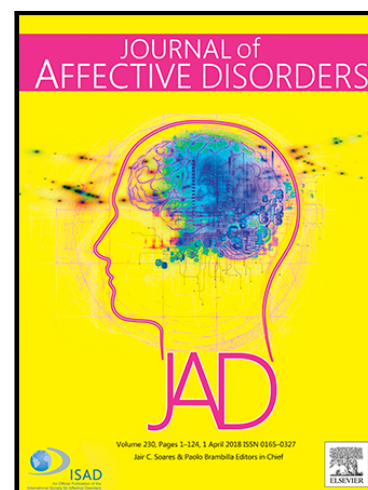


Accepted Manuscript

The Prevalence of Intrusive Memories in Adult Depression: A Meta-Analysis

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PII: S0165-0327(18)30444-0
DOI: <https://doi.org/10.1016/j.jad.2019.04.055>
Reference: JAD 10716



To appear in: *Journal of Affective Disorders*

Received date: 16 September 2018
Revised date: 8 February 2019
Accepted date: 8 April 2019

Please cite this article as: Alexandra Payne , Aleksandra Kralj , Judith Young , Richard Meiser-Stedman , The Prevalence of Intrusive Memories in Adult Depression: A Meta-Analysis, *Journal of Affective Disorders* (2019), doi: <https://doi.org/10.1016/j.jad.2019.04.055>

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Highlights

- An estimated 76.0% of adults with depression report intrusive memories.
- Depressed adults are more likely to report intrusive memories than healthy controls.
- The prevalence of intrusive memories in depression is comparable to that in PTSD.
- Intrusive memories may be an important target for intervention in adult depression.

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TITLE

The Prevalence of Intrusive Memories in Adult Depression: A Meta-Analysis.

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Abstract

Background: Intrusive memories have typically been associated with post-traumatic stress disorder (PTSD) but some studies have suggested they can also occur in depression-alone.

Objective: This meta-analysis aimed to estimate the prevalence of intrusive memories in adult depression and to explore methodological and other factors that may moderate this prevalence.

Method: The databases PsycINFO, PsycARTICLES, MedLine, PubMed, CINAHL and Embase were searched for relevant articles, published up to and including July 2016. Studies measuring point prevalence of intrusive memories in adults aged 18 years or above with depression were included and assessed for quality. Meta-analysis was completed under a random effects model.

Results: Seven studies measuring point prevalence of intrusive memories in adult depression were included. The overall pooled prevalence estimate calculated was 76.0% (95% CI 59.4 – 89.4%), reducing to 66.0% (95% CI 51.0 – 79.5%) when restricted to intrusive memories experienced within the week prior to assessment. Heterogeneity was high. Between-groups analyses indicated that adults with depression are as likely to experience intrusive memories as adults with PTSD, and more likely to experience intrusive memories than healthy controls (risk ratio of 2.94, 95% CI 1.53 – 5.67).

Limitations: The strength of conclusions is limited by the small number of studies included. Consideration of the relationship between depression, intrusive memories and trauma exposure is required.

Conclusions: Intrusive memories are experienced by a large majority of adults with depression and may therefore be an important target for cognitive intervention. Larger scale measurement of clinical outcome is needed with identification of individual factors predicting treatment response.

Keywords: Prevalence, Depression, Intrusive Memory, Meta-analysis

The Prevalence of Intrusive Memories in Adult Depression: A Meta-Analysis

Considered globally to be the leading cause of disability, depression is not only among the most debilitating of mental health difficulties for affected individuals but an identified target for advancing mental health care worldwide (World Health Organization [WHO], 2009, 2013). The most recent National Health Survey for England estimated the lifetime prevalence of depression at 19% in adults aged over 16 years (Craig et al., 2014). Therapeutic interventions within a cognitive behavioural framework are recommended in the psychological treatment of depression at all stages of severity under a stepped-care model and numerous studies have been presented in recent years attesting to their efficacy (National Institute for Health and Care Excellence [NICE], 2009). Although highly researched, evidence comparing the effectiveness of cognitive behaviour therapy (CBT) to other psychological interventions is mixed and rates of relapse and recurrence following treatment remain high (Hofmann et al., 2012; Richards, 2011; Vittengl et al. 2007). Cuijpers et al. (2013) report a large effect size in the superiority of CBT over control samples in their recent meta-analysis but describe considerable publication bias and argue that the efficacy of CBT in the treatment of depression has been overestimated.

