Psychological therapies for major depressive disorder and prolonged grief in bereaved adults


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Psychological therapies for major depressive disorder and prolonged grief in bereaved adults (Protocol)

Roulston A, Clarke MJ, Donnelly M, Candy B, McGaughey J, Keegan O, Duffy M

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Psychological therapies for major depressive disorder and prolonged grief in bereaved adults

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the effectiveness of CBT (e.g. cognitive therapy, cognitive behavioural therapy, rational emotive behaviour therapy, prolonged grief CBT) compared with non-CBT therapies (e.g. psychodynamic, humanistic, family or systemic therapies) for treating people with bereavement-related MDD or PGD.

To assess the effectiveness of CBT compared with usual care or waiting list for treating people with bereavement-related MDD or PGD.

To assess the effectiveness of CBT compared with pharmacological interventions (e.g. antidepressant medications and other drug therapies used explicitly for treating depressive disorders (Sadock 2009)) for treating people with bereavement-related MDD or PGD.

BACKGROUND

Grief is a normal reaction following the death of someone close, and most bereaved individuals adequately adjust through healthy grieving. However some of the bereaved population will develop a debilitating clinical condition as a result of the loss, such as Prolonged Grief Disorder (PGD) or bereavement-related Major Depressive Disorder (MDD). Several psychological therapies have been proposed to treat MDD and PGD, and there is a growing evidence base demonstrating their effectiveness; the goal of this systematic review is to evaluate the efficacy of Cognitive Behaviour Therapy (CBT) for bereavement-related MDD and PGD.

Description of the condition

There is evidence that bereaved individuals may develop a range of mental health problems, including depression (Zisook 1994), anxiety disorders (Jacobs 1990), Post-Traumatic Stress Disorder (PTSD) (Murphy 1999; Schut 1991), or prolonged grief (Maercker 2013). This review will examine bereavement-related...
Major Depressive Disorder and Prolonged Grief Disorder, which are described below.

**Major Depressive Disorder (bereavement-related)**

According to the World Health Organization (WHO), MDD is a common mental disorder affecting 322 million people worldwide, and is a major contributor to global disability and to deaths by suicide (WHO 2017). Evidence suggests that bereavement-related MDD is often recurrent, genetically influenced, impairing, and treatment-responsive (Kendler 2008). Adverse life events such as unemployment, bereavement, being a victim of a physical assault or major disaster, or experiencing psychological trauma can precipitate MDD, which is more common in women (WHO 2017). The most widely-used criteria for diagnosing MDD are APA's Diagnostic Statistical Manual of Mental Disorders (DSM) and the World Health Organization's International Statistical Classification of Diseases and Related Health Problems (ICD). There are a number of similarities between the definitions of depression and the symptoms identified in the ICD-10 (WHO 2016) and DSM-5 criteria (APA 2013), which are used to diagnose if someone has mild, moderate or severe depression. For example, both refer to changes in weight, sleep, activity or concentration, and both highlight suicidality. However, the ICD-10 also refers to self-esteem and guilt. The 5th edition of the DSM (APA 2013) categorises MDD as depressed mood or a loss of interest or pleasure in daily activities for more than two weeks, which represents a change from the person's baseline mood, and impaired function: social, occupational and educational (APA 2013). The key symptoms for depression in the ICD-10 (WHO 2016) are persistent sadness or low mood, loss of interests or pleasure, and fatigue or low energy. The DSM-IV-TR (APA 2000) definition of mental disorder excludes grief as a disorder on the grounds that it was “an expectable and culturally sanctioned response to a particular event”. Clinicians using the DSM-IV were advised to refrain from diagnosing MDD within the first two months following a bereavement, which became known as the ‘bereavement exclusion’. The DSM-5 (APA 2013) subsequently removed the ‘bereavement exclusion’ from the recommended criteria for MDD (Fawcett 2010), which led to some criticism (Horowitz 2011) and further research to support its removal (Jozwiak 2013; Zisook 2012; Zisook 2013). According to DSM-5 guidance (APA 2013), individuals should be screened for conditions that mimic or co-exist alongside MDD such as bereavement, and symptoms should persist for more than two months into bereavement or the individual should show marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms or psychomotor retardation. Given the unique differences between ordinary or uncomplicated grief and MDD, as well as the differences between bereavement-related MDD and PGD, it has been suggested that removing the bereavement exclusion should help avoid MDD being overlooked and should promote sound clinical judgement, taking into account the individual’s previous history and cultural norms (Ibrahim 2014), before the appropriate treatment is offered. Population-based studies have explored the validity of bereavement-related MDD. One study conducted in the USA (Kendler 2008) compared bereavement-related MDD and depressive episodes related to other stressors (e.g. separation/divorce, illness or job loss). It reported some differences in the demographic characteristics of the participants with bereavement-related MDD (i.e. older and female), lower levels of treatment-seeking, neuroticism and guilt, but higher levels of fatigue and loss of interest. However, the conclusion was that similarities overshadowed the differences, which echoed findings from another study exploring bereavement-related MDD (Wakefield 2007). A study conducted in Lebanon (Karam 2009) failed to find any significant differences in duration, impairment, and bereavement exclusion symptoms between bereavement-related and bereavement-unrelated MDD episodes. Mojtabai 2011 reported that participants with bereavement-related, single, brief depressive episodes were more likely to experience later onset, but were less likely to have had impairment in role functioning, comorbid anxiety disorders, or a treatment history at baseline. He also found that those participants with bereavement-related, single, brief episodes were less likely than those with bereavement-unrelated, single, brief episodes to experience fatigue, increased sleep, feelings of worthlessness, and suicidal ideations. The risk of new MDD episodes during the follow-up period among participants with bereavement-related, single, brief episodes was similar to people from the general population with no baseline history of MDD.

