010), and a consideration of evidence around how an intervention's delivery might impact long-term behaviour change (Gardner et al., 2012; Lally & Gardner, 2013; Michie et al., 2011). It is hoped that this thesis may be a useful complement to ongoing work looking at how acute treatments can have better enduring effects, on primary prevention, and on reducing those risk factors that lead to depression in the first place such as childhood maltreatment.

In order to provide an updated view of developments in non-pharmacological interventions since the review in Chapter 2 which was the basis of most work in this thesis, I repeated the full bibliographic searches and sifted for relevant trials (registered with PROSPERO, CRD42023385475). In the near decade between searches from early 2013 to late 2022, there have been a total of eight further MBCT studies (Dimidjian 2016, Elices 2017, Kuyken 2015, Meadows 2014, Shallcross 2018, Williams 2014, Moore 2022, Shawyer2016/Farb 2018) in addition to the previously identified seven. Six further CBT studies have been conducted (De Jonge 2019, De Rubeis 2020, Klein 2018, Bockting 2018, Van Tol 2021, Teismann 2014) in addition to the previously identified ten . No further IPT trials have been conducted, however there has been one trial which focused on mother-infant relationships (Cooper 2015). In terms of 'care programs' (interventions which involved several different elements of care), there has been an update to Apil 2012 with 2-year follow-up (Apil 2014), and a trial of a combination of psychoeducation and crisis management delivered online, with or without expert 'chats' over 2 years (Kordy 2016). There has also been a trial of supported self-help in primary care (Biesheuvel-Leliefeld 2017). Other interventions tested were Transcranial Magnetic Stimulation (Benadhira 2017), and exercise (Van der Waerden 2013).

Throughout this thesis I have emphasized the importance of accessibility of interventions, and this has been echoed in the field more broadly. The increase in focus on accessibility is clear, with several trials testing therapies adapted to be of lower intensity. For example, five of the CBT trials tested 'Preventive Cognitive Therapy', but in one study this has been adapted for delivery online (Klein 2014). Kordy 2016 online access with or without chat, Hitchcock 2021 had a face to face introduction then self-guided workbook sessions, Hoorelbeke 2021 was 10 online sessions,

and Biesheuvel-Leliefeld 2017 was self-help with weekly brief counsellor guidance. This increased focus on brief and low-intensity interventions is in line with much of this thesis, and the PRotect intervention may be usefully compared with these other interventions in future in terms of clinical and cost-effectiveness.

This thesis also looking more broadly than conventional psychological therapies, and the broadening of types of interventions being tested more widely in other work is also clear, with more trials of novel interventions which are not traditional psychotherapies being identified in the updated searches. There is a new 'group' of interventions focusing around 'cognitive training'. They vary from "cognitive bias modification" (Basanovic 2020), a program to improve memory skills (Hitchcock 2021) and 'cognitive control training' (Hoorelbeke 2021). These types of intervention were already suggested on the basis of an earlier evidence based within the PRotect intervention in the 'Inner workings' module. The updated review may show further options to reference within the PRotect intervention that are outside of the classic psychotherapeutic domain and previously had not been the subject of randomized controlled trials.

Strengths and limitations of this thesis

A key strength of this thesis is selection of an appropriate methodology to answer each research question: systematically reviewing cohort studies of depression to look at relapse risk and randomised controlled trials to look at the effectiveness of existing interventions; critically examining established characterisations of depression and applying a broader theoretical framework to set-out my understanding of relapse prevention and from which to base intervention development, and using trials methodology to establish whether a larger trial might be feasible. Selecting an appropriate method to answer each specific research question means that evidence collected is appropriate, and is more likely to lead to an innovation which might become routine in the future (Murray et al., 2010; Skivington et al., 2021). Given the potential implications of this research in people's everyday lives and health, it is important to incorporating qualitative work which represents the experience of people who participated and who research findings would apply.

Another strength of this work is that most of the methods and processes follow established and regularly updated guidance within the field of evidence-based healthcare. For example, the thesis as a whole followed the MRC guidance on development and evaluation of complex interventions in healthcare (Campbell et al., 2000; Craig et al., 2008; Skivington et al., 2021), including the structure of questions and building of evidence throughout the thesis. As described in this guidance, building interventions on the basis of a theoretical framework means any underlying assumptions can be tested, and then adjusted in the future on the basis of research evidence. The systematic review in Chapter 2 followed PRISMA reporting guidance (Moher et al., 2009), and the intervention description in Chapter 4 followed TIDieR guidance (Hoffmann et al., 2014), Chapter 5 and 6 also followed established guiding on the design, conduct, and reporting of feasibility trial protocol and results (Moher et al., 2001; Thabane & Lancaster, 2019). Following reporting standards ensures that research is replicable, can be understood and critiqued, and can be interpreted within the body of evidence established from other studies (Cooper, 2008).

There are limits in the extent this thesis was able to draw together a focus on wellness and wellbeing, with the field of relapse prevention which has more of a clinical focus. There is a detailed characterisation of relapses of depression but a better characterisation of wellbeing might be useful and might help to show how this work might fit in with interventions more broadly than for people who have experienced depression. It is also worth noting that this thesis is derived from an understanding of depression through its classification and symptomatology within western psychiatric thinking, and the intervention and trial are within a specific setting of a psychological treatment service. There are also limits to the examination of medication use and of comorbid conditions such as anxiety disorder within this thesis. In chapter 1 it is clear both are important and related to relapse risk. Medication use and anxiety were monitored in the pilot trial and there was some evidence anxiety scores were in line with depression scores (Chapter 6). The intervention content is to some extent flexible to different settings as it asks that participants select their own wellbeing plans.

Clinical and research implications

This thesis focuses on a ‘dimensional’ approach to understanding and describing depression, highlighting it as continuous rather than categorical. This may be of clinical importance within relapse prevention specifically, in order that we move further beyond thinking of ‘well’ and ‘unwell’, towards maintaining and improving mental health over longer-time periods (Vos et al., 2004). This may also highlight that there needs to be effective treatment or intervention within healthcare settings but also proper research into the ‘self-help’ strategies people are using outside of those settings. It has been argued that a change of culture from seeing depression as categorical to continuous might even reduce the stigma around seeking mental health support, or ‘coaching’ (Ring, 2016).

This shift might be facilitated by using a three-dimensional approach whenever describing depression or relapse prevention, where each of the three component parts of a depression diagnosis are made clear and explicit: the specific symptoms referred to, the level of severity, and the length of time. All three dimensions are important and if specified could be examined and explored separately, with various potential clinical and research implications as follows:

- Specifying the first ‘dimension’, the depression symptoms, allows for better testing of the diagnostic category, it’s sub-types and its relationship to other conditions. At the start of the thesis ‘depression’ was described as a short-hand for a variety of experiences which is useful for consistent reporting or monitoring of disease, but specifying the symptoms could allow for cross-cultural comparisons in other diagnostic or disease classification systems. Chapter 1 also describes that it is possible to have two people with depression but no overlap in symptoms, and that comorbid problems such as anxiety are important in relapse risk. Identifying the specific symptom cluster within and outside of the depression category that best represents a person’s mental distress could be useful clinically or by individuals wishing to monitor their mental health outside of treatment settings.
- Specifying the second dimension, severity or level of impairment, could make the graduation between all stages of health and ill-health more visible, and allow for a better

consideration of sub-threshold symptoms and suffering, as well as their associated risk with deteriorations (Buckman et al., 2018). For example, the results of a larger effectiveness trial of the PRotect intervention could use the Psychiatric Status Ratings (PSR) from the LIFE measure in more detail than to identify relapses: a person who had a PSR of 4 would be experiencing significant functional impairment, and equally a PSR of 1 is preferable to 2. This mirrors sentiment within the positive psychology movement: *In one metaphor, psychology was said to be learning how to bring people up from negative eight to zero but not as good at understanding how people rise from zero to positive eight.*(Gable & Haidt, 2005).

- Specifying the third dimension, the amount of time, could be used to bring a focus on reducing the length of time a person is suffering (so for example showing difference between a shorter or longer relapse). It could also be useful for further examination of the validity and appropriate timeframe by which to make any distinctions between terms such as between relapse and recurrence, investigations which were called for by the originators of the proposed distinction (Frank et al., 1991) but have not been sufficiently conducted (Rush et al., 2006 and Chapter 1).

The clinical effectiveness of a 'systems' approach to mental health and particularly of this approach as delivered through the PRotect intervention, remains to be seen pending an effectiveness trial. On the basis of the success of the feasibility trial researchers may wish to look at the recruitment strategy and ways that feasibility work and consultation with services was considered prior to any recruitment in the design of the intervention and of the trial methods. The experience reported by trial clinicians was that the aim to design a trial which fit well into existing systems worked. It is well known that developing an intervention with real-world application in mind from the outset increases the chances it will be feasible to deliver within an evaluation (Skivington et al., 2021).

There are some limited clinical implications that psychological therapies services may wish to consider. On the basis of the participant experience in the pilot feasibility trial, services may wish to consider implementing follow-up phone calls with clients in the months following treatment

completion. Measuring ‘patient satisfaction’ with and without these follow-up calls may indicate whether they would be seen as a useful addition by clients, ahead of any formal research into their clinical and cost-effectiveness.

There is also limited implications of the ‘whole system’ perspective used in this thesis for individuals looking at how to maintain their mental health outside of a clinical setting. If people have access to the relapse prevention interventions described in Chapter 2 and are keen to engage in them, this could be a good option to improve or protect their long-term health. People might also wish to consider broadening the potential domains of influence on their mental health than within one biological, psychotherapeutic, or environmental domain. In a practical sense whatever a person enjoys or is motivated to do, and fits into everyday life so could provide long-term input, could be a good option to try.

Future directions

The work presented in this thesis could be taken forward in three directions. Firstly, an update to the systematic review reported in Chapter 2 using the same methods should be reported with a meta-analysis of clinical effectiveness, and the findings considered when further developing the PRotect intervention. The searches for this review are complete and included studies presented earlier in this discussion to provide context for the work within this thesis.

Secondly, the PRotect intervention should be further developed given the positive feasibility outcomes and experience of clinicians and participants. Work should look to incorporate some of the learning from the feasibility trial. The introductory calls should not include a brief motivational interview but should continue as they served the function of booking people onto workshops, with some flexibility in allowing participants to book in by text or email. Flexibility in mode of delivery of the workshops such as to delivery online should be considered. Delivery online could allow the intervention to be offered across more services therefore ensuring group sizes are larger and participants have more choice, and preserve the group element of sharing expertise that was identified as important by several of the participants and clinicians. In response to some participants’ experience that the intervention didn’t add anything to what they already knew, more

in-depth (and updated) research evidence and links should be added to the booklet and workshop as optional extras that do not increase the reading age and accessibility of the core intervention materials. Expansion of the pool of potential participants to people who have not experienced acute psychological therapy but have recovered from an episode of depression using medication could be considered. Delivery of the intervention by 'peer workers' ('experts by experience' of mental health problems) who work within therapies service was suggested by the trial clinicians as this would fit with the intervention principles of a 'level playing field'.

Finally, in order to establish whether the PRotect intervention is clinically effective and whether it should be offered on a wider scale, a larger randomised controlled trial is warranted. The design should largely follow the pilot: replicating recruitment materials and method but increasing the pool of potential participants to select from, and adding a behaviour change measure as a potential mediator of effect. A behaviour change measure would be useful to identify whether the intervention leads to any changes in people's everyday lives and as such is a test of our proposed mechanisms of action. The impact of data collection through an in-depth interview which encourages reflection might be considered given the strong feeling from participants that these research interviews were mutative. Using self-report clinical measures delivered online may reduce the therapeutic potential within data collection, and could serve as an additional control group to isolate any impact of the reflective research interviews on relapse.

Conclusion

This thesis attempts to reframe depression to better understand and reduce risk of relapse. The effectiveness of existing non-pharmacological relapse prevention interventions is described and potentially important differences between study designs were highlighted. Using a complex systems approach to focus on the continuous nature of depression and recovery and maintaining wellbeing over time, the principles behind a novel intervention were developed. A brief wellbeing focused intervention was developed in consultation with service users and staff of an existing therapies service. The intervention was largely feasible to deliver in this service as part of a randomized controlled pilot trial. Clinicians and participants felt the intervention was helpful, and they provided examples of behavior changes they identified as originating from their participation. An appropriately powered randomized controlled trial is warranted in order to assess the clinical and cost effectiveness of the PRotect intervention.