Of recent interest in the adult depression literature has been the experience of intrusive memories, defined as uninvited memories that occur spontaneously and intrude on conscious thought (Brewin et al., 1996a). Intrusive memories have long been considered central to posttraumatic stress disorder (PTSD), listed in diagnostic criteria alongside other involuntary re-experiencing symptoms including recurring dreams and ‘flashbacks’ or reliving with dissociation (American Psychiatric Association [APA], 2013; WHO, 1992). However, with increasing recognition that experience of intrusive memories is not unique to

PTSD, evidence of this experience as common to many psychological disorders is growing with a move toward viewing intrusive memories as a transdiagnostic process (Harvey et al., 2004). The first to examine intrusive memories in depression, Kuyken and Brewin (1994) interviewed depressed women with histories of childhood abuse. They reported intrusive memories in approximately 85% of their sample accompanied by high avoidance, with higher scores for intrusiveness and avoidant behaviour associated with increased depression severity. Brewin et al. (1996b) later replicated these findings in a mixed sex sample of depressed adults. They identified intrusive memories following a range of negative life events, evidencing that this experience is not exclusive to survivors of abuse. Comparing adults with depression to adults with PTSD and a non-clinical control group, matched for histories of life events and trauma, Reynolds and Brewin (1998) reported a range of intrusive cognitions in all groups. Exploring intrusive memories in greater depth, they observed frequent intrusive memories and comparable levels of associated avoidance across matched samples of adults with depression and adults with PTSD (Reynolds & Brewin, 1999). Further, whilst dissociative re-experiencing continues to be considered a hallmark of PTSD, the experience of highly vivid intrusive memories with accompanying feelings of reliving and physiological sensation is one shared by adults with depression (Reynolds & Brewin, 1999; Patel et al., 2007).

Over the last two decades, researchers have assessed many aspects of intrusive memories in depression, including memory characteristics, content and qualities (e.g. Newby & Moulds, 2011a; Newby & Moulds, 2012; Parry & O’Kearney, 2014; Williams & Moulds, 2007a), memory appraisals (e.g. Newby & Moulds, 2010; Starr & Moulds, 2006) and cognitive avoidance (e.g. Newby & Moulds, 2011b; Williams & Moulds, 2007b). Further, longitudinal research has reported intrusive memories to be predictive of depressive symptomology six months later, a relationship that holds when severity of depression at

baseline is controlled (Brewin et al., 1999). In their recent meta-analysis exploring the association between intrusive memories and depression, Mihailova and Jobson (2018) report positive associations of moderate size between intrusive memory frequency and depression and between distress experienced in response to these memories and severity of symptoms. Further, negative appraisals of intrusive experience, cognitive avoidance and rumination were seen to be moderately, positively associated with depression, thus proposing that the maladaptive appraisals and ineffective strategies employed in emotional regulation understood to be implicated in the onset and maintenance of depression with respect to processing of verbal cognitions are relevant also in the processing of negative, autobiographical memories (Mihailova & Jobson, 2018; Weßlau & Steil, 2014; Williams & Moulds, 2010).

Indeed, recognition that distressing intrusive memories are frequently observed in depression and may be implicated in its course and maintenance has sparked interest in the potential utility of cognitive interventions targeting this experience (Brewin et al., 2010; Newby et al., 2014). Given the success of psychological techniques (particularly elements of trauma-focused CBT) in addressing intrusive memories in the context of PTSD (Cusack et al., 2015), targeting such phenomena in depression may be an important adjunct to current therapies for depression. However, there remains uncertainty in the published literature as to the prevalence of intrusive memories in depression, thus rendering the potential application of this research programme unknown. The primary aim of the current study was to conduct a meta-analysis to provide a best estimate of the prevalence of intrusive memories in adults with depression, with a view to appraising the extent to which depression is characterised by the presence of intrusive memories. If intrusive memories are a common or even core feature of adult depression, this would have implications for assessment and treatment plans in routine clinical practice. It must be acknowledged that, as is common in meta-analysis, the

review presented here includes a small number of studies and it is therefore prudent to outline the limitations this brings. IntHout et al., (2015) observed that of 2,009 meta-analyses reporting dichotomous outcomes, selected from the Cochrane Database of Systematic Reviews published between the years 2009 and 2013, the number of studies included ranged from 2 to 7 studies, with a mean average of 4 studies. Performing a meta-analysis with a small number of studies under a random-effects model increases the risk of error in estimating between-studies variance, inviting suggestion that meta-analysis with small numbers of studies should be avoided. However, Borenstein et al. (2009) argue that providing a statistical review of results with known limitations, albeit with likely high heterogeneity, is preferable to not doing so and thus leaving conclusions to be drawn unconcernedly from individual studies without systematic review. Although it must be recognised that the sample sizes of selected studies and the total number of studies included in a meta-analyses may result in significant between-studies heterogeneity, thus raising questions regarding reliability, it is also observed that combining several small studies in meta-analysis can achieve more accurate effect size estimates than can a single large study alone (IntHout et al., 2012). Thus, despite the limitations discussed, the current meta-analysis feels timely to provide initial indication of the potential application of rapidly expanding research exploring the experience of intrusive memories in adult depression. As recommended by Schmidt and Hunter (2015), this paper will serve to synthesise the results of the extant literature, inviting update as research in this field continues to grow.