**Prolonged Grief Disorder**

Grief is a normal reaction to bereavement following the death of a partner, parent, child, or other close person and most bereaved individuals will adequately adjust through healthy grieving, which typically involves completion of loss-focused and restoration-focused tasks (Stroebe 1999). These tasks enable the bereaved to come to accept their changed circumstances and reconnect with society or re-engage in normal, pleasurable activities (Bonanno 2002). However, it has been reported that some bereaved people will experience a bereavement-related disorder, commonly known as abnormal, pathological, complicated or traumatic grief and Prolonged Grief Disorder (Kuiken 2018). It has also been suggested that the prevalence rates may vary depending on the nature of the loss (i.e. non-violent or non-traumatic loss, violent death, or those who experienced a disaster), the variation of instruments and cutoff scores used for assessment measures (Kuiken 2018) and the lack of consensus on the diagnostic criteria (Rusner 2011). In response to increasing evidence for the specificity of a Prolonged or Complex Grief Disorder, and as a compromise between the two proposed diagnostic criteria for Prolonged Grief Disorder (Horowitz 1997; Prigerson 2009) and complicated grief (Zisook 2009), a new diagnostic category, Persistent Complex Bereavement...
ment-Related Disorder (PCBD) was included in the DSM-5 as requiring further study (APA 2013; Killikelly 2018). In terms of PGD, a new diagnostic category was recommended for inclusion in the 11th edition of the ICD (Maercker 2013; WHO 2018). Despite the ongoing debate surrounding terminology and definitions, we have selected for this review the term ‘Prolonged Grief Disorder’ (PGD) to reflect the ICD-11 terminology and the extended period of time beyond the acute phase of grief (Duffy 2017).

PGD is a debilitating clinical condition (Boelen 2007). According to the ICD-11 diagnostic criteria (WHO 2018), PGD is characterised by a daily or disabling yearning for the deceased following the death of a significant other, which is accompanied by five or more of the following: confusion about one’s role in life or a diminished sense of self; difficulty accepting the loss; avoidance of reminders of the reality of the loss; inability to trust others since the loss; bitterness or anger related to the loss; difficulty moving on with life; emotional numbness since the loss; feeling that life is unfulfilling, empty or meaningless since the loss; feeling stunned, dazed or shocked by the loss. According to ICD-11 criteria (WHO 2018), at least six months should have passed since the death. In addition, the disturbance should cause significant social, occupational or functional impairment and should not be better accounted for by Major Depressive Disorder, Generalised Anxiety Disorder or Post-Traumatic Stress Disorder. It is suggested that diagnosis can only be made by clinical assessment after six months, to differentiate between maladaptive reactions and normal distress (Jordan 2014; Prigerson 2006; Prigerson 2009). This is in contrast to DSM-5 criteria, which stipulate that diagnosis of PCBD cannot be made until 12 months after the death (APA 2013).

PCBD is characterised by unshakeable grief that does not follow the general pattern of improvement over time, but individuals continue to experience persistent and intense emotions or moods and unusual, severe symptoms that impair major areas of functioning, or that cause extreme distress (Shear 2011). In addition to the presence of persistent yearning for the deceased, intense sorrow and emotional pain in response to the death, preoccupation with the deceased for at least 12 months following the death of a close other, there should be clinically significant difficulty accepting the death; disbelief or emotional numbness over the loss; difficulty with positive reminiscing about the deceased; bitterness or anger related to the loss; maladaptive appraisals about oneself in relation to the deceased or the death; excessive avoidance of reminders about the loss; a desire to die to be with the deceased; difficulty trusting other people since the death; feeling detached from other people or alone since the death; feeling that life is meaningless or empty without the deceased or the belief that one cannot function without the deceased; confusion about one’s role in life or a diminished sense of one’s identity; or difficulty or reluctance to pursue interests or to plan for the future since the loss. In addition, the disturbance should be causing clinically significant distress or impairment in social, occupational, or other important areas of functioning, and the bereavement reaction must be out of proportion or inconsistent with cultural or religious norms (APA 2013).

**Differences between MDD and PGD**

According to published sources, normal grief, MDD and PGD differ in a number of ways. In normal grief, painful feelings are often mixed with positive memories of the deceased, and self-esteem is normally preserved, whereas in MDD, mood and ideation are almost constantly negative, and feelings of worthlessness and self-loathing are common (APA 2013). According to Jordan 2014, PGD differs in how the symptoms relate to the loss of the deceased, such as rumination presenting as a preoccupation with the deceased, despair and depressed mood linked to separation from the deceased, and guilt relating to self-blame associated with the individual’s death (Duffy 2017). Furthermore, yearning and being overwhelmed by the loss were specific to PGD but not to MDD (Prigerson 2009). Diagnosing MDD in the context of bereavement would therefore incorrectly label a normal process as a disorder.

A growing body of evidence suggests that PGD has distinct characteristics when compared to bereavement-related MDD (Boelen 2003). However, diagnostic criteria for MDD were not available until the DSM-III (APA 1980), and diagnostic criteria for PGD were not available until DSM-IV (APA 1994). Furthermore, Prigerson and colleagues (Prigerson 1995a; Prigerson 1995b; Prigerson 1996) did not confirm the distinction between traumatic grief and bereavement-related depression until the mid-1990s, which means that earlier studies may have misclassified people with MDD, rather than PGD. Randomised trials comparing treatments for PGD (Boelen 2007; Shear 2005) clearly support the efficacy of PGD-specific treatments, highlighting the importance of an accurate diagnosis (Prigerson 2009). Given the scope of this review, we will report interventions and outcomes for MDD and PGD separately and will acknowledge if the included trials were conducted prior to the diagnostic criteria and distinction being confirmed in the published literature and DSM guidance.

**Description of the intervention**

**Interventions for MDD**

Although antidepressants are the mainstay treatment for MDD in primary health care (NICE 2018), and have a proven efficacy for treating acute depression (Arroll 2009; Cipriani 2009), adherence rates are very low (Anderson 2012; Van Geffen 2009) and many people prematurely discontinue antidepressant therapy (Sansone 2012) due to fears about possible dependency and adverse effects (Hunot 2007; Sansone 2012; Van Geffen 2011), to uncertainty about the treatment effects (Anderson 2012), to sociocultural beliefs around taking medication for depression and stigma around
depression (Van Veerbeck-Heida 2006), and due to lack of patient education and to poor follow-up (Sansone 2012).

The 2009 National Institute for Health and Care Excellence (NICE) clinical guidelines for depression (NICE 2009), recommend a collaborative care model (Archer 2012). A Cochrane Review demonstrated significantly greater improvement in a range of depression outcomes for adults treated using the collaborative care model (Van der Feltz-Cornelis 2010). Updated NICE guidelines for the assessment and treatment of depression (CG90) promote a stepped-care model which provides a framework for pharmacological and psychological interventions based on the severity of the depression and preferences of the patient (NICE 2018).