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Appendices

Appendix A Search string for Embase, MEDLINE, and PsycINFO (using the Ovid interface)

	Searches
1	depression/ or agitated depression/ or atypical depression/ or depressive psychosis/ or dysphoria/ or dysthymia/ or endogenous depression/ or involutional depression/ or major depression/ or masked depression/ or melancholia/ or "mixed anxiety and depression"/ or "mixed depression and dementia"/ or organic depression/ or pseudodementia/ or recurrent brief depression/
2	1 use emez
3	depression/ or depressive disorder/ or depressive disorder, major/ or dysthymic disorder/
4	3 use mesz
5	"Depression (Emotion)"/ or Endogenous Depression/ or Major Depression/ or Recurrent Depression/ or Atypical Depression/ or Treatment Resistant Depression/ or Pseudodementia/ or Dysthymic Disorder/
6	5 use psyh
7	(depress* or dysthymi* or melancholi* or dysphori* or pseudodementia).ti,ab,kw.
8	2 or 4 or 6 or 7
9	disease course/ or relapse/ or recurrence risk/ or recurrent disease/ or chronic disease/ or chronicity/
10	9 use emez
11	recurrence/ or chronic disease/ or disease progression/
12	11 use mesz
13	Relapse Prevention/ or "Relapse (Disorders)"/ or Preventive Medicine/ or Chronic Mental Illness/ or "Chronicity (Disorders)"/
14	13 use psyh
15	(recur* or relaps* or ((depress* or dysthymi* or melancholi* or dysphori* or pseudodementia) adj3 (long?term or chronic* or prevent*))).ti,ab,kw.
16	10 or 12 or 14 or 15
17	8 and 16
18	exp clinical trials/ or (crossover procedure or double blind procedure or placebo$ or randomization or random sample or single blind procedure).sh.
19	18 use emez
20	exp clinical trial/ or (cross-over studies or double-blind method or random allocation or single-blind method).sh. or randomized controlled trials as topic/
21	20 use mesz
22	exp clinical trials/ or (placebo or random sampling).sh,id.
23	22 use psyh
24	(clinical adj2 trial$).ti,ab.
25	(crossover or cross over).ti,ab.

26	(((single$ or doubl$ or trebl$ or tripl$) adj5 blind$) or mask$ or dummy or singleblind$ or doubleblind$ or trebleblind$ or tripleblind$).ti,ab.
27	(placebo$ or random$).ti,ab.
28	(clinical trial$ or controlled clinical trial$ or random$).pt. or treatment outcome$.md.
29	animals/ not human$.mp.
30	animal$/ not human$/
31	(animal not human).po.
32	(or/19,21,23-28) not (or/29-31)
33	17 and 32

Appendix B Search string for CENTRAL

	Searches
1	(Depress* or dysthymi* or Melancholi* or Dysphori or Pseudodementia):ti,ab,kw
2	("long term" or Chronic* or prevent* or relaps* or recur*):ti,ab,kw
3	SR-DEPRESSN
4	1 and 2 and 3

((ft((recur* OR relaps* OR (depress* OR dysthymi* OR melancholi* OR dysphori* OR pseudodementia)) NEAR/3 (long?term OR chronic* OR prevent*)) OR su.Exact("relapse" OR "relapse prevention" OR "disease recurrence" OR "chronic disease" OR "chronic diseases" OR "recurrence" OR "recurrence rates" OR "disease progression" OR "preventive medicine")) AND (ft(depress* OR dysthymi* OR melancholi* OR dysphori* OR pseudodementia) OR su.Exact("depressive disorder" OR "melancholia" OR "depressive disorder, major" OR "depression (18270)" OR "mental depression" OR "depression, involutional" OR "beck depression inventory" OR "anxiety-depression" OR "depression (psychology)" OR "beck depression inventory (bdi)" OR "dysthymic disorder" OR "depression"))) AND (su.Exact("clinical randomized controlled trials" OR "clinical trials" OR "clinical trials as a topic" OR "clinical trials, phase i as a topic" OR "clinical trials, phase ii as a topic" OR "clinical trials, phase iii as a topic" OR "controlled clinical trials" OR "controlled clinical trials as a topic" OR "cross-over studies" OR "randomization" OR "random samples" OR "double-blind method" OR "random allocation" OR "clinical randomized controlled trials" OR "double blind randomized controlled trials" OR "randomized controlled trials" OR "randomized controlled trials as a topic") OR ab(random? OR control? OR experiment? OR trial))

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	49, 57
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	49
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	51-54
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	57
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	59, 60, 71 and 72
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	59
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	59 and Appendix A, B and C
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	59
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	60
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	60
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	60, 61
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	61
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	60, 61
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	71, 72
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	60, 61

Section and Topic	Item #	Checklist item	Location where item is reported
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	60
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	60, 61
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	60
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	77
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	62
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	62-64
Study characteristics	17	Cite each included study and present its characteristics.	64-70
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	72-73
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	74-76
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	72-73
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	74-76
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	77
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	77-78
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	78
	23b	Discuss any limitations of the evidence included in the review.	83
	23c	Discuss any limitations of the review processes used.	83

Section and Topic	Item #	Checklist item	Location where item is reported
	23d	Discuss implications of the results for practice, policy, and future research.	83
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	50
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	50
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Published paper
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Published paper
Competing interests	26	Declare any competing interests of review authors.	Published paper
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Published paper

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

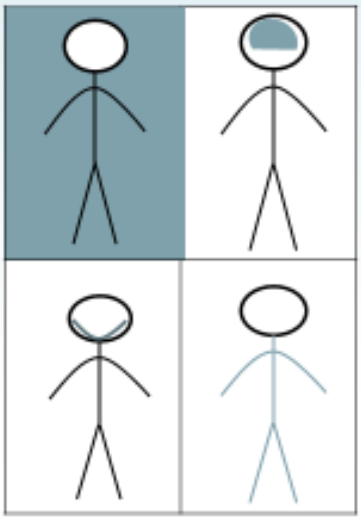
UCL

This phase is: "Identify the components of the intervention and the underlying mechanisms by which they will influence outcomes…."

Your choice: What ideas are practical, positive and could be permanent for you?

Four parts

- Your world
- Your brain
- Your thoughts
- Your body

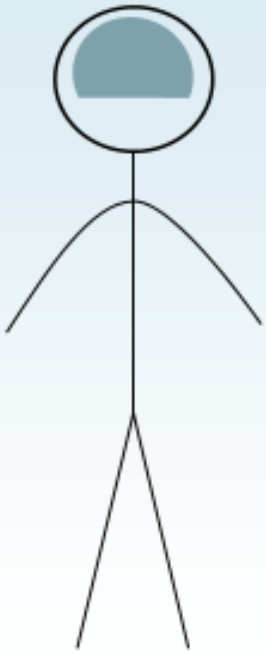


UCL

Your brain

Encouraging activities which may have positive impact on automatic processes linked to mental health/depression:

- Online links to cognitive control training
- Meditation exercises

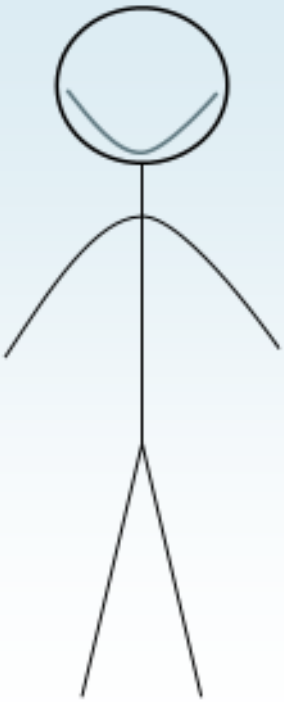


UCL

Your thoughts

Encouraging people to practice positive thoughts:

- Take a personality strengths questionnaire
- Letters of thanks
- 3 funny things that have happened today
- Do a favour for someone



UCL

Your body

Encouraging people to focus on their physical health and wellbeing as this will impact their mental health.

- Nutrition e.g. eat 5 portions of fruit or vegetables per day
- Exercise
- Effects of drug and/or alcohol use
- Physical health conditions

INTRODUCTORY phone call procedure

If you have any questions or concerns at all, however small, don't hesitate to contact Kat by email (k.clarke@ucl.ac.uk) or by phone (02031083260 or 07947392839).

Data Protection
Any participant names or contact details must be sent as encrypted files attached to emails, and no personal data should be in the body of the email itself. No other information such as outcome assessments should be sent in the same email as any name or contact details. Email accounts must be accessible only with a password.

Managing risk
You should follow your normal risk procedure if you are concerned about the safety of a client during any contact you have with them. As the client has been discharged from the care of IAPT service, you may need to inform their GP about any risk issues (as the client's current care provider). If you have concerns, please also get in contact with Kat.

You will receive an email with the names and contact details of participants that have been allocated to the intervention arm of the trial. Try to telephone the clients within 7 days if possible.

Introductory phone call (10 minutes)

Introduce yourself and the intervention
Hello, this is NAME calling from iCope. Do you have ten minutes to talk?

No- *When would be a better time to call?*

Yes- *Great. I'm just phoning to introduce myself, and to give you a bit of an introduction to the PRotect wellbeing course you are being offered. Did you receive the letter and booklet about this?*

No- *Oh, I'll make sure we send another copy. We sent a letter to let you know that as part of the PRotect trial you are a participating in, you are being offered the wellbeing intervention. Can I tell you a bit about the intervention?*

Yes- *Introduce the intervention*

- *It's an add-on for people who have improved from an episode of low-mood or depression.*
- *It's based around a booklet, with a 2-hour workshop and a 20 minute review phone call one month later.*
- *It combines research with expertise from people who have been depressed in the past.*
- *We will focus on 4 wellbeing 'routes'-*

1. *positive inputs, which are things in the world around you or in your diary that have a positive influence on you.*
2. *'Inner workings' which are the subconscious parts of your brain and thinking.*
3. *'Positive outputs', which are activities that may have a good effect on other people, and*
4. *physical health as well.*

- *You are welcome to look through the booklet before the workshop, but don't need to.*

Ask about the participant (and identify any potential barriers to attendance).
How are you feeling about coming? Do you have any concerns about it?

Introductory phone call prompts

I have written a list of prompts you can use to get the client talking in the introductory phone call. The important thing to remember is to leave long gaps and silences, and listen really carefully to what the client is saying. To start a conversation you can ASK- WAIT- REFLECT- CLARIFY. Ask a question, leave a lot of silence for the client to elaborate on their answer and use short cues to encourage them to speak more, reflect back to them what they have said, and clarify any points that they brought up that you didn't quite get.

SMALL PROMPTS TO GET THE CLIENT TO SAY MORE

Mm, I see, oh, OK, (etc. you get the idea)

ASK- *How are you feeling about coming to the workshop?*

WAIT- *Oh I see.*

WAIT-*That's interesting.*

REFLECT- *It sounds like you're feeling quite enthusiastic/ stressed/unsure/…*

CLARIFY- *What did you mean when you said 'X'?*

FURTHER QUESTION- *Why is that, do you think?*

CLARIFY- *Would it be fair to say you have mixed feelings about it?*

ASK- *Do you have any concerns about the workshop?*

WAIT- Oh right/mm/I see/etc.

REFLECT- *So you're concerned about X/Y/Z*

FURTHER QUESTION- *Why is that a concern for you?*

FURTHER QUESTION- Is that important to you?

CLARIFY- Am I right in saying that on the one hand you feel X, but on the other hand you feel Y?

ASK- *Is there anything that's putting you off attending?/What are you hoping for from the workshop?*

(AFTER ARRANGING WORKSHOP ATTENDANCE)

QUESTION- *How do you feel about an evening workshop?*

QUESTION- *Will you be in the area or will you have to travel?*

QUESTION- *How will you travel there?*

REVIEW phone call procedure

If you have any questions or concerns at all, however small, don't hesitate to contact Kat by email (k.clarke@ucl.ac.uk) or by phone (02031083260 or 07947392839).