Assessment of the prevalence of intrusive memories is challenged by methodological differences across studies including assessment of depression, handling of comorbid difficulties including PTSD and, in particular, the operationalisation and assessment of intrusive memories. This study therefore also aimed to explore the potential methodological factors influencing the prevalence rate, particularly with regard to assessment of clinical

presentation and identification of intrusive memories. Additional analyses were considered to assess the impact of potential moderator variables but were not conducted due to the small number of studies included and subsequent lack of statistical power.

Method

This review was registered on the PROSPERO register of systematic reviews (7th June 2016, CRD42016040129). The current review was conducted in line with the meta-analysis of observational studies in epidemiology guidelines (MOOSE; Stroup et al., 2000) and utilised the preferred reporting items for systematic reviews and meta-analyses framework (PRISMA; Moher et al., 2009) to record the search process and paper selection.

Literature Search

An initial literature search of the databases PsycINFO, PsycARTICLES, MedLine, PubMed, CINAHL and Embase was conducted in July 2016 to identify published research measuring the point prevalence of intrusive memories in adult depression. Articles were selected where the search terms (*intrusi** OR *involuntary*) AND (*memor**) AND (*depress** OR *dysthymi**) appeared within the title or abstract. The search was restricted to peer-reviewed articles published in English. Studies were included if they: (a) provided a measure of the prevalence of intrusive memories; (b) comprised a sample of adults aged 18 years or over; and (c) employed a sample with clinically significant depression, as assessed through screening or through use of diagnostic interviews. Studies were excluded if: (a) the sample consisted exclusively of adults with depression who reported experience of intrusive memories, i.e. they were selected for the presence of intrusive memories; (b) the sample was selected for mental or physical health comorbidity or trauma exposure; or (c) an experimental manipulation occurred prior to measurement of the prevalence of intrusive memories, including where retrieval of intrusive memories was cued. Articles identified through the initial search were screened for eligibility by the first author through inspection of the title

and abstract. Identified articles were read in full by the first and second authors, with any disagreements resolved through discussion. The reference sections of selected papers were then hand searched.

Quality Assessment

Quality assessment of the seven included studies was guided by the criteria offered by Richardson et al. (1999), adapted for appraisal of articles considering prevalence of symptomology, as opposed to disease prevalence, with hierarchy of levels identified prior to assessment. Each article was rated green (criterion fully met), amber (criterion partially met) or red (criterion not met) against each quality criterion, as detailed in Supplementary Material A. All articles were assessed independently by two reviewers to determine whether (a) the clinical sample of adults with depression was clearly defined and recruited against explicit diagnostic criteria; (b) the sample was representative, assessed according to source of participant recruitment (community sampling vs. clinical recruitment only); (c) consideration was given to comorbid PTSD in the assessment and inclusion of participants; (d) the experience of intrusive memories was clearly operationalised; and (e) a clearly identified time frame for point prevalence was given. An overall quality rating was then calculated for each article, with green ratings scoring 2, amber ratings scoring 1 and red ratings scoring 0, giving a total score out of a possible maximum of 10.

Statistical Analysis

All analyses were performed in OpenMeta[Analyst] (Wallace et al., 2012). The primary variable of interest across studies was the prevalence of intrusive memories in adults with depression. This was considered a measure of effect size with a single prevalence estimate extracted from each study, presented as percentages to aid comprehension. Where depressed samples were split into trauma-exposed depressed (TED) and depressed adults without trauma (DWT), these groups were combined to give a single prevalence estimate.

With prevalence estimates as high as 96.0% (Newby & Moulds, 2010), the Freeman-Tukey double arcsine transformation was performed (Freeman & Tukey, 1950), as recommended by Barendregt et al. (2013) to avoid weighting bias where prevalence estimates approach upper and lower limits. To allow comparison of the prevalence across groups in controlled samples, estimates of the prevalence of intrusive memories in adults with PTSD and in healthy control samples (HC) were extracted, where available. Where control samples were split into recovered depressed and never depressed, these groups were combined to give a single prevalence estimate. With one study reporting prevalence of 100% in PTSD, risk ratios are presented rather than odds ratios (Deeks et al., 2011).

Considerable heterogeneity was expected given the inclusion of studies with diverse demographics including in severity of depression, recruitment from community and clinical settings with some participants accessing pharmaceutical or psychological treatment and variation in the assessment of intrusive memories. In acknowledgement of this, a random-effects model was employed, with each sample supposed to provide a prevalence estimate from among the range of possible prevalence rates observed within the population and weighted according to the inverse of its variance (Borenstein et al., 2009; DerSimonian & Laird, 1986). The heterogeneity of studies included in each analysis was tested through use of the Q statistic, to determine the proportion of variance that may be attributed to sampling error, and the I^2 statistic (Higgins & Thompson, 2002), to assess between-studies variability. Confidence intervals are provided to supplement point estimate I^2 statistics to account for bias observed when the number of studies included in a meta-analysis is small (von Hippel, 2015), calculated according to the formulae offered by Borenstein et al. (2009). Sensitivity analyses were undertaken to test whether key methodological aspects of the included studies (e.g. excluding studies that did not use a structured interview to assess depression or the presence of intrusive memories) altered the pattern of results.