Psychological interventions are broadly categorised into four different theoretical or philosophical schools: cognitive, behavioural, psychodynamic and humanistic. For the purposes of this review, cognitive therapy (Beck 1979) and behaviour therapy (Ellis 1962) approaches have been merged to form CBT. Although the acronym ‘CBT’ suggests a unitary therapy (Roth 2008), it is now regarded as a family of allied therapies (Mansell 2008) that draw on a common base of behavioural and cognitive models of psychological disorders and use a set of overlapping techniques (Roth 2008). The following cognitive behavioural approaches (e.g. cognitive therapy, rational emotive behaviour therapy and prolonged grief-CBT) will be the main experimental intervention, which will be compared to the non-CBT interventions outlined below.

According to a meta-analysis of studies involving psychotherapy and pharmacotherapy (Oestergaard 2011), combined psychotherapy and pharmacotherapy was more effective than pharmacotherapy alone in attaining remission and preventing relapse in people with MDD. In another meta-analysis of randomised trials of behaviour treatment of depression, the authors concluded that behaviour therapy is an effective treatment for depression (Ekers 2008). Studies have shown that CBT is as effective as antidepressant medication for treating depression, and seems to reduce the risk of relapse even after its discontinuation (Hollon 1992; Rush 1977). The Centre for Reviews and Dissemination (Centre for Reviews and Dissemination 2008) conducted a systematic review on interventions for people bereaved by suicide (e.g. active outreach, bereavement groups, writing exercises, CBT, first talk through, and psychological debriefing). Although the findings revealed methodological flaws and resulted in the authors concluding that there was a lack of robust evidence to be able to offer clear guidance for clinical interventions, they did suggest that the following interventions may be beneficial: psychologist-led group therapy for children who lost a parent; combined health professional- and volunteer-led group therapy for adults who lost a family member; and family cognitive behavioural therapy with a trained psychiatric nurse (Centre for Reviews and Dissemination 2008).

Interventions for PGD

It is now accepted that PGD requires a specific diagnosis and intervention to enable bereaved individuals to overcome the barriers to loss-orientation and restoration-orientation tasks (Shear 2005).

Despite how PGD has been classified and how concepts and diagnostic criteria for grief have evolved over time, core symptoms overlap, such as intense yearning and preoccupation with the loss, reactive distress symptoms and social/identity disruption (Rosner 2014). PGD is also associated with significant morbidity and suicide risk, and it has been suggested that grief support groups may be helpful for some bereaved people (Simon 2015). It has been reported that psychotherapies using cognitive and behavioural principles to directly target PGD are effective (Boelen 2007; Bryant 2014; Shear 2005; Shear 2014; Simon 2013).

The following cognitive behavioural approaches (e.g. cognitive therapy, rational emotive behaviour therapy and prolonged grief-CBT) will be the main experimental intervention, which will be compared to the non-CBT interventions outlined below.

How the intervention might work

In CBT, therapists and patients work collaboratively to understand the link between thoughts, feelings and behaviours. They identify and modify unhelpful thinking patterns, underlying assumptions and idiosyncratic cognitive schemata (e.g. core beliefs, underlying assumptions or associated strategies) about the self, others and the world (Beck 1979; Beck 2004). Cognitive change methods for depression target the automatic thought level in the first instance and include thought catching, reality testing and task assigning as well as generating alternative strategies (Williams 1997). Behavioural experiments are then used to re-evaluate underlying beliefs and assumptions (Bennett-Levy 2004). According to NICE Guidelines (NICE 2009), treatment is normally delivered over 15 to 20 sessions, depending on the severity of depression. CBT-based models have been developed to treat PGD. For example, rational emotive behaviour therapy (Malkinson 2000) is used to target ‘irrational beliefs’ and teaches the bereaved to practice more adaptive thinking and to re-organise their life to maintain bonds with the deceased (Duffy 2017; Malkinson 2000). Similarly, CBT techniques such as imaginal exposure (Eisma 2015; Foa 2001) are useful in treating individuals with PGD, where the moment of death is a distressing experience (Duffy 2017). Prolonged Grief CBT (PG-CBT) offers 25 sessions (five of which are optional) which focus on stabilising and motivating the patient, exploration of the grief situation, teaching relaxation, focusing on confrontation and reinterpretation of the cognitions and perceptions of themselves, and on future prospects while maintaining a healthy bond to the deceased (Rosner 2014). Results suggest that PG-CBT is highly effective in reducing grief severity and compares well to other treatments for PGD (Rosner 2014). Further research is planned to test PG-CBT against Present-Centred Therapy (PCT) (Rosner 2018).

CBT interventions which combine exposure therapy and cognitive restructuring (Boelen 2006) have been demonstrated to be
effective in alleviating symptoms of PGD (Boelen 2007; Shear 2005). Boelen 2007 compared CBT and supportive treatment for bereaved individuals with PGD who each received 12 weeks of treatment (cognitive restructuring, exposure, and social support). Findings indicated that those who had CBT improved more than the social support group, and that exposure which included behavioural and emotional elements was more effective than cognitive construction (Boelen 2011). Wagner and Maercker tested the longer-term effects of an Internet-based cognitive-behavioural intervention and reported that the reduction in symptoms of complicated grief observed at post-treatment was maintained at 18 month follow-up (Wagner 2007).

Non-CBT approaches

a) Complicated Grief Treatment (CGT) was developed for PGD (Shear 2005; Shear 2014). It is based on attachment theory, and integrates the use of interpersonal therapy, CBT and motivational interviewing over 16 weekly sessions (Shear 2010). Shear 2014 reported that CGT had a significantly greater effect and higher tolerability, when compared with grief-focused Interpersonal Therapy (IPT) among older adults who had experienced a loss.

b) Psychodynamic or psychoanalytic approaches (e.g. brief psychotherapy, countertransference, transference, Freudian, Jungian, Kleinian, person-centred therapy, interpersonal therapy) (Klerman 1984). Grounded in psychoanalytic theory (Freud 1949), psychodynamic approaches use the therapeutic relationship to explore and resolve unconscious conflict through transference and interpretation (Strupp 1984). A number of randomised trials have demonstrated the effectiveness of both Interpersonal Therapy (IPT) and CGT for treating PGD, with significantly better outcomes reported with CGT (Glickman 2016; Shear 2005; Simon 2015). A systematic review of interventions for depression indicated that IPT was more effective than CBT (De Mello 2005).

c) Humanistic approaches (e.g. existential therapy, gestalt therapy, transactional analysis). Whilst contemporary models differ in their clinical approach, all focus on the therapeutic relationship (Cain 2002), within which the ‘core conditions’ (Rogers 1951) are cornerstones for facilitating recipient insight and change.

d) Family or systemic therapy focuses on the family and aims to enhance the ability of family members to support each other, or to develop coping skills for various life situations, including long-term illness (Carr 2009). Family therapy has been used to support relatives of people with cancer during the palliative phase and into bereavement, and has been reported to reduce the severity and development of PGD (Kissane 2016).