Data Protection
Any participant names or contact details must be sent as encrypted files attached to emails, and no personal data should be in the body of the email itself. No other information such as outcome assessments should be sent in the same email as any name or contact details. Email accounts must be accessible only with a password.

Managing risk
You should follow your normal risk procedure if you are concerned about the safety of a client during any contact you have with them. As the client has been discharged from the care of IAPT service, you may need to inform their GP about any risk issues (as the client's current care provider). If you have concerns, please also get in contact with Kat.

Review phone call in the style of a brief motivational interview (20 minutes)

You should try and phone participants for their review phone call one month after their attendance at the workshop.

The goal of the phone call is to

- Listen to the clients experience of implementing their PRotect plan
- Normalise any feelings of discouragement
- Affirm small steps
- Build feelings of self-efficacy through exploring activities the clients are doing that help their wellbeing (small everyday activities).
- Allow the client to lead the way with thinking about ideas for the future
- Answer any questions about the PRotect course
- Encourage self-efficacy through signposting

Flexibility, and responding to the client's needs are important for this phone call. For this reason, we have only given the key topics to cover, and some sample questions.

Essential topics

- Introduce yourself and the reason you are calling
- Ask how the client is
- Talk about the workshop and their plan/the previous month
- Ask if they have any advice for others who have recovered from an episode of depression (and note down/record)
- Ask about the future
- Ask if the client has any questions for you

Sample questions
How are you?
How have you been doing?
How did you find the workshop?
Was there anything you found particularly interesting or stood-out?
Tell me about your time since the workshop
Do you remember what was in your PRotect plan?
How is your PRotect plan going?
Are you doing anything at the moment that's good for your wellbeing?

Placeholder screen- have projected for when people are arriving. There should also be 'posters' of the four routes stuck in 4 corners of the room, along with the resource packs for the corresponding route.

Questionnaires (IAPT minimum dataset) to be completed outside the room/as people arrive. Check people have booklet with them, if not, give them another copy.

Welcome…

Introductions – us

Camden Psychological Therapies Service – we provide 1-to-1 interventions for common mental health problems as well as psychoeducational groups and workshops such as today's. We are trained to deliver this workshop for after people have received treatment for low mood or depression and are feeling better.

House-keeping

(fire/toilets)

Phones off please

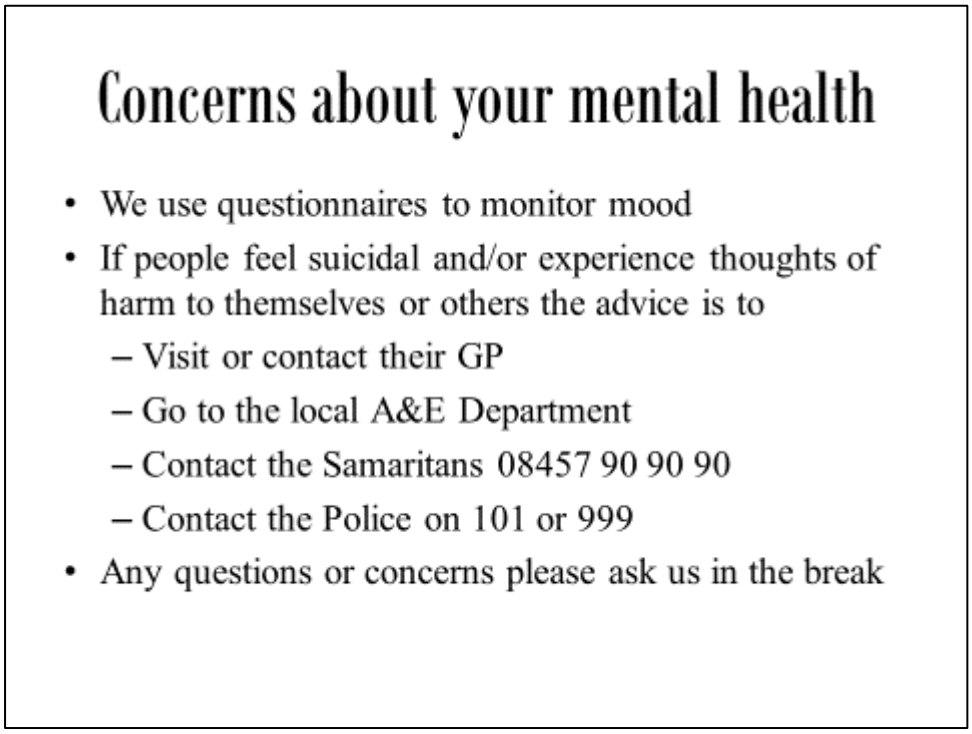
Outline today's session;

2 hours long

15 mins break halfway though

We want the session to be interactive so do ask anything you want and contribute your ideas. Respect what other people say so that we have a supportive atmosphere. Equally, you will never have to share anything you don't want to.

Opportunity to feedback at the end of todays session/ ask any final questions



Questionnaires – we ask that people complete some brief questionnaires about current symptoms of low mood and anxiety when attending workshops. These help us to identify current symptoms and help us to monitor your individual progress should you have any further contact with our service. All information that we collect from you is confidential and stored on a secure NHS database.

Risk - One of the questions asks specifically about suicidal thoughts over the past two weeks, the reason we ask this is because it is very common for people to experience these types of thoughts if feeling low and/or anxious.

Please note that we are not a crisis service therefore if you have experienced any of these thoughts or are concerned about your mental health then we recommend that you:

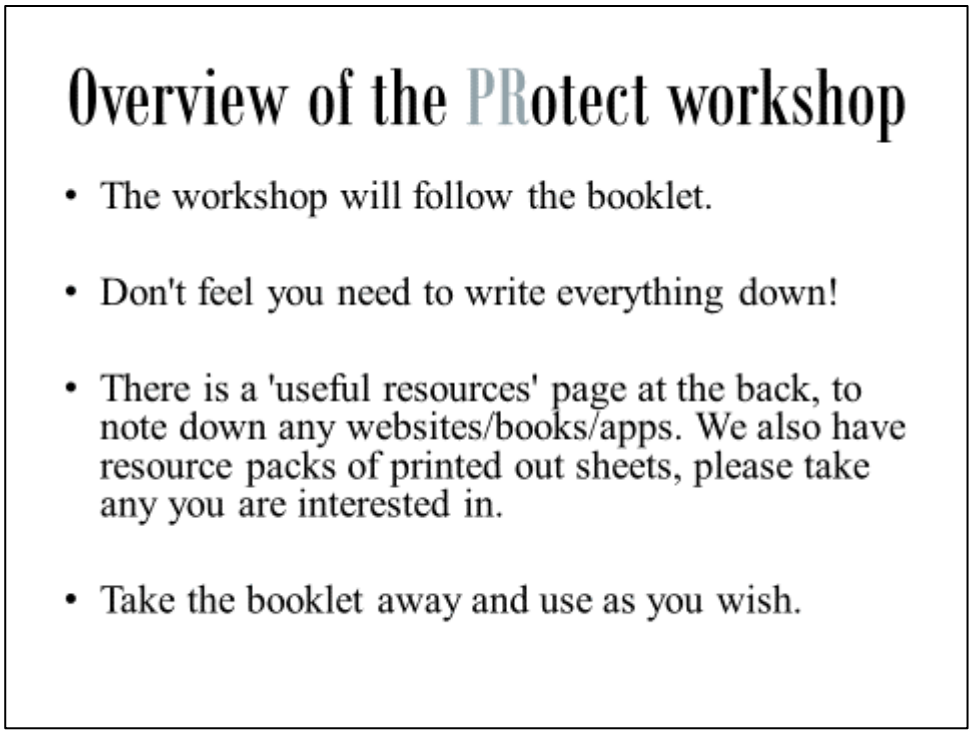
Visit or contact your GP

Go to your local A&E Department

Or if you feel that either yourself or another person is in danger then call the police

We have included all this information and other useful helpline numbers in your packs. We recommend that you familiarize yourselves with this information in your own time.

Break – We will have a short 15 minute break and will be available to answer any questions that you may have

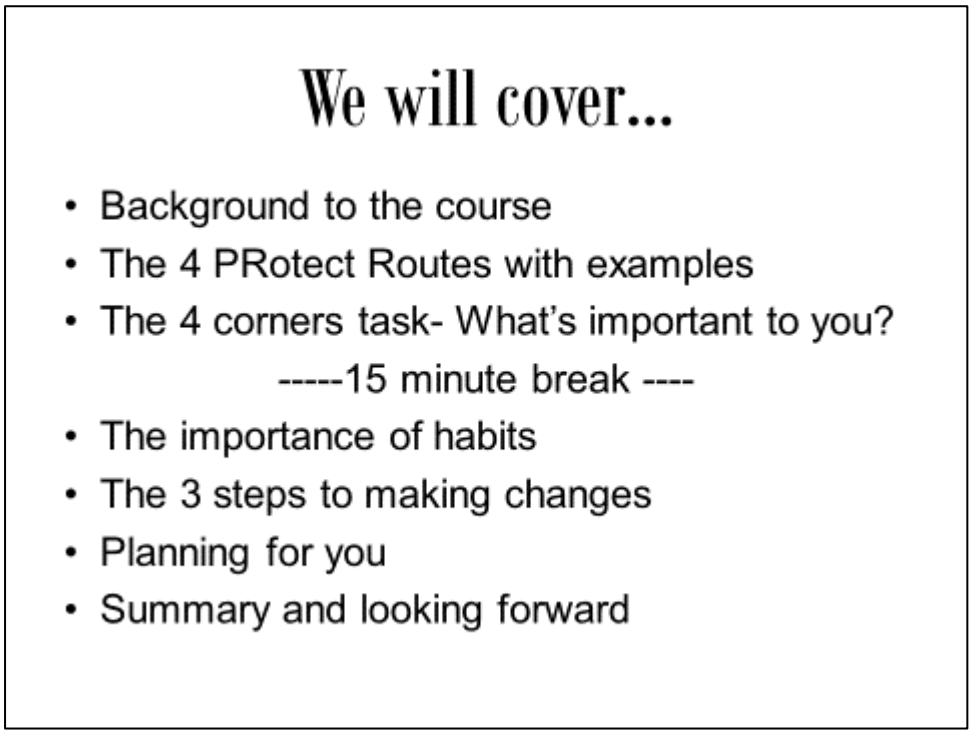


-We will follow the booklet during the workshop, but don't feel you need to write everything down in it. Everyone is different, it might not be helpful for you. You could write in it at home, or write on the post-it notes provided.

-The booklet has a 'useful resources' page at the back. If you want to note down any websites/books/apps at any point, do so there.

-Can take away and use it as you wish in your everyday life.

-Check everyone has a booklet with them. If not, give another.



These timings are allowing 10 minutes before this slide to gather everyone and cover the previous slides

Background

The 4 PRotect Routes with examples

The 4 corners task- What's important to you?

BREAK

Importance of habits

The 3 steps to making changes

Final task- Planning for you

How common is depression?

This is a Wimbledon crowd from 2008. How many of them do you think would have experienced depression in the previous year? (there are 159 people there)

The last household survey in England was in 2007, and in that year alone, 12.3% of people had experienced an episode of depression or depression and anxiety.

Most people recover from depression. Some go on to have a relapse, but a considerable number remain well after recovery.

There are **'risk' factors**, that increase a person's chances of depression, and also **'protective' factors**, that increase a person's chances of staying well.

*McManus, S., Meltzer, H., Brugha, T. S., Bebbington, P. E., & Jenkins, R. (2009). Adult psychiatric morbidity in England, 2007: results of a household survey. Retrieved from http://discovery.ucl.ac.uk/164862/

-Best information we can get about mental health problems is from population surveys (household surveys), as a lot of people never seek support or treatment.