Results

Search Results

The results of the literature search and overview of paper selection are presented in Figure 1. The initial search generated 368 unique results that were screened for eligibility by the first author. The 32 identified articles were read in full by the first and second authors (Supplementary Material B), with any disagreements resolved through discussion, resulting in identification of 9 eligible papers. The reference sections of these articles were hand searched, revealing one additional paper. Where more than one paper presented the same data, paper selection was based on the inclusion of a comparison group, if applicable, or earliest publication date; this resulted in the exclusion of three papers. This gave a final sample of seven original articles to be included in the meta-analysis involving a total of 262 adults with depression, marked by asterisks in the reference list (Table 1).

Consideration of Publication Bias

Given the inclusion of fewer than 10 studies, a funnel plot was not generated, in line with Anzures-Cabrera and Higgins' (2010) recommendations. Other statistical approaches were instead considered but the measure of prevalence of intrusive memories was invariably among a range of outcome variables in the included studies and was often not the variable of primary focus. Taking a statistical measure of publication bias based on the prevalence rates reported therefore felt less appropriate and a formal measure of publication bias is therefore not presented. Although the observed prevalence rate may be less likely to have directly impacted on paper publication, the findings of the current meta-analysis should be considered alongside the possibility that studies recording a low prevalence rate may have obtained insufficient data to measure the outcome variable of interest and may therefore have remained unpublished.

Methodological Quality

Following the rating of each study against the five identified quality criteria, the initial rate of agreement between the first and second authors was 86%. Disagreements were resolved through discussion reaching consensus. Agreed quality ratings are presented in Table 2. All studies fully met or partially met at least four of the five quality criteria, with a minimum overall quality rating assigned of five and a maximum assigned of nine. Full descriptions of the assessment of depression, measurement of the prevalence of intrusive memories and assessment of PTSD across studies are provided in Tables 3, 4 and 5, respectively.

[INSERT FIGURE 1 HERE]

[INSERT TABLE 1 HERE]

[INSERT TABLE 2 HERE]

[INSERT TABLE 3 HERE]

[INSERT TABLE 4 HERE]

[INSERT TABLE 5 HERE]

Pooled Prevalence

Prevalence of intrusive memories reported in the seven studies included was pooled to obtain an overall prevalence estimate of 76.0% (95% CI 59.4 – 89.4%), with considerable heterogeneity observed between studies, $I^2 = 87.6%$ (95% CI 76.86 – 93.40%), $Q(6) = 48.53$,

$p < .001$ (Figure 2). Removing each study in turn to assess the impact on the model obtained prevalence estimates ranging from 71.8% (95% CI 54.7 – 86.3%) to 80.7% (95% CI 66.0 – 92.2%), indicating that the overall prevalence estimate was not unduly affected by any one study. Considerable heterogeneity continued to be observed in all analyses (Table 6).

Sensitivity Analyses

The analysis was run only including the five studies in which depression was assessed via clinical interview against explicit diagnostic criteria by the research team (Table 3). It is possible that the use of self-report measures and acceptance of unconfirmed diagnoses made by referring clinicians may have resulted in the inclusion of participants presenting with symptoms falling outside of clinical significance. However, the prevalence estimate obtained was 71.6% (95% CI 50.5 – 88.9%) and therefore close to the overall prevalence estimate, with considerable heterogeneity remaining between studies, $I^2 = 88.2\%$ (95% CI 75.1 – 94.4%), $Q(4) = 34.01$, $p < .001$.

Of the seven studies included, four controlled for the presence of PTSD, excluding adults with PTSD from the sample or from the depression group, where a control sample of adults with PTSD was employed (Table 5). Adjusted prevalence estimates were calculated for those studies that did not exclude comorbid PTSD but where the number of participants with comorbid PTSD was reported, making the conservative assumption that each of these participants reported intrusive memories. The analysis was run with these adjusted prevalence rates entered and with the one study excluded that did not exclude on the basis of PTSD and did not report the number of participants meeting criteria for this diagnosis. This gave a prevalence estimate of 73.5% (95% CI 53.1 – 89.8), with considerable heterogeneity, $I^2 = 90.58$ (95% CI 82.2 – 95.0%), $Q(5) = 53.05$, $p < .001$, and thus close to the overall prevalence estimate.