Why it is important to do this review

There is evidence demonstrating the effectiveness of different psychological therapies for treating MDD and PGD. These are based on randomised trials using a range of measures and instruments for MDD and PGD.

There are already some published systematic reviews exploring bereavement and PGD. One assessed interventions linked to bereavement following suicide (McDaid 2008), but the included studies varied in the type of intervention, participants, and how the intervention was delivered, with the authors concluding that evidence for interventions was not robust. Another review explored the prevalence of PGD in an adult bereaved population (Lundorff 2017), but excluded violent deaths and intervention-based studies. We are aware of two published reviews focusing on the effects of psychological therapies for PGD. One examined interventions following perinatal deaths (Koopmans 2013), and the other explored preventative and treatment interventions, which had very limited inclusion criteria and did not search the grey literature (Wittouck 2011).

In view of bereavement-related depression and PGD being classified as distinct disorders, and the need to base treatment decisions on reliable, up-to-date evidence, it is important to compare the effectiveness of psychological therapies for individuals with bereavement-related MDD or with PGD, which we will do in this review. Our findings may inform treatment decision-making by trained healthcare professionals, therapists, counsellors or policy makers and may inform the development of guidelines for routine treatment for bereavement-related MDD and PGD.

Objectives

To assess the effectiveness of CBT (e.g. cognitive therapy, cognitive behavioural therapy, rational emotive behaviour therapy, prolonged grief CBT) compared with non-CBT therapies (e.g. psychodynamic, humanistic, family or systemic therapies) for treating people with bereavement-related MDD or PGD.

To assess the effectiveness of CBT compared with usual care or waiting list for treating people with bereavement-related MDD or PGD.

To assess the effectiveness of CBT compared with pharmacological interventions (e.g. antidepressant medications and other drug therapies used explicitly for treating depressive disorders (Sadock 2009)) for treating people with bereavement-related MDD or PGD.

Methods

Criteria for considering studies for this review
**Types of studies**

We have prepared this Methods section using the template text provided by the Cochrane Common Mental Disorders Group. We will include individually-randomised trials and cluster-randomised trials, regardless of setting, sample size, or duration. We will not include cross-over trials, as this is a design rarely used in psychological therapy trials.

We will include studies regardless of language of publication. If necessary, we will seek resources to translate studies not published in English, because this will allow us to present a more global picture.

We will include studies if a structured or semi-structured diagnostic clinical interview was conducted by a mental health professional or a trained researcher using the Structured Clinical Interview for DSM-5 (First 2016), or where other appropriate psychometric data were assessed and reported (e.g. acceptable inter-rater reliability).

**Types of participants**

**Participant characteristics**

We will include studies with bereaved individuals who were diagnosed and treated for a MDD or for PGD. We will only include MDD-related studies if they clearly identify that the study population were diagnosed with MDD following a bereavement, and only if half or more of the study population meet the agreed inclusion criteria.

We will set no restrictions on gender or ethnicity. With regard to age, we will only include studies involving bereaved adults, or where most of the study population includes adults. We define adults as individuals aged 18 or over, which is based on the groups covered in the NICE Guideline on depression in adults (NICE 2018), and UK child protection law (HMSO 1995), which defines individuals under the age of 18 as children.

Based on our understanding of how the nature of the relationship between the deceased and the bereaved impacts on bereavement outcome (Roulston 2017), we will include individuals who are related to or were in a relationship with the deceased (e.g. spouse, partner, adult child, parent, sibling).

As the prevalence of PGD differs according to cause of death (Killikelly 2018), we will include any health condition, accident, homicide, suicide, road traffic crash, act of terrorism or natural disaster.

Given the lack of consensus between diagnostic criteria for PGD (Rosner 2011), the potential for misclassifying MDD prior to the clear distinction between MDD and PGD being confirmed in the literature (Prigerson 1995a; Prigerson 1995b; Prigerson 1996), as well as the debate about the ‘bereavement exclusion’ in DSM (Ibrahim 2014) and the ICD-11 criteria that at least six months should have passed since the death (WHO 2018), we will not place any restrictions on when the individual was bereaved. To avoid compromising generalisation from the systematic review, we will include all studies, but will use sensitivity analysis to explore the impact of the PGD studies that include individuals bereaved for less than six months.

**Diagnosis**

We will include studies where the participants were included on the basis of a MDD diagnosis, which was determined by standardised diagnostic criteria including the Diagnostic and Statistical Manual of Mental Disorders (DSM versions III, IV (APA 1994) and 5 (APA 2013)), the NICE Guidance (NICE 2018) for classifying depression, the Inventory International Statistical Classification of Diseases ICD-10 (WHO 2016) and ICD-11 (WHO 2018). We will include studies if a structured or semi-structured diagnostic clinical interview was conducted by a mental health professional or by a trained researcher using the Structured Clinical Interview for DSM-5 (First 2016). We will also include studies where participants were selected based on reaching a predefined cut-off point on a validated depression measure tool such as the Beck Depression Inventory (Beck 1961; Beck 1996); Hamilton Depression Rating Scale (Hamilton 1960); Centre for Epidemiological Studies - Depression Scale (Radloff 1977); Hospital Anxiety and Depression Scale (Zigmond 1983); or Montgomery Depression Scale (Montgomery 1979).

We will include studies where participants were included following a diagnosis of PGD, identified using standardised diagnostic criteria outlined in DSM-IV (APA 2000), DSM-5 (APA 2013) and ICD-11. In addition, we will include studies where participants were recruited based on reaching the predefined cut-off score on any validated measures, such as the Inventory of Complicated Grief (ICG) (Prigerson 1995a); Inventory of Complicated Grief-Revised (ICG-R) (Jacobs 2010); Prolonged Grief Interview-13 item version (PG-13) (Prigerson 2008); Traumatic Grief Inventory Self-Report version (TGI-SR) (Boelen 2017); Brief Grief Questionnaire (Ito 2012) or any other validated measure. We will include validated measures administered through self-report, structured clinical interview or informant report, where the informant is a member of staff or relative.

**Comorbidities**

We will include studies where participants have other health conditions (e.g. physical or mental), as long as the comorbidity is not the main focus of the study.