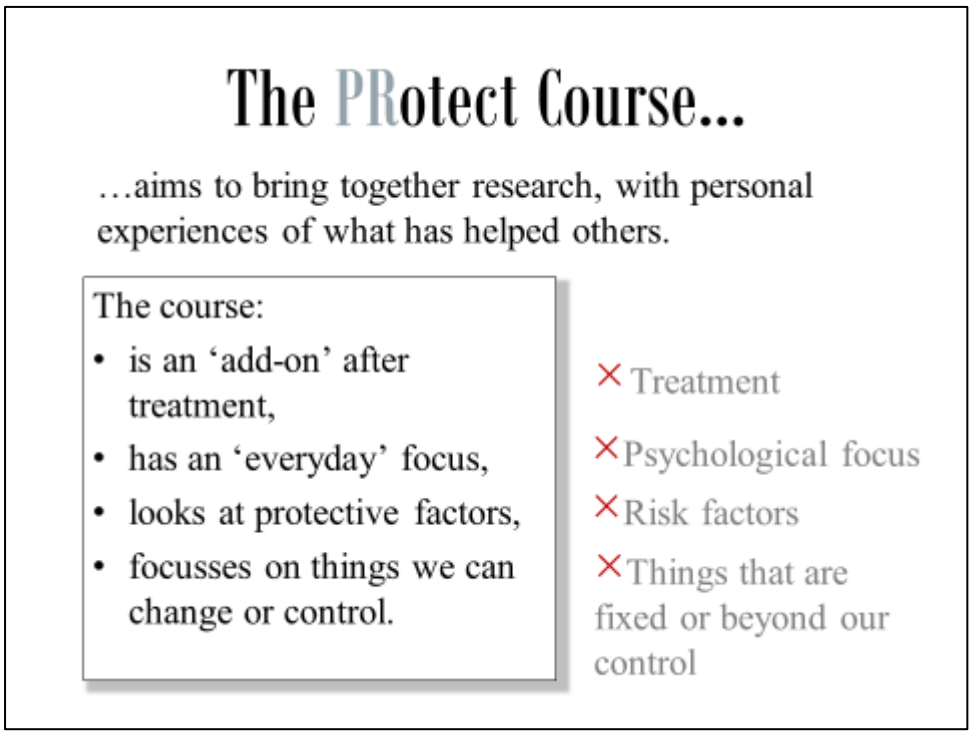
-Every 7 years there is survey of households in England which gives us a picture of people's mental health.

-The last one was 2007. That year, 12.3/100 people had an episode of depression or mixed anxiety and depression.

ANSWER to previous slide- it's very difficult to say. But our best evidence would suggest around 20 people.

Reference

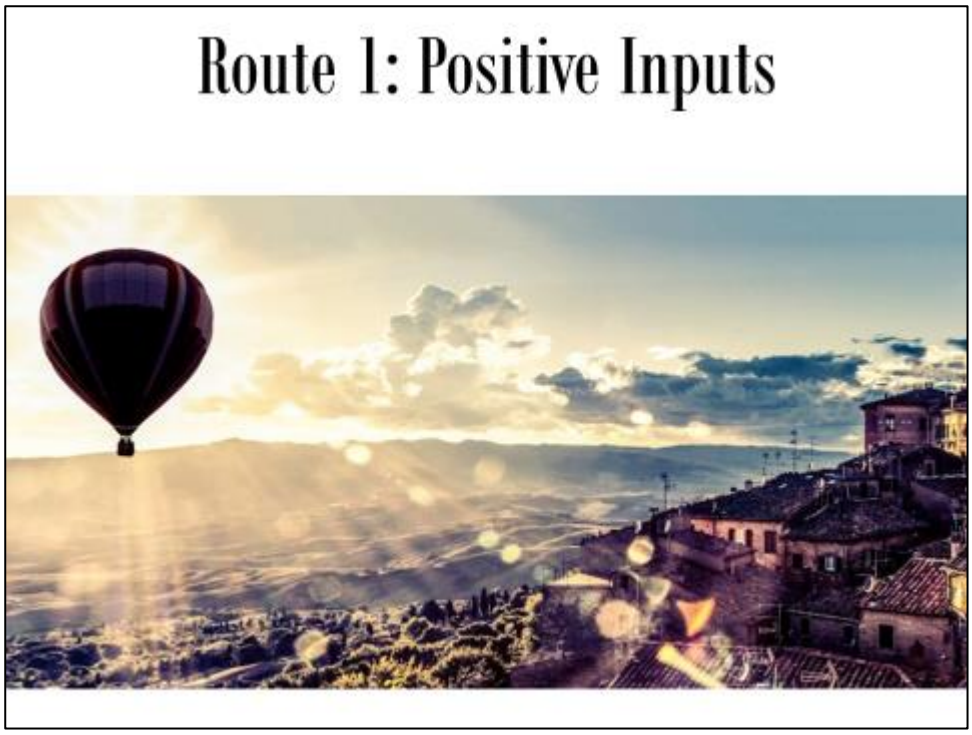
McManus, S., Meltzer, H., Brugha, T. S., Bebbington, P. E., & Jenkins, R. (2009). Adult psychiatric morbidity in England, 2007: results of a household survey. Retrieved from http://discovery.ucl.ac.uk/164862/



This course aims to bring together research with personal experiences of what has helped and does help other people. Depression and other mental health problems are so common, people are taking action every day to protect their mental wellbeing. We aim to harness this expertise and share it.

There are lots of things that could be part of recovering from depression and staying well, but the PRotect course has a specific focus.

- This is an 'add-on' for after a person has finished treatment or is feeling quite a bit better. Everything that has been covered in acute treatment is still important, and worth continuing with (we just won't focus on that here).
- The focus of this course is on everyday activities that will be part of many people's lives whether or not that person realises they are helping your mental health.
- We look at potential for protection from activities. Risk factors may still be there, but by adding protective factors this may help
- We have only looked at things you can control, and ignored anything that's fixed or beyond our control.



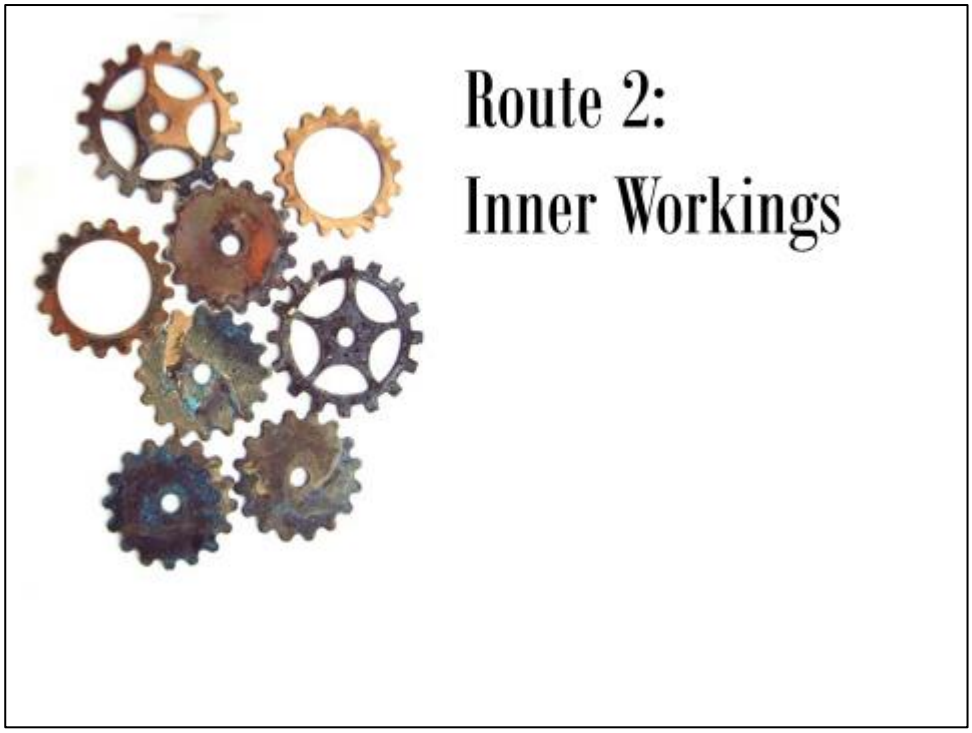
Explore- what does this mean?

Research suggests that things that happen around you have an impact on the chemicals in your brain, and so your wellbeing.

A positive influence could come from having a hobby you enjoy, having friendships or contact with people, enjoying work, or going to a peer support group.

For example- ADD IN YOUR OWN EXAMPLE IF POSSIBLE (or run through examples from booklet)

Task- Talk with the person/people next to you. Think through the last 7 days- is there anything that you came across, or did, that had a positive impact on you? Note down on post-it notes, and stick anything you're willing to share to the 'route 1' poster which is in one corner of the room.



Explore- what does this mean?

Research suggests that these automatic processes may make a difference to your mental health.

Some people like to think of the brain as a muscle that needs regular exercise to ensure it stays strong and works well.

For example-

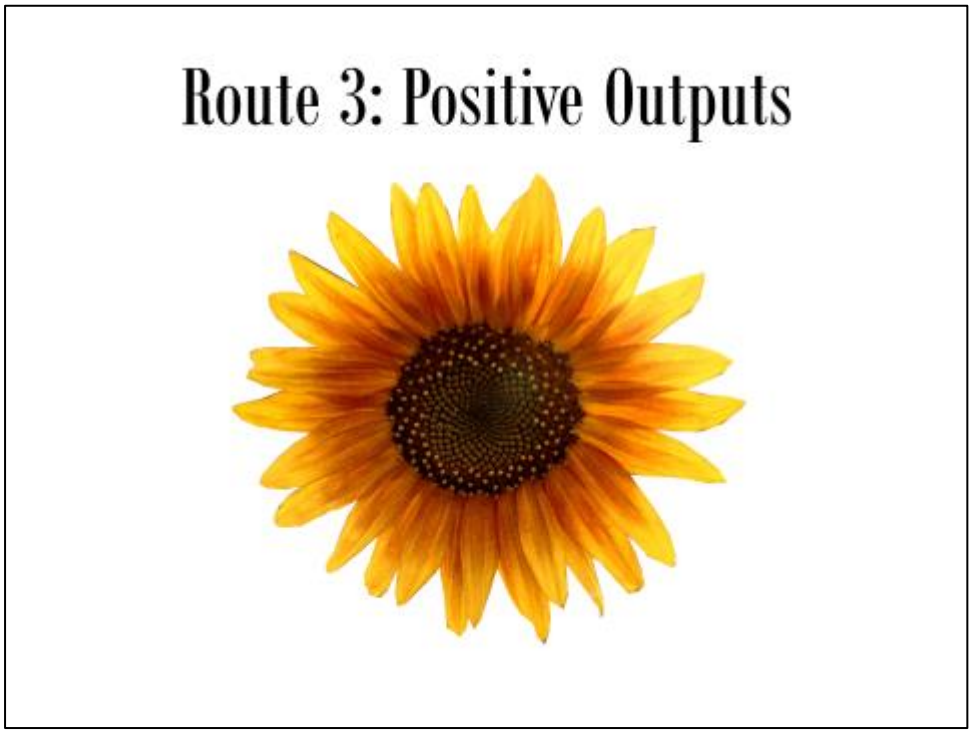
-meditation or mindfulness

-apps that aim to improve ‘cognitive biases’ or ‘cognitive control’

-games (crosswords/puzzles/sudoku)

ADD IN YOUR OWN EXAMPLE IF POSSIBLE (or run through examples from booklet)

Task- guided meditation/relaxation (play recording).



EXPLORE- What does this mean?

‘Outputs’ are our thoughts and actions

Thinking positive thoughts on purpose can make some people feel happier and increase their self-esteem. This could be thinking of things you enjoy, are grateful for, or are proud of. These feelings then lead naturally to more positive thinking.

Positive actions, such as helping a friend or praising a colleague can also improve your own mood. At the same time, you may help the other person’s wellbeing.

GROUP TASK- Brief strengths survey. Identify your top 3 strengths from the list

Route 4: Physical Health

Most people will know exactly what this route is- it's the most well-known. However

- Its not just exercise and diet, also includes managing physical health problems, and self-care.
- Sometimes people think only of the physical benefits, but there are mental ones too.

TASK- think of your friends and family, and write any small actions they do to help their physical health. Write on post-it notes, and stick any ideas you're willing to share to the 'route 4' poster which is in one corner of the room.

You

- Which of the routes do you already follow?
- Which of the routes interests you the least?
- Which interests you most?

We will have a break in 15 minutes. Now a task where we will get up and move around a bit.