Estimates reported in the five studies with a point prevalence defined as occurring within the previous week were pooled (Table 4), obtaining a prevalence estimate of 68.4% (95% CI 49.2 – 85.0%), with considerable heterogeneity, $I^2 = 86.00\%$ (95% CI 69.3 – 93.6%), $Q(4) = 28.57$, $p < .001$. Included in this analysis were two studies that asked first for intrusive memories in the previous week but, where none were reported, provided prompts; Newby and Moulds (2010) prompted for the most recent intrusive memory, limited to those occurring within the previous 12 months, whilst Patel et al. (2007) prompted for intrusive memories from a ‘typical’ week or experienced during the last depressive episode. With these studies excluded, the prevalence estimate reduced to 66.0% (95% CI 51.0 – 79.5%), with heterogeneity falling below significance, $I^2 = 64.21$ (95% CI 0.0 – 89.7%), $Q(2) = 5.59$, $p = .06$.

Finally, the analysis was run using only the five studies that measured the prevalence of intrusive memories via interview, which may be assumed to have allowed the researchers to confirm participants’ understanding of the concept of intrusive memories prior to assessing their experience. The prevalence estimate obtained was very close to the overall prevalence estimate calculated, at 75.9% (95% CI 58.0 – 90.2%) with considerable heterogeneity, $I^2 = 85.38\%$ (95% CI 67.7 – 93.4%), $Q(4) = 27.36$, $p < .001$.

Between Groups Analyses

Risk ratios were analysed for the experience of intrusive memories in depression against adults with PTSD and healthy controls. For the three studies including a comparison group of adults with PTSD, risk ratios between the prevalence estimates recorded in depression and those recorded in PTSD were pooled to obtain an overall risk ratio of 1.25 (95% CI 0.99 – 1.58), approaching significance at $p = 0.06$ with considerable heterogeneity between studies, $I^2 = 79.8\%$ (95% CI 36.0 – 93.6%), $Q(2) = 9.90$, $p = .007$. This suggests a

trend toward an increased risk of experiencing intrusive memories in PTSD than in depression.

For the three studies including a group of healthy controls, risk ratios between the prevalence estimates recorded in adults with depression and those without were pooled to obtain an overall risk ratio of 2.94 (95% CI 1.53 – 5.67), with heterogeneity falling below significance, $I^2 = 0\%$ (95% CI 0.0 – 94.9%), $Q(2) = 1.135$, $p = .57$. The zero value of I^2 here should be considered with caution given the small number of studies included in this analysis and the wide confidence interval presented. The risk ratio calculated was significant at $p = .001$ and indicates that adults with depression are significantly more likely to experience intrusive memories than healthy controls.

Discussion

A growing trend in recent years, research aiming to identify the effective components of cognitive interventions has seen consideration of intrusive memories as a transdiagnostic process, observed not only in PTSD but across a range of mental health presentations. The suggestion that intrusive memories occur frequently in depression and may play a role in its course and maintenance has inspired thought as to the potential utility of this experience as a cognitive target for intervention. However, the likely impact of such interventions has been obscured by the lack of consistency in observed prevalence across studies. To address this disparity, the current meta-analysis aimed to calculate an overall estimate of the prevalence of intrusive memories in adult depression and to explore potential factors influencing this prevalence rate. A total of seven studies met the inclusion criteria, measuring the prevalence of intrusive memories in adults aged 18 years or over with clinical depression, yielding a total of 262 participants. The results indicate an overall prevalence estimate of 76.0% (95% CI 59.4 – 89.4%), remaining stable when each study was omitted in turn. The overall prevalence estimate was not markedly affected by assessment of depression (diagnostic interview vs.

self-report) or assessment of intrusive memories (interview vs. questionnaire). These findings indicate that intrusive memories are reported by a large majority of adults with depression and therefore indicate that the development of cognitive treatments targeting this experience may be of value.

Consideration of Heterogeneity

Studies were screened for inclusion against a list of criteria considering recruitment, sample selection and measurement of intrusive memory prevalence with the aim of reducing heterogeneity and allowing comparison across papers. However, considerable heterogeneity was observed in the overall pooled prevalence analysis. This remained across all other analyses with the exception of the sensitivity analysis exploring the impact of the given time frame for intrusive memory identification. Specifically, the prevalence rate reduced to 66% (95% CI 51.0 – 79.5%) when restricted to intrusive memories occurring only within the week prior to assessment, with heterogeneity falling below significance. This indicates that when assessment is constrained to this measure of point prevalence, results across studies are comparable, whilst permitting inclusion of intrusive memories over a broader time frame introduces considerable variability.

Comparison of Intrusive Memories in Depression vs. PTSD

Of significant interest in the current review is the finding that controlling for PTSD within samples did not significantly alter the prevalence of intrusive memories. Between-groups analysis examining studies that included a comparison sample of adults with PTSD obtained a risk ratio of 1.25, falling below significance, indicating that adults with depression are at comparable risk of experiencing intrusive memories as adults with PTSD. These findings provide some evidence that intrusive memories occur in depression independently of PTSD and highlight that the headline finding of high prevalence applies to depression both comorbid with and in the absence of PTSD. However, these findings must be considered with

a degree of caution given the small number of studies employing a PTSD comparison group and in the absence of sufficient information evidencing trauma exposure among samples.