**Setting**

All types of setting will be eligible for inclusion: inpatient (psychiatric setting), outpatient, and primary care.
Types of interventions

Experimental Intervention

- The principal psychological intervention will be CBT (e.g. cognitive therapy, cognitive behavioural therapy, rational emotive behaviour therapy, PG-CBT) delivered to individuals or groups as treatment for bereavement-related MDD or PGD. We will include face-to-face and online-based CBT programmes. There will be no restrictions on the duration or frequency of treatment interventions. We will explore training levels, qualifications and supervision of individuals delivering the intervention when comparing any differences in outcome scores.

Comparator intervention

Studies with the following comparisons will be included in the review.

- CBT versus non-cognitive behaviour therapies (e.g. psychodynamic, humanistic or integrative therapies, family therapy or systemic therapies).
- CBT versus selected pharmacological interventions (e.g. antidepressant medications and other drug therapies used explicitly for treating depressive disorders (Sadock 2009)).
- CBT versus usual care (e.g. participants could receive appropriate medical care during the course of the study on a naturalistic basis, deemed necessary by the clinician).
- CBT versus waiting list (e.g. delayed delivery of the intervention to the control group until after participants in the intervention group have completed treatment).

We will include any mode of delivery, such as face-to-face contact, telephone or online interventions, and we will include individual, group and family therapy. Due to the wide range of treatments being examined, we will place no restrictions on the duration or frequency of treatment interventions.

Types of outcome measures

We will include all eligible studies in the review, but will only be able to include those that provide the necessary outcome data in the relevant meta-analyses.

Primary outcomes

- Treatment response: the number of participants showing an improvement in MDD or PGD symptoms measured separately or clinically significant changes (treatment response/endpoint functioning) versus no significant change in the severity of MDD or PGD symptoms measured separately, captured using the standardised DSM or ICD diagnostic criteria, or NICE Guidance (NICE 2018). Where treatment scores are captured using validated measures, the authors will highlight clinically significant changes. For example, people who have been clinically diagnosed using the BDI (Beck 1961) where scores from 0 to 9 represent minimal depressive symptoms, scores of 10 to 16 indicate mild depression, scores of 17 to 29 indicate moderate depression, and scores of 30 to 63 indicate severe depression. The authors will do likewise with other validated measures for MDD or PGD.

Secondary outcomes

- Adverse events outcome: dropout for any reason.
- Occurrence of bereaved relatives attempting or completing suicide (if incidence reported in selected studies). We will summarise in narrative form adverse effect outcomes such as dropout due to completed suicide.
- Reduction in MDD or PGD scores, measured using a validated continuous scale as outlined above in diagnosis.
- Changes in the use of routinely-prescribed antidepressant medication or other interventions (e.g. bereavement support groups).

Timing of outcome assessment

Where available, we will assess outcomes at short term (end of treatment), medium term (six months after treatment), and long term (more than six months after treatment). Our primary time point will be medium term, because this will demonstrate if there were sustained benefits from the intervention. Where data are available, other time points will help to demonstrate if there were immediate and longer term benefits.

Hierarchy of outcome measures

We will include any validated measures for depression or complicated or prolonged grief. We will prioritise clinician-administered scales over informant-rated scales and self-reported scales. If multiple outcome measures of the same type are used (e.g. two self-report measures for PGD), we will choose the outcome measure that is most frequently used across the included studies.

Search methods for identification of studies

Cochrane Common Mental Disorders Controlled Trials Register (CCMDCTR)

The Cochrane Common Mental Disorders Group (CCMD) maintains two archived clinical trials registers at its editorial base in York, UK: a references register and a studies-based register. The CCMDCTR-References Register contains over 40,000 reports of randomised trials in depression, anxiety and neurosis. Approximately 50% of these references have been tagged to individual,
coded trials. The coded trials are held in the CCMDCTR-Studies Register and records are linked between the two registers through the use of unique Study ID tags. Coding of trials is based on the EU-Psi coding manual, using a controlled vocabulary, information on which is available from the CCMD Information Specialists. Reports of trials for inclusion in the Group's registers are collated from routine (weekly) generic searches of MEDLINE (1950 to 2016), Embase (1974 to 2016) and PsycINFO (1967 to 2016); quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL) and review-specific searches of additional databases. Reports of trials are also sourced from international trial registers via the World Health Organization's trials portal (the International Clinical Trials Registry Platform (ICTRP) (Ghersi 2009)), pharmaceutical companies, the handsearching of key journals, conference proceedings and other (non-Cochrane) systematic reviews and meta-analyses. Details of CCMD's core search strategies (used to identify randomised trials) can be found on the Group's website with an example of the core MEDLINE search displayed in Appendix 1.

The Group's Specialised Register is up-to-date as of June 2016, when the editorial group moved from the University of Bristol to York University.

Electronic searches

The Cochrane Common Mental Disorders Group's Information Specialist will run searches on the following databases.

- CCMDCCTR (Studies and References Registers) (all available years).
- Cochrane Central Register of Controlled Trials (CENTRAL) (current issue).
- Ovid MEDLINE databases (1946 onwards) [Appendix 2].
- Ovid Embase (1974 onwards).
- Ovid PsycINFO (all available years).
- Ebsco CINAHL (1980 onwards).

Search strategies for the CCMDCCTR are displayed in Appendix 3 and will be translated across to all other databases using relevant subject headings (controlled vocabularies) and search syntax, appropriate to each resource. We will also apply filters to identify randomised trials.

We will apply no restrictions on language or publication status to the searches, but we will consider applying a date limit in keeping with the advent of the diagnostic criteria for MDD in DSM-III (1980 onwards) and PGD in DSM-IV (1994 onwards).

We will search international trial registries through the World Health Organization's trials portal (ICTRP) (Ghersi 2009) and ClinicalTrials.gov, to identify unpublished or ongoing studies.

We will rerun all searches close to publication of the full review if the initial search date is more than 12 months earlier.

Searching other resources

Grey literature

We will search the following sources for grey literature and dissertations and theses.

- Open Grey (www.opengrey.eu).
- Electronic Theses Online Service (EThOS) - British Library (ethos.bl.uk/Home.do).
- DART - Europe e-theses Portal (www.dart-europe.eu/basic-search.php).
- Networked Digital Library of Theses and Dissertations (NDLTD) (search.ndltd.org).
- PQDT Open - open access dissertations and theses (pqdtopen.proquest.com/search.html).
- Proquest Dissertations & Theses Global (search.proquest.com/pqdtglobal/dissertations).

Reference lists

We will check the reference lists of all eligible studies (Horsley 2011) and relevant systematic reviews for relevant studies that are not identified in the original electronic searches.