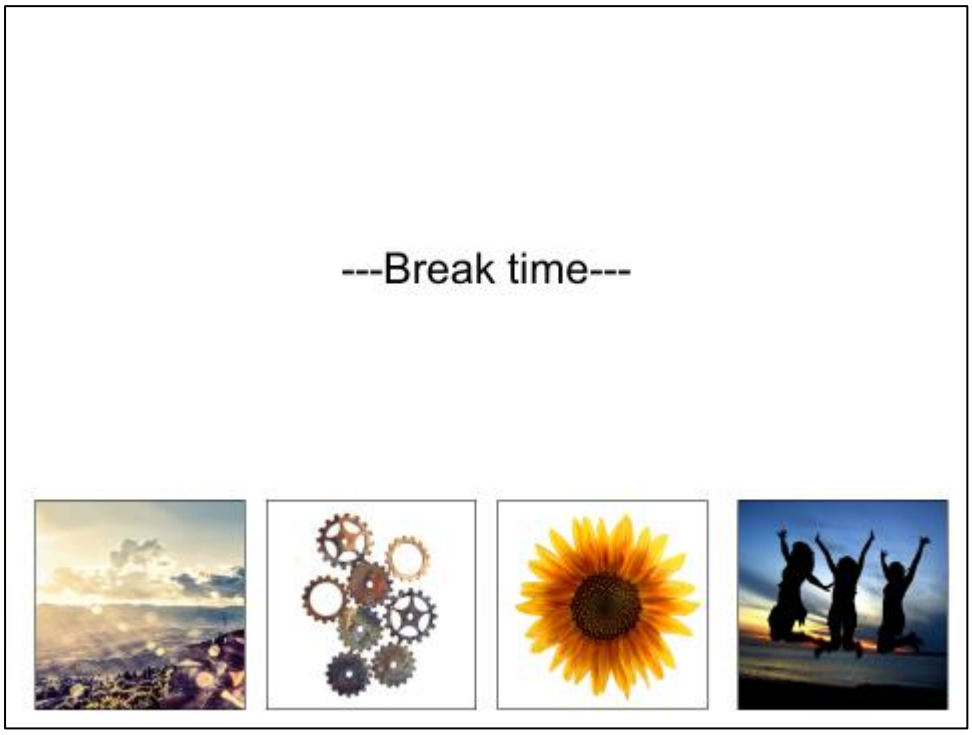
Introduce where the 4 routes are. We will have three questions and you can go and stand by the route in response to the question.

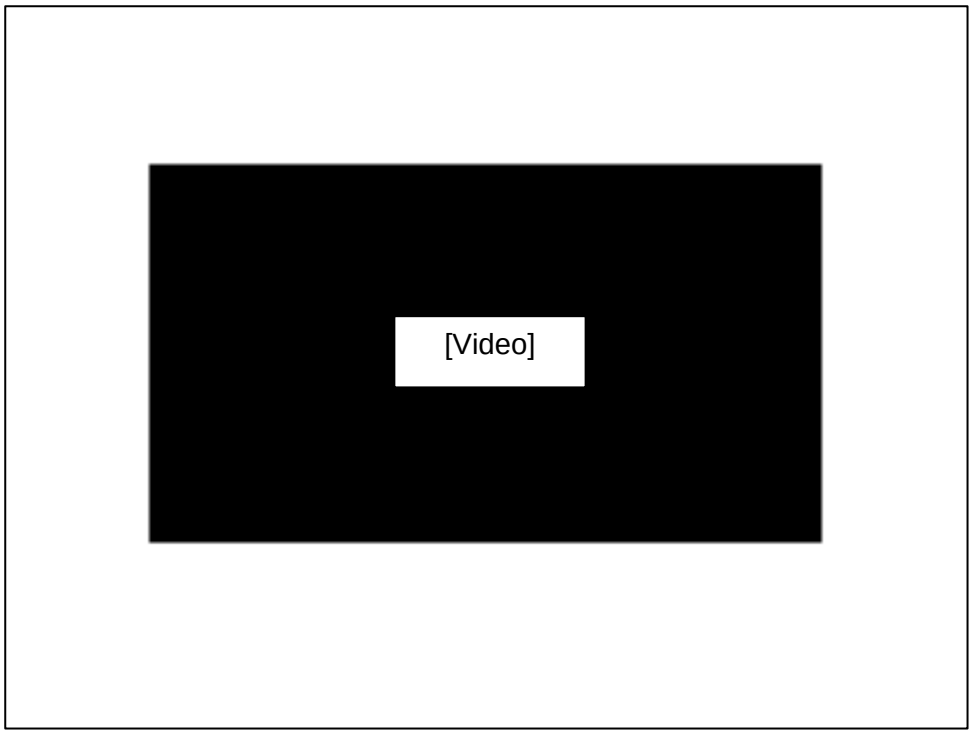
Go and stand by the route which you already follow (to some extent). Discuss with others that are there/write down on post-its any examples you're willing to share/tips you would give to other people about what works for you.

Go and stand by the route you're least interested in. Discuss with the others the reason for 2 minutes.

Go and stand by the route you're most interested in. Discuss with others the reason for 2 minutes.

We are scheduled to have a break at 7. You could spend some time now looking through the resources pack that's there and see if anything interests you/add any post-its you want to. We will start back seated at 7.15.



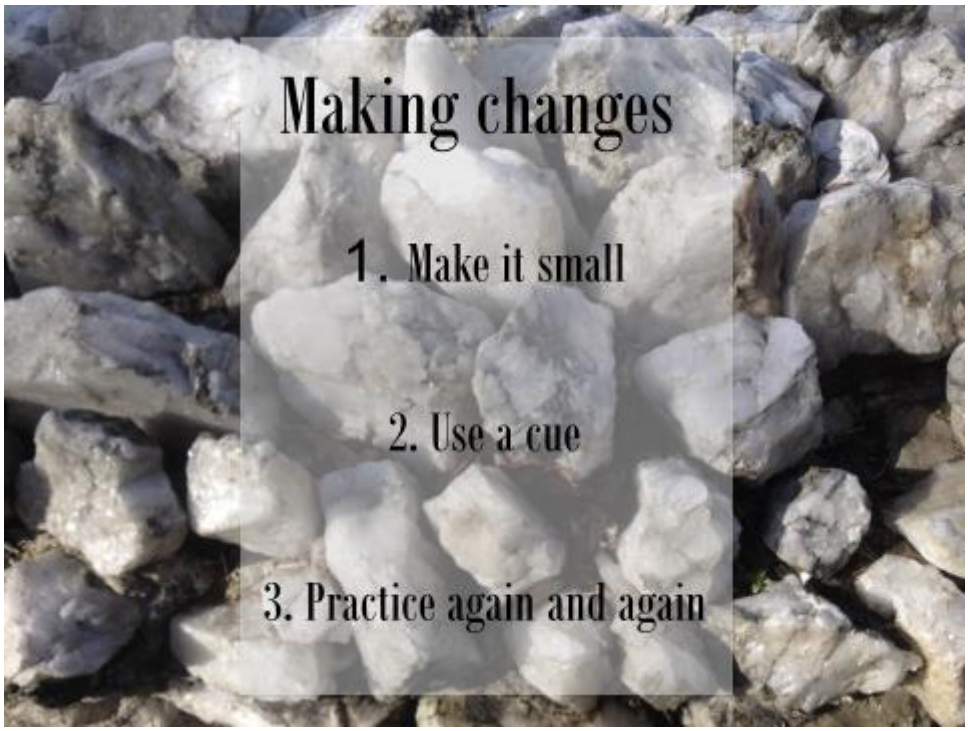


This next section of the workshop will be on some research about habit formation. This is for any habit at all, regardless of whether it is related to wellbeing.

Explain benefits of trying to make something a habit

- They last a long time
- Habits conserve our energy. We don't have to always act intentionally we can act automatically.
- High effort to start with, no effort later.

Short video about learning and brains: https://youtu.be/ELpfYCZa87g

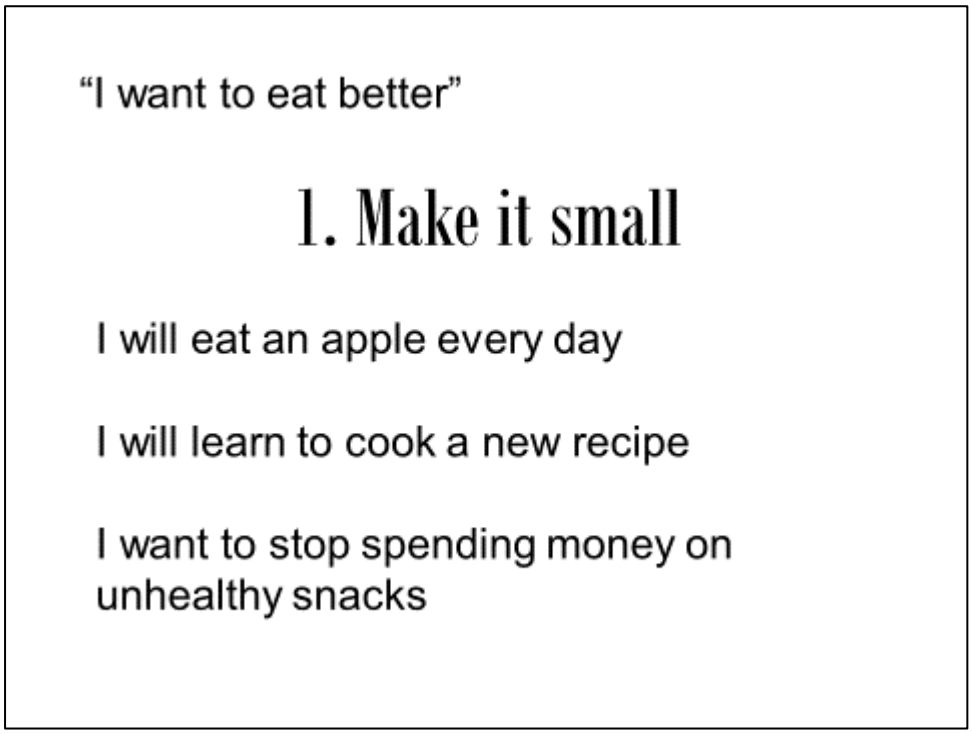


There are three important steps to forming a habit.

The first, is ‘make it small’. Small, simple actions can become habits. For example, ‘I want to be more active’ could be changed to ‘I will take the stairs rather than the escalator’.

The second, is to use a ‘cue’, which is something you do anyway, or something in your environment. For example- the cue for taking the stairs could be ‘seeing an escalator’.

The third, is to practice again and again. As we saw in the video, every time you see a cue and then do the small action, the connection between these two is strengthened in your brain. If you perform the action every single time you see the cue, you will form a habit that becomes easier with time.



Group practice of ‘make it small’. If an aim is too broad/complex it can’t become a habit (and people often try and then feel bad when they don’t succeed). Ask the group what small actions could be potentially become a habit.

3 examples are given- these could be different for everyone

"I would like to take my asthma medication regularly"

2. Use a cue

- Cues from the time of day
  - Take medication when alarm clock goes off/when eating breakfast/when brushing teeth
- Cues from location
  - Putting medication next to alarm clock/putting it next to the kettle/on your desk at work
- Cues from 'reminders'
  - Setting an alarm on your phone/using a medication reminder app/putting a note in a calendar/tying a piece of string as a reminder round a regular coffee cup

Everyone is different! What cues might work in your life? They can be unrelated to the action. Be creative!

Example from PWPs life?

And the third step is practice consistently. Every time you repeat the action when you see the cure, this strengthens the connection in your brain.

Now we will have 10 minutes to plan something for yourself and your own wellbeing.

Think of something from the 4 routes that you might like to try to protect your well-being.

Feel free to wander around the room- there are resource packs in each corner and post-it notes for ideas.

Go through the 3 steps of habit formation, which we will leave up on the projector

Do what's write for you- make notes or don't make notes, discuss with someone or sit alone.

We have covered...

- Background
- The 4 PRotect Routes with examples
- The 4 corners task- What's important to you?

-----15 minute break ----

- Importance of habits
- The 3 steps to making changes
- Final task- Planning for you

Take your booklet and any resources you want with you.

Think about any plans you want to take forward. One is enough!

You could discuss with friends or family. We have extra booklets if you want to pass any on.

Use cues that work for you.