Clinical Relevance and Application

Estimates of the prevalence of intrusive memories in healthy controls ranged from 23% to 73% in studies employing a comparison sample, suggesting that intrusive memories are not uncommon among adults without mental health difficulties. However, between-groups analysis across studies that recruited adults with depression and a comparison sample of healthy controls revealed a risk ratio of 2.94 (95% CI 1.53 – 5.67). Although again calculated from a small number of studies, this finding was highly significant, indicating that adults with depression are significantly more likely to experience intrusive memories than adults without depression. Coupled with the suggestion above that adults with depression are at near comparable risk of intrusive memories as adults with PTSD, this finding supports the notion of intrusive memories as a transdiagnostic process and highlights this experience as of clinical importance in depression.

From the introduction of cognitive therapy, the role of mental imagery in psychological difficulties has been acknowledged, with early observation that modifying distressing imagery can realise affective change (Beck, 1976). However, cognitive therapy in adult depression has typically focused on verbal restructuring and techniques exploring imagery have received less attention (Holmes et al., 2007; Wheatley & Hackmann, 2011). As discussed, intrusive memories are considered a diagnostic feature and hallmark of PTSD and cognitive treatments typically focus on intrusive experience. The current findings indicate that the application of such interventions may be extended to adults with depression. Such interventions include eye movement desensitisation and reprocessing (EMDR; Wood & Ricketts, 2013) and mindfulness-based cognitive therapy (Seagal et al., 2002; Ma & Teasdale, 2002). However, research exploring the efficacy of these approaches has not

focused on intrusive memories as the *central active component* of intervention, rather than examining the overall impact of treatments that include imagery-based components on depression. The efficacy of components targeting intrusive memories therefore cannot be evaluated separately from the efficacy of the overall treatment approach. However, the effectiveness of specifically targeting the experience of intrusive memories in depressed adults has been afforded through the application of imagery rescripting to depression, which has been of interest in the recent literature

Imagery rescripting requires the client to revisit their memory, describing in detail the narrative and emotional content, and to construct an alternative scenario in collaboration with the therapist that offers a more positive outcome (Hackmann, 1998). In a series of papers, Wheatley and colleagues have explored the application of imagery rescripting to depression (Wheatley et al., 2009; Wheatley & Hackmann, 2011; Wheatley et al., 2007). Although acknowledging that questions remain regarding the underlying mechanisms by which change is achieved, Wheatley and Hackmann (2011) propose that imagery rescripting offers a powerful adjunct to CBT where distressing intrusive memories are reported to be present. Brewin et al. (2009) term this approach 'modular treatment', by which therapeutic components are matched to individual symptom profiles. They go on to propose imagery rescripting as a stand-alone, brief treatment for adults with depression experiencing intrusive memories, evidenced to be effective in reducing depressive symptomology with maintenance at one year follow-up. The current findings support such suggestions, indicating that for upwards of two thirds of adults with depression, imagery rescripting may prove a successful stand-alone intervention or a beneficial module to enhance cognitive interventions. However, questions remain regarding the underlying mechanisms by which change is achieved and Wheatley and Hackmann (2011) highlight the need to explore individual factors for consideration in identifying clients for whom imagery focused interventions may be

appropriate. Brewin et al. (2009) call for larger scale investigation, preferably in the form of a randomised controlled trial, to strengthen preliminary findings and to evidence the applicability of interventions to a broader audience.

Limitations

Overall, the strength of conclusions that can be drawn from the current meta-analysis is restricted by the small number of studies measuring the prevalence of intrusive memories in depression and, in particular, the small number of studies including each of the two comparison groups considered. Roloff et al., (2013) observe that where the results of meta-analysis are inconclusive, additional study is typically recommended to enhance statistical power. However, they argue that where heterogeneity is anticipated between studies, for example in the collection of observational data such as that recorded in assessment of prevalence, running a single additional study, no matter its size, may prove insufficient to achieve the desired level of power. Rather, a preferable approach would be to update the presented meta-analysis as further research is published, rerunning the analyses to include the new data (Schmidt & Hunter, 2015; Schmidt & Raju, 2007).