Correspondence

We will contact trialists and subject experts for information on unpublished or ongoing studies, or to request additional trial data, as required (Young 2011).

Data collection and analysis

Selection of studies

Two review authors will independently screen all titles and abstracts identified as a result of the search, and will code them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. At least two review authors will independently screen the retrieved full-text study reports/publication to identify studies for inclusion based criteria listed above in the section 'Criteria for considering studies for this review'.

We will accept studies with any publication status (e.g. full-text, abstract only, in-press, etc). We will resolve any disagreements about the eligibility of a study through discussion after having retrieved the full paper or, if required, we will consult the original authors or another review author. We will identify and exclude duplicate records and collate multiple reports that relate to the same study, so that each study rather than each report is the unit of interest in the review. We will record the selection process in sufficient detail to complete a PRISMA flow diagram and a 'Characteristics of excluded studies' table.
Data extraction and management

Our methods for data extraction and management will follow those outlined in chapter seven of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We will use a data collection form that has been piloted on at least one eligible study to extract study characteristics and outcome data. At least two review authors will extract the following study characteristics and outcome data from eligible studies.

- **Source:** study ID, Report ID, review author ID, citation and contact details.
- **Eligibility:** confirm eligibility criteria for review, reason for exclusion.
- **Methods:** study design, total study duration, number and location of study centres, study setting, dates study was conducted, withdrawals, sequence generation, allocation sequence concealment, blinding and other concerns about bias.
- **Participants:** N, mean age, age range, gender/sex, ethnicity, country, recruitment, diagnostic criteria, severity of depression or PGD, nature of death, duration of time since being bereaved, nature of relationship to the deceased, comorbid conditions, inclusion criteria and exclusion criteria.
- **Interventions:** total number of intervention groups, specific interventions, intervention details, integrity of intervention, comparison, and concomitant medications.
- **Outcomes:** primary and secondary outcomes specified and collected, method of collection, and time points collected and reported. For each outcome of interest: outcome definition (with relevant diagnostic criteria), unit of measurement, upper and lower limits for each measurement scale (clarifying if high or low score is good).
- **Results:** number of participants allocated to each intervention group. For each outcome of interest the sample size, missing participants, summary data for each intervention group, estimate of effect with confidence interval and P value, subgroup analyses.
- **Other information:** funding source for trial, references to other relevant studies, correspondence required and notable conflicts of interest of trial authors.

In the 'Characteristics of included studies' table, we will record if we are unable to use outcome data as reported. We will resolve disagreements between the data extractors by consensus or by consultation with another review author. One review author will transfer data into the Review Manager 5 software (RevMan 2014). A second review author will check that data have been entered correctly by comparing data presented in the systematic review with data provided in the study reports.

Assessment of risk of bias in included studies

At least two review authors will independently assess risks of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We will resolve any disagreements by discussion or by involving another review author. We will assess the risk of bias according to the following domains.

- Random sequence generation.
- Allocation concealment.
- Blinding of participants and personnel.
- Blinding of outcome assessment.
- Incomplete outcome data.
-Selective outcome reporting.
- Other potential bias.

We will judge each potential source of bias as high, low or unclear, and provide a supporting quotation from the study report together with a justification for our judgement in the 'Risk of bias' table. We will summarise the 'Risk of bias' judgements across different studies for each of the domains listed. For psychological interventions, blinding of healthcare providers or participants to the treatment is not usually feasible, and so we will only evaluate trials of psychological interventions for blinding of the outcome assessors. Where necessary, we will contact the authors of the studies for further information (Young 2011). Where information on risk of bias comes from unpublished data or correspondence with a trialist, we will note this in the 'Risk of bias' table. We will use blinding of outcome assessments as a marker of trial quality for the purposes of undertaking sensitivity analyses.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome. For any cluster-randomised trials that we identify, we will assess the risks of bias by considering recruitment bias, baseline imbalance, loss of cluster, incorrect analysis and comparability with individually-randomised trials (Higgins 2017).

Measures of treatment effect

Dichotomous data

We will analyse dichotomous data using the risk ratio (RR) in terms of the proportion of trial participants experiencing the outcome of interest in the treatment groups being compared. We will calculate the 95% confidence interval (CI) for each comparison and will present it in this form for ease of interpretation. Where available, we will favour the findings of intention-to-treat (ITT) analyses over other approaches, such as per protocol or as-treated.

Continuous data

Where studies have used the same outcome measure for comparison, we will pool data by calculating the mean difference (MD) using a 95% CI. Where available, we will favour comparison of the changes over time for outcome measures which have a smaller standard deviation in the change scores (i.e. from baseline to follow-up) than in the final scores, and the findings of ITT analyses over other approaches, such as per protocol or as-treated.
We will enter data as the least biased way to present data as a scale with a consistent direction of effect. We will undertake meta-analyses only where this is meaningful, i.e. if the treatments, participants and the underlying clinical question are similar enough for pooling to make sense. We will use narrative description if skewed data are reported as medians and interquartile ranges. Where multiple intervention groups are reported in a single trial, we will include only those groups that are relevant to the meta-analysis in question.

**Unit of analysis issues**

**Cluster-randomised trials**

Application of meta-analysis is conventionally based on the assumption that the primary unit of randomisation is the individual study participant. However, some trials have randomised intact social units of individuals to intervention groups. If we identify any cluster-randomised trials, we will include them if proper adjustment for the intra-cluster correlation can be undertaken using steps described in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2017).

**Studies with multiple treatment groups**

Where studies have additional intervention groups that are not eligible for this review, we will only include the data relating to the eligible intervention and one control group in the review. When a study has more than two intervention groups that meet our inclusion criteria (e.g. two psychological therapies and a control group) we will split data from the control group equally to produce two (or more) pair-wise comparisons.

**Dealing with missing data**

We will contact investigators or study sponsors to verify key study characteristics and to obtain missing numerical outcome data when possible (e.g. when the only information we have for a study is a conference abstract) (Young 2011). We will document all correspondence with trialists and will report which trialists responded in the full review.

We will not use a trial’s data for an outcome measure if more than 50% of the relevant data are missing for that trial. For continuous outcomes, we will calculate missing standard deviations from other available data, such as confidence intervals, standard errors, and P, T, or F values. As we will be using only summary measures for the analysis, we will assume that missing data for each study are randomly distributed and thus do not influence the quality of estimates. If we find any published studies describing the missing data as non-random, we will statistically weight the estimates for studies based on the level of data missingness, that is, when we create a weight factor for each published study in deriving the overall estimate, we will consider the quantity of missing data, as well as the sample size.