In 1 month we will have a review phone call to see what is working, and ask for any tips you might want to pass on to other people.

Thanks for your participation

Any questions or comments?

Review phone call in one month

Good luck!

PRotect

Promoting Recovery
after depression

PRotect

Promoting Recovery after depression

Welcome. This booklet has been designed for people who want practical tips to help protect their mental wellbeing. It is tailored to people who have recently had low-mood or depression, but we think it could be used by anyone wishing to invest in their own mental health. We hope you find it enjoyable, useful, and that it sparks ideas to try yourself.

Some people recover from depression and stay well. However, as you may know, some relapse or struggle with low mood over a longer time. There are various reasons for this, many of which are beyond our control.

We wanted to focus on things that you can control, that might help protect wellbeing. We have brought together a broad range of research about depression, with personal experiences of what helps others.

What's the point of this booklet?

For you to continue your journey into wellness and recovery. To extend your skills at 'being your own therapist' so that you are less likely to relapse in the future.

How?

We look at four possible routes to protecting your mental health. There is a short activity to make you think about each route. We give the research background, and examples from normal life. You can add your own ideas.

It's up to you...

Which routes are important to you? Which ideas could fit into your everyday life? There is no right or wrong way, we are all different.

Going forward

We will give some tips on how to make changes that stick. You can make a 'PRotect plan'. Later you can review how things are going, and think of tips you would like to pass on to others.

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Background

The route to PRotect

To start, here is an overview of some of the thinking and research that led to the making of this booklet.

Humans are complex and unique, and depression and wellbeing are probably different for each of us. Life experiences, the environment, genetic factors, and thinking patterns have all been linked to depression.

But we all have one thing in common, a complex organ that brings together all these factors: our brains.

There are more neurons in our brains than number of stars in our galaxy. These 100 billion cells are each connected to 10,000 others, making 100 trillion connections. It is in these connections that electrical messages are sent. Every time we see a smile, or smell cut grass, there is an electrical and chemical reaction in our brains. Every time we think, electrical signals in our brain strengthen the connection between certain neurons.

The great thing is that, even as adults, our brains change and adapt. If I repeat an action, my brain will learn the connections needed for this action, and it will be easier in the future.

The aim of the PRotect booklet is to think about ways to 'train our brains' in a way that might offer long-term protection of wellbeing.

The world around us impacts our mental health. For example, identical twins have the same genes but might have different mental health. Major life events like loss of work or the breakup of relationships can sometimes lead to depression. On the other hand, positive inputs from the world around us can help protect our wellbeing. We will focus on these positive inputs in:

PRotect Route 1: Positive Inputs

Our brains and minds are constantly making lightning-speed calculations, too quickly for us to be aware of. Computer tasks and reaction tests in research studies have shown that these can be different when a person is depressed. Some studies have also suggested ways we could 'train' these inner workings in a way that protects from future problems. We will suggest some of these in:

PRotect Route 2: Inner Workings

Thoughts and actions are affected by depression. It's common to have a negative view of yourself and the world, and to focus on this a lot of the time. This can make you avoid activites, even ones that might usually make you feel good. We will look at ways to plan positive thoughts and actions in:

PRotect Route 3: Positive Outputs

People with physical health problems are more likely to become depressed. People with depression are at risk of physical health problems too. When your mood is low everyday activities to care for yourself like showering can become difficult. We will look at health and self-care in:

PRotect Route 4: Physical Health

PRotect Route 1 Positive Inputs

5 minute activity: Write a rough diary of your last 7 days. Is there anything you came across, or did, that had a positive impact on you?

The Research

Research suggests that things that happen around you have an impact on the chemicals in your brain, and so your wellbeing.

A positive influence could come from having a hobby you enjoy, having friendships or contact with people, enjoying work, or going to a peer support group.

What works for you?

You can't control all of these things! But thinking of ways that you can have regular positive inputs can make any negative influence less important.

Benefits

-these are pre-planned so don't depend on your current mood
-can be consistent over time

'Inputs' are everything that we come across that has an impact on us

Here are some tips from others:

"I try to phone my mum when I'm walking home from work. It's good when life is really busy to take the time out and have a chat. I can tell she's pleased too."

"I haven't been able to work in a while which has been difficult. I volunteer at a charity shop now and it's great – reminds me of my strengths and it's a nice bunch of volunteers there."

"I easily get too busy and that makes me stressed. I need an evening to myself each week, so now I block that out in my diary which makes it easier to say 'no' if someone asks me to do something."

"I buy myself a bunch of flowers each time I do a big shop. Just a cheap bunch but I get a lot of enjoyment from seeing them in my bedroom"

What are your thoughts about this route?

PRotect Route 2 Inner Workings

5 minute activity

Move into a comfortable position and close your eyes. Start to pay attention to how your breath feels. Notice the sensation as air comes in through your nose, travels down into your lungs and comes back out again through your mouth. Try not to change your breathing, you don't need to. It's normal for your mind to wander, so don't worry when this happens. Gently bring your focus back to your breathing.

The Research

We are not consciously aware of all the inner workings of our brains. Research suggests that these automatic processes may make a difference to your mental health.

Some people like to think of the brain as a muscle that needs regular exercise to ensure it stays strong and works well. Again, everyone is different, so it is best to try a few things and see what works best for you personally.

What works for you?

There are some activities that other people find helpful. You could try to see if they suit you. Examples are:

-meditation or mindfulness
-apps that aim to improve 'cognitive biases' or 'cognitive control'
-games (crosswords and puzzles)

Benefits

-activities are often fun
-can be done when convenient

Here are some tips from others:

"I have tried some 'cognitive bias modification' games online. I like computer games so it's pretty good to think I can do ones that are good for keeping my mood OK. I'm not that sociable so it suits me to be able to do something to help my mental health that I can do on my own and whenever I feel like, even if I'm feeling low. Also I think it makes me less stressed."

"I am going to learn meditation. When I have tried it in the past I have felt good - not happy necessarily, but just good somehow."

"I find that thinking clearly is a real sign that I'm well and I want to do exercises to strengthen the muscle that is my brain. I do a Sudoku or puzzle with my breakfast in the morning. I find it really absorbs me and wakes me up for the day."

Does any of this appeal to you?

PRotect Route 3 Positive Outputs

The Research
It is easy to miss the good things, and to be hard on yourself. This is especially true when you are feeling low, but can be the case for anyone.

Thinking positive thoughts on purpose can make some people feel happier and increase their self-esteem. This could be thinking of things you enjoy, are grateful for, or are proud of. These feelings then lead naturally to more positive thinking.

Positive actions, such as helping a friend or praising a colleague can also improve your own mood. At the same time, you may help the other person's wellbeing.

What works for you?
Looking at positive outputs can seem 'fake' or strange at first. You might decide it's worth a try.

Benefits
-activities become easier over time
-other people may benefit too

'Outputs' are our thoughts and actions

5 minute activities

- *Write a note of thanks to someone that has done something kind.*
- *Imagine a friend was asked to say 3 good things about you. What might they say?*
- *Consider a moment in your life when a negative event led to positive consequences that you were not expecting.*

Here are some tips from others:

"I've started keeping a diary which is good to keep track of my mood. I write something everyday that I've done well. It's not normally a big achievement but it's nice to notice them."

"When I brush my teeth at night I think of three things I'm grateful for. I do repeat the same things sometimes!"

"I have been doing some online positive psychology questionnaires. There's one about personality strengths and I scored high for humour and teamwork. Just because I have been depressed doesn't mean that's everything, there are lots of other parts of who I am".

How does this route sound to you?

PRotect Route 4 Physical Health

The Research
Our bodies and minds are linked in many ways and affect each other. Some activities that we think of as mainly being for your physical health, actually also improve well-being. For example:

-taking prescribed medication
-eating a balanced diet
-exercising
-reducing alcohol consumption
-avoiding drug misuse

What works for you?
Everyone is different, and each of our health concerns will be quite different.

Benefits
-you could improve your physical as well as mental health.

5 minute activity

List as many examples as you can, of ways people take care of their physical health. Be specific! Think of your own habits, as well as friends or family.

Here are some tips from others:
"Eating properly is crucial for me because it's making the effort to look after myself."

"I would say exercise definitely helps as everyone says it increases endorphins etc. Listening to music to relax works too. I have a friend who is struggling with stuff and whenever she gets too bad she'll go into her room, blast pop music and just dance by herself. She also does Zumba which helps her a lot."

"It's easy to have a bit too much to drink. I downloaded an app where I monitor what I'm drinking, it makes it easier to keep track of what I'm consuming and spending too."

Is an aspect of physical health important for you?

You

Which of the routes is important to you?

Which of the routes is less important to you?

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Which of these routes do you already follow? Can you think of specific examples?

Have you had any ideas about new things you want to try?

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Making changes

The great thing about habits is that they are automatic: once you are used to doing something it is easy to keep doing it. So how do you form new habits? Researchers have looked at lots of new habits in hundreds of people, and found there are 3 vital steps:

1. Make it small

Small, simple actions can become habits. If you have an aim, break it into small tasks, such as thinking of 3 things you're grateful for each day (rather than a bigger more complicated aim like 'think positively'). Small actions are important, and lead to bigger changes. If you don't make it small there is a risk of setting yourself up to fail, and then feeling worse for having tried.

2. Use a cue

Try to form a habit based on something you do anyway. For example, put a band around your toothbrush to remind you to think of 3 things you're grateful for whilst brushing your teeth.

3. Practice again and again

At first it will take effort to always repeat the small, simple action when you see the cue. The more times you practice your new habit the more automatic it will become. You will not need to put a lot of thought or energy into it after a while.

5 minute activity: Try to apply the 3 steps to one of these 'broad aims'

"I want to feel healthier, go the gym more and eat better"/"I want to learn to speak Spanish"/"I want to get more sleep"

What small, simple activity could be started? What everyday cue could be used to remind the person of the new activity?

Example- I want to get more sleep

1. Make it small

I will only spend 15 minutes on my laptop before bed each night.

2. Use a cue

I will leave a post-it note on my laptop that says '15 minutes'. When I see it I'll remember to set a timer, and will close the laptop when the timer goes off.

3. Practice again and again

If I'm strict at first and close my laptop when the timer goes off, over time it will become second nature

Personal PRotect Plan

-What activity from the 4 routes do you want to try?

-How will you apply the 3 steps to making changes?

Here is some space to make your own plan. You can do this in whatever way works for you, but start with one idea, and you can always add more later.

Review

-How has your time been since you made your personal PRotect plan?

-Is the plan working for you, or would you like to try something different?

-Would you like to add any other activities?

Here is some space to review how things are going.

Tips to pass on

Do you have any advice to pass on of how to stay well after depression? What works for you?

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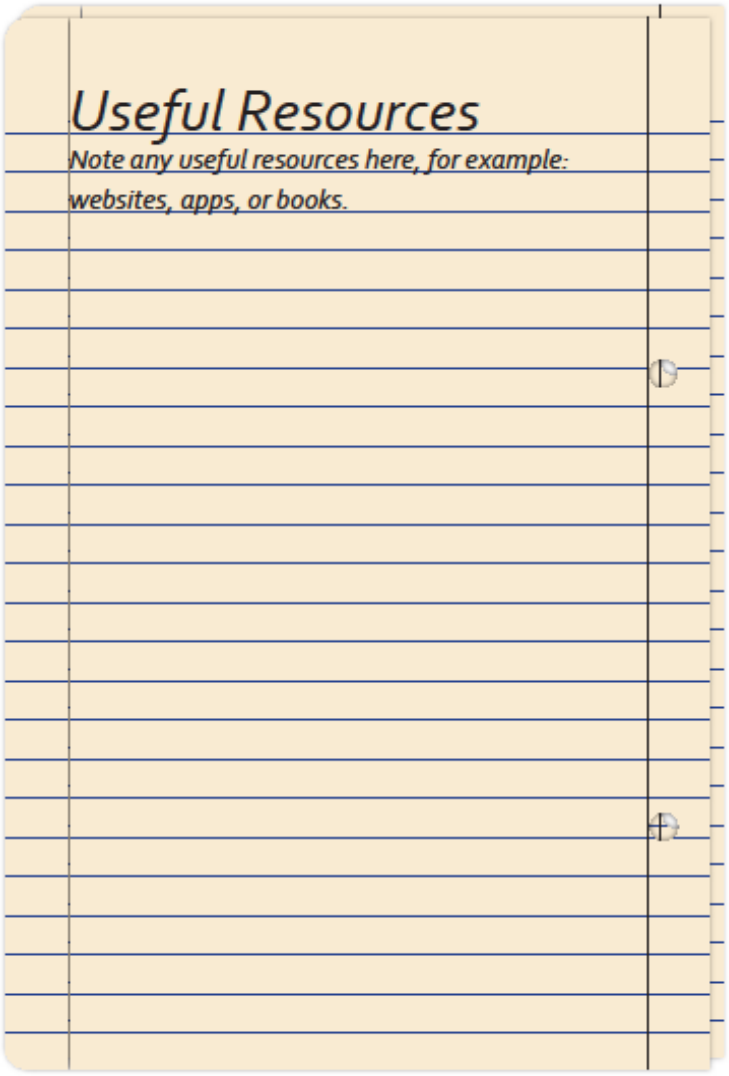

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LONDON'S GLOBAL UNIVERSITY

PRotect trial- Participant Information Sheet

We would like to invite you to take part in a new study about wellbeing after a period of depression or low mood.