The potential impact of trauma exposure and presentation of comorbid PTSD should also be considered when interpreting the current findings. Firstly, three studies did not exclude adults presenting with PTSD from the depression group (Brewin et al. 1996b; Patel et al., 2007; Smets et al., 2014), one of which did not assess for the presence of PTSD (Brewin et al., 1996b). In recognition that intrusive memories are considered a defining feature of PTSD (APA, 2013; WHO, 1992), it must be considered that the inclusion of adults with PTSD may have led to an overestimate of the prevalence of intrusive memories in depression. However, sensitivity analyses indicated that when utilising adjusted prevalence estimates to control for comorbid PTSD, a large majority of adults with depression continued to describe intrusive memories. Secondly, just two studies assessed trauma exposure within

depressed and control samples (Birrer et al., 2007; Parry & O’Kearney, 2014), with only one of these reporting prevalence independently for trauma-exposed and non-trauma-exposed depressed participants (Birrer et al. 2007). Given the well documented link between adverse life events and the development of depression, attempts to fully partial out trauma exposure from the relationship between depression and intrusive memory prevalence may be somewhat futile and lacking in clinical relevance. However, research exploring this relationship further would allow consideration of the impact of trauma exposure on intrusive memory prevalence and may provide useful information regarding the profiles of individuals likely to benefit from interventions targeting intrusive memories.

Conclusions

The current meta-analysis estimates a 76.0% point prevalence rate of intrusive memories in adult depression and suggests that adults with depression are at near comparable risk of experiencing intrusive memories as adults with PTSD. The prevalence rate observed was robust to methodological variation, remaining almost unchanged when controlling for comorbid presentation of PTSD and when separated by assessment method (interview vs. questionnaire), thus indicating that intrusive memories are an experience shared by a large majority of adults with depression. It can be argued therefore that intrusive memories are a core clinical feature of adult depression, consideration of which may be beneficial in clinical assessment. Intrusive memories may be an important cognitive target for therapeutic intervention for a significant proportion of depressed adults. The current results support the existing programme of research exploring the utility of imagery rescripting in depression and suggest that interventions addressing intrusive memories may be of clinical utility with depressed adults. As recommended by Brewin et al. (2009) and Wheatley and Hackmann (2011), larger scale investigation measuring clinical outcome is warranted to identify the profiles of individuals for whom such interventions may be appropriate and individual factors

predicting treatment response, including the relationship between depression, intrusive memories and trauma exposure. Overall, given indication that intrusive memories may play a role in the course and maintenance of adult depression alongside the high prevalence rate noted here, it is encouraging to see a renewed and timely interest in intrusive memories and interventions targeting this experience.

Contributors

Alexandra Payne and Richard Meiser-Stedman designed the meta-analysis. Alexandra Payne completed the literature searches and quality ratings, with identified articles also read in full and rated for quality by Aleksandra Kralj. Alexandra Payne and Richard Meiser-Stedman undertook the statistical analyses. Alexandra Payne wrote the first draft of the manuscript, which was reviewed by Richard Meiser-Stedman, Aleksandra Kralj and Judith Young. All authors have approved the final manuscript.

Role of the Funding Source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

None.

Declaration of Interest

Conflicts of interest: None

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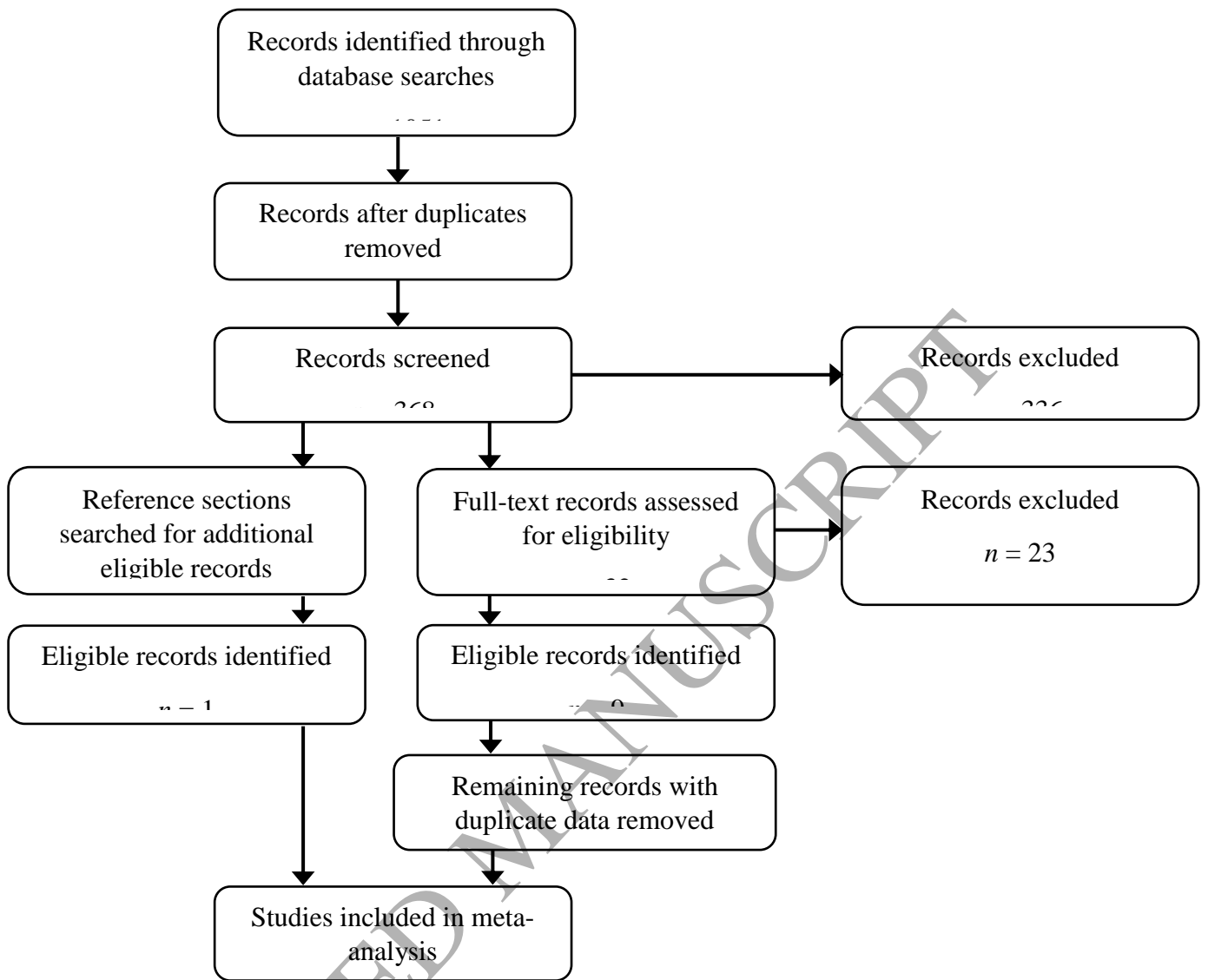