As noted above, we will seek to conduct ITT analyses, which are usually recommended (Newell 1992) as the least biased way to estimate intervention effects. We will follow guidance in Chapter 16 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) for these ITT analyses for dichotomous and continuous data.

**Assessment of heterogeneity**

We anticipate that eligible studies will present various types of heterogeneity, conventionally classified as clinical, methodological, and statistical heterogeneity. In assessing clinical heterogeneity, we will examine differences between factors associated with intervention or participant characteristics across studies included in any meta-analysis. We will conduct the Chi^2 test to assess whether observed differences in results might be due to chance alone, using a P value of 0.10 as evidence of heterogeneity of intervention effects. We will also use the I^2 statistic to consider the extent of any statistical heterogeneity and analyse its potential influence on the summary effect size estimate, and will explore this in our Discussion. We will interpret the I^2 statistic by adhering to the criteria outlined in the *Cochrane Handbook*.

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

When inspecting methodological heterogeneity, we will identify differences between methodological factors across studies that may result in substantial diversity in outcome measurements. We will pay attention to whether outcome variables are defined in the same way, if they are measured by the same scale and quantity, and whether methodological diversity affects the quality of the summary effect size estimate. Where one or more studies have strong outlying results, we will exclude those results from further analysis.

**Assessment of reporting biases**

We will try to minimise the impact of reporting biases by completing comprehensive searches of multiple sources to increase the likelihood of identifying unpublished material. We will try to identify outcome reporting bias in trials by recording all trial outcomes, planned and reported, and by noting where there are missing outcomes. In the event of missing outcomes, we will contact the authors in an attempt to obtain any available data (Young 2011).
Data synthesis

Given the potential heterogeneity of psychological approaches for treating MDD and PGD, together with the likelihood of differing secondary morbid mental disorders in the bereaved population, we will use a random-effects model in all analyses (Shinohara 2013). We will provide a narrative summary for comparisons with only one available study and for those with a moderate or high level of statistical heterogeneity following exploration of heterogeneity.

Main planned comparisons

- CBT versus waiting list or usual care for bereavement-related MDD and for PGD
- CBT versus non-CBT therapies for bereavement-related MDD and for PGD
- CBT versus antidepressant medications and other drug therapies used explicitly for treating depressive disorders for bereavement-related MDD and for PGD

Subgroup analysis and investigation of heterogeneity

- CBT approach (cognitive therapy, cognitive behavioural therapy, rational emotive behaviour therapy, PG-CBT). Different CBT approaches have a varying underpinning theoretical basis (e.g. Beck 1979; Boelen 2006; Boelen 2007; Ellis 1962; Shear 2005; Wagner 2006). We will test if the effectiveness differs depending on the CBT approach used.
  - Comparator
   - Non-CBT psychological therapies (CGT, psychodynamic, humanistic, family or systemic therapy approaches). Different therapies may have different effect sizes and acceptability to participants. We will test if the effectiveness of CBT differs depending on the type of non-CBT approach used as a comparator.
   - Control (waiting list, usual care). We will test if the effectiveness of CBT differs depending on whether usual care or waiting list are used as comparators.
   - Pharmacological intervention (antidepressants versus other commonly prescribed drugs). Different antidepressants and other drug therapies used explicitly for treating depressive disorders for bereavement-related MDD and for PGD may have different effect sizes and acceptability to participants. We will test if the effectiveness of CBT differs depending on the type of pharmacological intervention used as a comparator.
- Treatment delivery (individual, online or group). Newer options for treatment delivery are emerging. Service providers, practitioners and service users may wish to know if the treatment outcomes differ. Increased Internet access and the increased therapeutic potential of computers for people living in rural areas, with physical disabilities or who fear stigma, suggest potential for Internet-based interventions (Wagner 2006). However, some approaches are heavily reliant on writing tasks, which may be an issue for participants with poor literacy skills.
  - Time since bereavement (less than six months, 6-12 months, more than 12 months). Rationale for different time points is due to differences in the ICD-11 (WHO 2018) and DSM-5 (APA 2013) regarding when you can diagnose PGD, which may impact on accessing treatment, and to determine if the time since bereavement impacts on the treatment response.

Sensitivity analysis

We will conduct sensitivity analyses for the primary outcome. For the purpose of investigating the potential impact of bias, we will exclude the following.
- Trials with high levels of post-randomisation loss (> 40%).
- Trials with unblinded outcome assessments or uncertain blinding of outcome assessments.
- Trials where bereavement was less than six months ago.

In order to assess the potential impact of fidelity to treatment, we will exclude studies that did not use an assessment of audio or videotapes of therapy sessions to assess fidelity to the psychological therapy models under evaluation.

'Summary of findings' tables

We will use the GRADE approach to summarise and interpret findings, and we will use the GRADE profiler to import data from RevMan to create 'Summary of findings' tables. We will construct a 'Summary of findings' table for each experimental and comparator intervention to address the following.
- Change in treatment response of major depressive disorder symptoms (medium-term).
- Change in treatment response of prolonged grief disorder (medium-term).
- Dropouts due to adverse effects (medium-term).
- Reported number of (a) deaths by suicide, or (b) suicide attempts.
- Change in the use of prescribed medication.

In keeping with Belsher 2017, we will assess the quality of evidence by examining the following: limitations in study design, indirectness of evidence, unexplained heterogeneity or inconsistency of results, imprecision of effect estimates, and potential publication bias. For each outcome, we will grade the quality of evidence according to the following categories.
• High quality: Further research is very unlikely to change our confidence in the estimate of effect.
• Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
• Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
• Very low quality: We are very uncertain about the estimate.

We will downgrade evidence from ‘high quality’ by one level for serious study limitations, indirectness of evidence, serious inconsistency, imprecision of effect estimates, or potential selective reporting bias.

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Disclaimer: The views and opinions expressed herein are those of the review authors and do not necessarily reflect those of the NIHR, the NHS, the Department of Health and Social Care or the Public Health Agency of Northern Ireland.