Taking part would involve answering some questions about how you are feeling in 3 and 6 months' time. It also may involve trying a brief wellbeing course.

Before you decide whether to be involved, here is some more information.

. **What is the purpose of the study?**

We want to research the period after recovery from depression. It is thought to be an important time, as the risk that a person will relapse reduces during this time. We also want to test a new wellbeing course and see whether it is useful, and whether it should be offered to more people.

. **Who is doing this research?**

The study is being conducted by researchers at University College London (UCL), led by Professor Stephen Pilling, in partnership with clinicians in Camden and Islington Improving Access to Psychological Therapies (IAPT) services. Our funding is from the British Psychological Society (BPS), although they have no role in deciding what happens in the study. Previous service users and members of the public have contributed to the study design and the wellbeing intervention.

Katherine Clarke, a researcher at UCL, is in charge of the day-to-day running of the study, and will talk to most participants at some point.

. **Why have I been invited?**

We are inviting people who have received treatment from IAPT clinicians for depression or low mood. We are looking to recruit 130 people to the study.

. **Do I have to take part?**

No! It is up to you to decide if you want to join the study. Also, you can decide to leave at any time- just ask us and we will stop contacting you and delete your contact details. You don't need to give us a reason, and it will have no impact on your normal care.

. **What will I have to do?**

We would like to ask you some questions in 3 months and again in 6 months, about how you have been feeling. We can do this over the phone or in person, whatever is best for you. All the answers you give us will be kept confidential. It will take about 30-45 minutes each time, and we will give you £15 in shopping vouchers each time to say thank you.

We would also like half of participants to try the brief wellbeing course. We want to see if it is useful, so we need to compare the experience of a group of people who have tried it, to a group of people who haven't. To do this fairly, we need to put people in each group at random. If you agree to be in the study, this means you will have a 50/50 chance of being in the course group, or in the evaluation-only group. The wellbeing course consists of an introduction telephone call, a 2-hour group workshop, and a follow-up phone call. We will also give you a booklet with tips and there will be tasks to think about between sessions.

We welcome your feedback about the intervention and trial, and would like to interview 8 participants about their experience.

. What are the advantages of taking part?

In previous trials we have found that participants often appreciate the opportunity to reflect on how they are doing during follow-up phone calls.

The aim of this research is to better understand and better assist people who have recovered from depression. Your participation will contribute to helping someone who recovers from depression in the future.

. What are the disadvantages?

Being a trial participant will take up some of your time for the follow-up phone calls, and potentially for the wellbeing course. We will do all we can to make sure the follow-ups are at a time convenient to you. We don't think this trial will put you at a significant risk.

. Who has reviewed this study?

The project has received ethical approval from the Camden and King's Cross Research Ethics Committee.

. What if something goes wrong?

If you have any concerns or wish to complain about any aspect of the way you have been approached or treated by members of staff due to your participation in the research, National Health Service or UCL complaints mechanisms are available to you. Please ask your IAPT therapist, or contact Katherine Clarke or Professor Stephen Pilling (contact details at the bottom of the page) if you would like more information on this.

In the unlikely event that you are harmed by taking part in this study, compensation may be available. If you suspect that the harm is the result of the Sponsor's (University College London) or the hospital's negligence then you may be able to claim compensation. After discussing with your therapist, please make the claim in writing to Professor Stephen Pilling, who is the Chief Investigator for the research and is based atUCL. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

. What about confidentiality? What will happen to the information you collect about me?

We will not tell your GP or anyone outside of the research and IAPT team that you are in the study. We will keep your name and contact details separately from any information we collect about your wellbeing. We will delete your name and contact details once the study is complete. The final results of the study will be summarized, and may be published in a journal. However this will not include any details that could identify you.

If during the study we become concerned about your safety, we will direct you towards appropriate services to help. We may also need to tell your GP, with or without your permission. However, this is the only time we would ever break confidentiality.

. What happens next?

If you agree to take part, your contact details will be passed on to Katherine Clarke at UCL. She will phone and ask you some questions to check that you are suitable for the study. If you are, we will randomly put you in the intervention group or the monitoring group. If you are in the intervention group, someone from IAPT will contact you to explain the wellbeing intervention and arrange for you to attend the workshop. If you are in the monitoring group, a researcher will let you know, and contact again in 3 months to ask about how you are.

Further information and contact details

Please do not hesitate to contact us if you have any questions or concerns, at any time:

Katherine Clarke (Principal Investigator) k.clarke@ucl.ac.uk **0203 108 3260**
Centre for Outcomes Research and Effectiveness (CORE)
1-19 Torrington Place, University College London, London WC1E 6BT

Alternatively, you can contact: Professor Stephen Pilling (**Chief Investigator,** Director of CORE and Katherine Clarke's academic supervisor) s.pilling@ucl.ac.uk with the email subject 'PRotect trial' 0207 679 1784

LONDON'S GLOBAL UNIVERSITY

UCL

PRotect trial- Participant consent Form

Centre Number:_____

Part 1: Consent to be contacted by UCL researchers

Please read each statement and then initial the box

☐ I confirm that I have the information sheet (Version..... dated ...../...../.....) and will take it with me to read through.

☐ I am interested in taking part in the study, and agree to be contacted by the researchers about the possibility o participating.

_____ _____ _____
Name of participant Signature Date

Please provide your preferred contact details

_____
Telephone number

_____
Postal address

_____
Email address

_____ _____ _____
Name of IAPT worker Signature Date

SCREENING phone call procedure

Data Protection
Any participant names or contact details must be sent as encrypted files attached to emails, and no personal data should be in the body of the email itself. No other information such as outcome assessments should be sent in the same email as any name or contact details. Email accounts must be accessible only with a password.

Managing risk
You should follow the research settings risk procedure during the screening phone call. Make sure to have a copy of the files in front of you when making phone calls: the Research Settings Risk Protocol and the Research Settings Risk Form. Explore risk if an issue comes up, assess, and advise the participant as appropriate. Complete the risk form and follow-up.

As the client has been discharged from the care of IAPT service, you may need to inform their GP about any risk issues (as the client's current care provider).

General documents needed:
- Research Settings Risk Protocol
- Research Settings Risk Form
- Participant Information Sheet

Documents for each participant:
- Participant's completed Consent form A (from IAPT clinician)
- Copy of Consent form B to be completed
- Envelope to be stamped and addressed for consent form

You will be given the contact details of clients who have agreed to be contacted about the study. You should try and phone participants for their screening phone call 48 hours after they were given the information sheet by their IAPT clinician.

- Ensure you have the documents listed above in front of you
- Open the database for inputting baseline and trial data

Part 1: Introduce yourself and the reason you are calling

Hello, I'm Katherine. I'm phoning about the Protect trial you agreed to be contacted about. Is now a good time to talk?

***NO-** Can we arrange a better time and I'll phone you back?*

***YES-** Great, this should take about X-X minute. First I will explain a bit about the study and see if you do want to be involved. Then I will then ask you some questions to see if you meet the criteria to be in the study. If you do, I will ask some final questions and then explain what will happen next. Does that sound OK?*

Part 2: Informed consent procedure
(NB: If there are any concerns about a participant's capacity to give informed consent, the phone call should be continued but these concerns should be raised with Stephen Pilling (s.pilling@ucl.ac.uk, 07931886334) ASAP.)

LONDON'S GLOBAL UNIVERSITY

UCL

PRotect trial- Participant Consent Form

Centre Number:_____

Part 2: Consent to participate in the PRotect trial

Please read each statement and initial the box

☐ a) I confirm that I have read the information sheet (Version..... dated ...../...../.....) for the PRotect trial and have had the opportunity to ask questions and have these answered.

☐ b) I understand that taking part in the study means I will have a 50% chance of being in the group who receives the PRotect course, and a 50% chance of being in the group who are monitored only.

☐ c) I understand that my participation is voluntary and that I am free to withdraw at any time without giving a reason, and my medical care and legal rights won't be affected.

☐ d) I understand that my information will only be available to my care team, and researchers involved in this project. It will be stored incompliance with the Data Protection Act (1998).

☐ e) I understand that relevant sections of my data collected during the study may be looked at by regulatory authorities or the NHS Trust, but that this will only be for the purposes of evaluating the research. I give permission for these individuals to have access to the study data.

☐ f) I agree to take part in the above study.

_____	_____	_____
Name of participant	Signature	Date
_____	_____	_____
Name of researcher	Signature	Date

Assessing and Reporting Risk in Research settings

The following principles and procedures govern risk assessment and reporting in follow-up assessments by researchers with participants experiencing psychopathological symptoms. This study does not include routine management of people at acute risk of suicide by trial clinical workers or research associates.

When to undertake a risk assessment

Risk assessments should be undertaken at the following stages:

a) Initial contact with the Research Team for the first research assessment.
b) Any subsequent contacts

Although formal assessment of risk is limited to the above situations, if significant risk (probable level B or C) is disclosed in the course of a research interview this should be reported to the participant's GP, in line with the procedures in this protocol.

General procedures

All research associates, research assistants and students will have received risk training. Whenever any significant risk is identified, a risk assessment should be completed and (counter-) signed by the clinical lead as soon after the assessment as possible.

- Any significant, but not imminent risk should be reported to the person's **GP** and, if appropriate, other health care professionals, as soon as is reasonably possible.
- Any imminent risk should lead to the **immediate** involvement of the appropriate emergency health services. Clinical leads must ensure that research associates, research assistants, and trial workers and students are fully informed and competent to follow the procedures.

When clinical leads are away they should ensure appropriate cover is arranged for any risk issues that might arise in their absence.

Knowing when a Risk Assessment is required

Following indication of risk from questionnaire items, or any clear report of suicide/self-harm ideation, a six-question risk assessment should be carried out.

Indicators include (one is enough):

- A score of 1, 2 or 3 on Q9 of the PHQ9 (*Thought that you would be better off dead or of hurting yourself in some way*)
- Suicidal ideation in the LIFE evaluation interview
- Suicidal or self-harming behaviour in the LIFE evaluation interview

Exploring Risk in Research Interviews

After asking the following questions the level of risk; A, B or C can be determined

To introduce the risk assessment*: "I'm quite concerned about your responses on some of the questionnaires that you've completed. I see you've mentioned that you're feeling 'xxx/having thoughts of harming or killing yourself'.*

It's really important for us to make sure that you're receiving the right kind of support. I hope it's okay with you if I follow this up with some more questions that will explore these feelings in a little more depth.