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* Indicates the major publication for the study
Appendix 1. OVID Medline: CCMD’s core search strategy used to inform the specialised register

A weekly search alert based on condition + RCT filter only

1. [MeSH Headings]:
   eating disorders/ or anorexia nervosa/ or binge-eating disorder/ or bulimia nervosa/ or female athlete triad syndrome/ or pica/ or hyperphagia/ or bulimia/ or self-injurious behavior/ or self mutilation/ or suicide/ or suicidal ideation/ or suicide, attempted/ or mood disorders/ or affective disorders, psychotic/ or bipolar disorder/ or cyclothymic disorder/ or depressive disorder/ or depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or seasonal affective disorder/ or neurotic disorders/ or depression/ or adjustment disorders/ or exp antidepressive agents/ or anxiety disorders/ or agoraphobia/ or neurocirculatory asthenia/ or obsessive-compulsive disorder/ or obsessive hoarding/ or panic disorder/ or phobic disorders/ or stress disorders, traumatic/ or combat disorders/ or stress disorders, post-traumatic/ or stress disorders, traumatic, acute/ or anxiety/ or anxiety, castration/ or korol/ or anxiety, separation/ or panic/ or exp anti-anxiety agents/ or somatoform disorders/ or body dysmorphic disorders/ or conversion disorder/ or hypochondriasis/ or neurasthenia/ or hysterical/ or munchausen syndrome by proxy/ or munchausen syndrome/ or fatigue syndrome, chronic/ or obsessive behavior/ or compulsive behavior/ or behavior, addictive/ or impulse control disorders/ or firesetting behavior/ or gambling/ or trichotillomania/ or stress, psychological/ or burnout, professional/ or sexual dysfunctions, psychological/ or vaginismus/ or Anhedonia/ or Affective Symptoms/ or *Mental Disorders/

2. [Title/ Author Keywords]:
   (eating disorder* or anorexia nervosa or bulimi* or binge eat* or (self adj (injur* or mutilat*)) or suicide* or suicidal or parasuicid* or mood disorder* or affective disorder* or bipolar i or bipolar ii or (bipolar and (affective or disorder*))) or mania or manic or cyclothymic* or depression or depressive or dysthymic or neurotic or neurosis or adjustment disorder* or antidepress* or anxiety disorder* or agoraphobia or obsess* or compuls* or panic or phobi* or ptsd or posttrauma* or post trauma* or combat or somatoform or somati* or unexplained or body dysmorphic* or conversion disorder or hypochondriasia* or neurasthenia* or hysteria or munchausen or chronic fatigue* or gambling or trichotillomania or vaginismus or anhedoni* or affective symptoms or mental disorder* or mental health).ti,kf.

3. [RCT filter]:
   (controlled clinical trial.pt. or randomized controlled trial.pt. or (randomi#ed or randomi#ation).ab.ti. or randomly.ab. or (random* adj3 (administ* or allocat* or assign* or class* or control* or determine* or divide* or distrib* or expose* or fashion or number* or place* or recruit* or substit* or treat*)).ab. or placebo.ab.ti. or drug therapy.fs. or trial.ab.ti. or groups.ab. or (control* adj3 (trial* or study or studies)).ab.ti. or ((singl* or doubl* or tripl* or trebl*) adj3 (blind* or mask* or dummy*)).mp. or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or randomized controlled trial/ or pragmatic clinical trial/ or (quasi adj (experimental or random*)).ti,ab. or ((waitlist* or wait* list* or treatment as usual or TAU) adj3 (control or group)).ab.)

4. (1 and 2 and 3)

Records are screened for reports of RCTs within the scope of the Cochrane Common Mental Disorders Group. Secondary reports of RCTs are tagged to the appropriate study record. Similar weekly search alerts are also conducted on OVID EMBASE and PsycINFO, using relevant subject headings (controlled vocabularies) and search syntax, appropriate to each resource. A quarterly search of the Cochrane Central Register of Controlled Trials (CENTRAL) is conducted c/o the Cochrane Register of Studies Online (CRSO).

Appendix 2. Review Search: Ovid MEDLINE

Ovid MEDLINE databases (MEDLINE(R), Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (1946 onwards)) will be searched using the following search strategy.

1. (bereave* or grief or grieving or mourning) adj disorder*.ti,ab.kf.
2. (complicated or complex or elevated or intense or maladaptive or morbid$ or persistent or prolonged or sever$) adj3 (bereav* or grief* or grief* or mourn*).ti,ab.kw.
3. (grief disorder adj5 depress*).ti,ab.kf.
4. persistent complex bereavement disorder$.ti,ab.kf.
5. (PGD and (grief$ or griev$ or bereav$)).ti,ab.kf.
6. 1 or 2 or 3 or 4 or 5
Psychological therapies for major depressive disorder and prolonged grief in bereaved adults (Protocol)

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Appendix 3. Review Search: CCMDCTR

1. Cochrane Common Mental Disorders Controlled Trials Register (CCMDCTR)

CCMDCTR-Studies
The information specialist will search the Group’s specialised register using the following controlled vocabulary terms to identify relevant studies:
Condition = (grief or bereavement)
Two review authors will screen all primary and secondary references tagged to these studies to check for eligibility and trial data.

CCMDCTR-References
The information specialist will run a search the CCMDCTR-References Register using a more sensitive set of terms to identify additional untagged/uncoded reports of RCTs:

#1 ((depress* or dythymi* or “affective disorder*” or “affective symptoms” or mood*):ti,ab,kw,emt,mh
#2 (bereav* or grief or grieving or morn* or “death of” or (death near “loss of”) or (death and “life chang* event*”) or widow* or orphan*):ti,ab,kw,ky,emt,mh
#3 ((death* or died or dead or suicide* or homocide* or genocide*) near3 (infant* or child* or adolescent* or teen* or husband* or partner pr partners or spous* or parent* or mother* or father* or family or families or sibling* or relation or (relative* not “relative risk”) or caregiver* or “care giver*” or friend* or colleague* or whanau or tribe or tribal or neighbour* or neighbor* or “significant other*”):ti,ab,kw,ky,emt,mh
#4 (#1 and (#2 or #3))
#5 ((prolonged or complicated) near2 (grief or grieving)):ti,ab,kw,ky,emt,mh
#6 (#4 or #5)

[Key to field tags. ti:title; ab:abstract; kw:keywords; ky:other keywords; mh:MeSH headings; mc:MeSH check words; emt:EMTREE headings]
Two review authors will screen all untagged references to check for eligibility. Where appropriate we will tag reports of the same trial together to ensure no trial is counted twice.
CONTRIBUTIONS OF AUTHORS
Audrey Roulston and Mike Clarke conceived, designed and secured funding for the review. Mike Clarke, Bridget Candy, Michael Donnelly and Michael Duffy provided methodological expertise and critical comments on protocol manuscripts. Michael Donnelly, Jennifer McGaughey and Orla Keegan identified areas for clarification within the protocol. Michael Duffy also provided subject expertise on the conditions and psychological interventions. All authors reviewed the final draft.

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