THOUGHTS

1. Do you know how you would kill yourself? Yes / No

If **yes –** details

PLANS

2. Have you made any actual plans to end your life? Yes / No

If **yes –** details

ACTIONS

3. Have you made any actual preparations to kill yourself? Yes / No

If **yes –** details

4. Have you ever attempted suicide in the past? Yes / No

If **yes –** details

PREVENTION

5. Is there anything stopping you killing or harming yourself at the moment? Yes / No

If **yes –** details

6. Do you feel that there is any immediate danger that you will harm or kill yourself? Yes / No

Details:

Researcher Risk Protocol

Actions by Researcher	*Tell Participant*
All answers 'no' apart from Q5 'yes': ↓ **A** →	*I can see that things have been very difficult for you, but it seems to me these thoughts about death are not ones you would act on – would this be how you see things? (if they say yes) I would advise you to make an appointment to see your GP to talk about these feelings.* ***(Also provide leaflet)***
1) 'Yes' for any one of Qs 1-4; plus 'yes' for Q5 and 'no' for Q6 **OR** **2) 'No' to all questions including Q5** ↓ **B** →	*Things seem to be very hard for you right now and I think it would help if you were to speak to your GP about these feelings. I will be writing to your GP to tell them that you have been here today and have been having some troubling thoughts. I would also advise you to make an appointment to see your GP to talk about these feelings.* Send letter *'Non-NHS recruitment suicide risk GP letter v1.0 – 05.12.14'*
1) Scoring 'Yes' for any one of Qs 1-4 AND 'no' to Q5 **OR** **2) Scoring 'yes' to Q6** ↓ **C (possibly) actively suicidal** →	*I am very concerned about your safety at this moment. I am not qualified to deal with this on my own as I am not a clinician, but I would like you to talk to one right now. I am going to contact someone to come and talk to you.*

If Q6 is answered "yes" participant needs immediate help – **do not leave them alone**. Follow the chain of supervisory clinical contact (below) and enact immediate risk procedure. If no clinical contact can be reached, order taxi to take participant to Accident & Emergency, University College Hospital, Euston Road, NW1 2BU.

After completing this risk assessment form, the *Research setting suicide risk reporting form v1.0* should be completed and discussed with the clinical lead as soon as possible.

Telephone Chain – Clinical Lead

1) Steve Pilling (text preferred: [redacted])
2) Patient's GP – or any available doctor
3) 999

Randomisation procedure

Data Protection
Any participant names or contact details must be sent as files attached to emails, and no personal data should be in the body of the email itself. Email accounts must be accessible only with a password.

General documents needed

- Excel randomisation log
- Intervention letter template
- Evaluation only letter template
- PRotect booklet (paper and electronic copy)

You will be emailed with the contact details and unique participant ID of trial participants. We aim to randomly allocate participants within 48 hours of receiving their information. You will need to

1. **randomly allocate participants to the intervention or control arm**
2. **notify necessary parties of the results of the randomisation.**

1. Randomisation

- Log in to the trial on www.sealedenvelope.com
- Randomly allocate all participants in the list to the intervention or control arm
- Record the allocation in the excel randomisation log

2. Notifying necessary parties

Participants
Notify participants of their allocation by letter and by email

If person is allocated to the control arm

- Edit evaluation only letter template with the participant's details
- Post to them
- Email them the letter as an email attachment

If person is allocated to the intervention arm

- Edit intervention letter template with the participants details
- Post letter along with the PRotect booklet to the participant
- Email them the letter and the PRotect booklet electronic version

Shah Alam at iCope

- Make a list (excel file?) of participants allocated to the intervention arm, include name DOB and address but **DO NOT INCLUDE UNIQUE PARTICIPANT ID.**
- Email this to the shah.alam@candi.nhs.uk as an attachment. Copy Adam in to the email.

INTRODUCTORY phone call intervention fidelity measure

Managing risk
You should follow your normal risk procedure if you are concerned about the safety of a client during any contact you have with them. As the client has been discharged from the care of IAPT service, you may need to inform their GP about any risk issues (as the client's current care provider). If you have concerns, please also get in contact with Kat (k.clarke@ucl.ac.uk, 02031083260).

Introductory phone call

Name of PWP:_____

Date of call: _____

	Tick when complete Add details where prompted	
	Yes	**No**
Introduce yourself		
Ask- Did they receive the booklet?		
Introduce the intervention		
It's an add-on for people who have improved from an episode of low-mood or depression.		
It's based around a booklet, with a 2-hour workshop and a 20 minute review phone call one month later.		
It combines research with expertise from people who have been depressed in the past.		
We will focus on 4 wellbeing 'routes'.		
You are welcome to look through the booklet before the workshop, but don't need to.		
Ask about the participant and any expectations/barriers to attending		
Expectations/barriers to attending given by client and explored		
(if time) Ask if the client has any questions for you		
Arrange workshop attendance	**Date:**	**If not, reason for this:**
Exact length of phone call (minutes and seconds)	**--:--**	
After the phone call Send the details of the workshop to the client via their preferred method.	**Sent?** **How?** **Date completed**	

Consent to Audio-record the Workshop

We would like to make an audio-recording of the workshop today. This is in order to

- Monitor how the workshop is being delivered
- Improve the workshop for the future

The recording would only be used for research purposes, and not for any training or clinical purposes. The recording will be passed to researchers at UCL after the workshop, and will be destroyed after it has been analysed (within 6 months). Any identifiable data will be removed.

Please tick one box:

☐ I consent to this workshop being audio-recorded, and these tapes being used by the research team at UCL to evaluate the workshop.

☐ I do not consent to this workshop being audio-recorded.

| --- | --- | --- |
| Name of participant | Signature | Date |

Appendix R Audio-recording workshop consent form

ONE MONTH FOLLOW UP phone call intervention fidelity measure

Managing risk
You should follow your normal risk procedure if you are concerned about the safety of a client during any contact you have with them. If you have concerns, please also get in contact with Kat (k.clarke@ucl.ac.uk, 02031083260).

Introductory phone call

Name of PWP:_____

Date of call: _____

	Tick when complete Add details where prompted	
	Yes	**No**
Introduce yourself		
Ask how the client is		
Talk about the workshop and their plan/the previous month		
Short summary:		
Any advice for others who have recovered from an episode of depression?		
Please note, giving as much detail as possible and write verbatim where possible:		
Ask about the future		
Short summary:		
Ask if the client has any questions for you		
Short summary:		
Exact length of phone call (minutes and seconds)	**--:--**	

PRotect Trial Interview Schedule

We will seek to conduct a brief semi-structured interview with all trial participants following completion of their six-month research interview. This will not be recorded so make notes about the participants answers in as much detail as possible, using their own words wherever possible.

Interview introduction

- Thank the person for their participation
- Explain that this was their final research interview
- Explain that we would like to understand the experience of trial participants
- Ask if they will answer a few further questions on this topic.

Thank you very much for answering those questions, and for participating in this trial over the last 6 months. This was your final research interview, and your participation has been invaluable for us. We would like to explore the experiences and views of people who have taken part in the trial so I will ask a few further questions about this if that is OK with you. Please be as honest as possible with your answers as your feedback is very useful and important to us. There are no right or wrong answers. You are free to comment or not comment on any issue that comes up, or to finish the call at any point.

Interview style

These interviews will be semi-structured. At first, let the interviewee tell their story freely. Use the points given below to focus the interview where needed.

Topic guide

1. **General trial experience**

How would you describe your experience of being part of this trial?

- Clarification of *what* experiences were part of the trial (e.g. the question does not relate to the acute treatment received from the IAPT service)
- Clarification of timeframes (e.g. *you joined the trial on X date and had a first phone conversation with X. You answered similar questions to those I asked you today*)
- Exploration of any points stated (e.g. *What do you mean by X? What does X mean to you?*)

2. **Experience of randomisation**

This was a randomised study, so 50% of participants were offered a wellbeing intervention, and 50% of participants were not. Do you remember if you were offered the wellbeing intervention?

- Clarification of what the wellbeing intervention entailed (e.g. it would have been offered by someone at the IAPT service, who might have invited you to a workshop)
- How did you feel about being offered the intervention/not being offered the intervention?

If the participant answered YES proceed to part 3, if the participant answered NO proceed Interview close.

3. Experience of the PRotect intervention

When you were offered the intervention, did you decide to participate?

- *What made you did you decide to participate/decide not to participate?*

What did you think of the intervention?

Repeat for each the introductory call, the workshop, and the review call. For each: first check that the person knows what is being referred to and recalls the call/workshop. After this is establish ask about their experience: *How did you find that? What happened? What was that like? How did you find the intervention?*

Did you find the intervention useful? Why/why not? Do you use anything from the intervention now? If yes ask for specific examples.

Interview Close

Thank you very much for answering those last questions, its useful for us to understand a little about your experience as a participant in this trial. Before we finish, do you have any questions that you would like to ask me?

PRotect: Trial Clinician Focus Group Plan

Set-up/Table plan

	Krupa Vakani	
Ruhana Hussain		Laura Franklin
Eleanor Popp		Shah Alam
Symone McEachron		Pinar Marasli
	Alice Winters	

- Water and cups on table
- Audio recorder and materials with Alice
    - Large piece of paper for part 2.
    - Paper and pens for part 3.
    - 8 copies of the PRotect booklet for part 5.
    - Cards with future considerations for part 6, plus some blank cards.

Introduction- Krupa to lead

Welcome. I am Krupa, I'm a masters' student working on the PRotect trial. I'll be running the focus group today alongside Alice, who has been working on the trial too.

The aim of the focus group today is to find out about your experiences delivering the PRotect intervention. We will pose 6 topics to the group. Please do talk with each other and discuss answers- there is no need to direct your answers just to me and Alice. I have a few things to mention before we start.

- *The session today will be recorded. It will be transcribed and your names will be removed before the transcript is passed on to Kat.*
- *The group will last 45 minutes. At the end Kat will magically appear with pizzas and drinks!*
- *Toilets are (then give directions).*
- *Ground rules: discuss amongst yourselves but please try to make sure everyone has a chance to speak. We have limited time so try not to repeat things. We will keep what is discussed in this room and not talk about it outside of this context (confidentiality).*

Any questions?

I will start recording now.

To start let's go around the group, introduce yourself, and say a few words about why you are interested in relapse prevention for depression. Do use your own names as this will help the transcriber to identify who is speaking later. The names will be removed from the transcript which is given to Kat.

1. **Context**

(Krupa to lead) *We would like to understand the context in which you started delivering the PRotect intervention. Can you tell me about the services you are working in?*

- *Have there been changes in the service during the trial period (2015-2017).*
- *How does the intervention fit into existing practice?*
- *How did the service impact the delivery of the PRotect intervention?*

2. **What is the intervention?**

(Alice to lead) *I'd like to now ask about your understanding of the PRotect intervention. Feel free to shout out and I'll note down on this flipchart paper your responses.*

- *What does the intervention consist of?*
- *What is the aim of the intervention?*
- *Who is the intervention designed for? Why do you say that?*

3. **Your experience of the intervention**

(Krupa) *Now we would like to talk about your experiences with delivering the intervention (including the workshop and review calls). Think about your own experiences. You have some paper on the table. Could you note down a good moment, and a challenge you encountered. I will give you a few minutes to think about this.*

- *OK has everyone got something? Who would like to share theirs?*
- *Did anyone have something similar/different?* Discuss

4. Evaluating the intervention

(Alice) *Moving on, we will now look more specifically at evaluating the intervention. I have some statements I will read you. Tell me on a scale of 1-10 how much you agree with each statement, and why.*

- *The group setting was beneficial to participants*
- *It would have been better as an individual session* (then try to explore any different responses to the first 2 statements)
- *The workshop didn't add anything new for clients above what they had covered in their treatment sessions.*
- *The 1 month review calls were useful*
- *The 1 month review calls were difficult to arrange*
- *The workshop suited some clients but not others (Why? Who did it work for?)*
- *Clients were motivated to take part because it was research, more than to improve their own wellbeing*

5. Evaluating the booklet

(Krupa) *I'd like to move on to the 5th part of the focus group, evaluating the PRotect booklet. Please take a booklet and have a look through.*

- *What do you like/dislike about the booklet?*
- *How do you think the booklet was used by clients?*
- *How would you change the booklet?*

6. The future

(Alice) *For the final part of today's focus group we will be looking forward. What do you think the next steps should be for the PRotect intervention?*

- *I have in my hand some cards with factors to consider when deciding the future of the intervention.*

Targets

Lower MDS scores in those who attend

Clinician time per client

Client satisfaction

Ease of implementation within current iCope systems

Current aims of the service

Current staffing levels of the service

- *Can you think of any others?* (When there are suggestions note them down on a new card)
- *As a group, can you try to sort these considerations in order of importance* (Make sure they discuss and justify why they are deciding a certain order)

TO FINISH (Krupa) Thank you and pizza time