Figure 1: Search Strategy and Paper Selection Documented Within the PRISMA Framework.

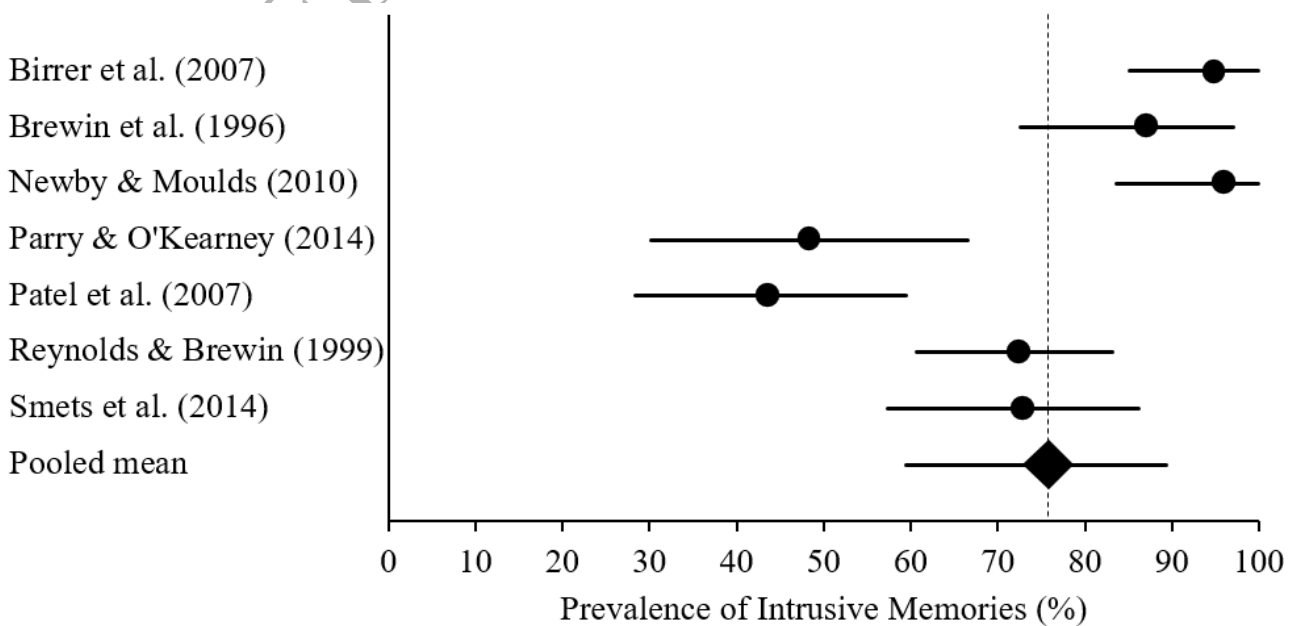


Figure 2: *Forest Plot of Pooled Mean Prevalence with 95% Confidence Intervals.*

ACCEPTED MANUSCRIPT

Table 1

Methodological and Sample Characteristics of Included Studies

Study	Country	Overall sample		Recruitment	Depressed sample		Type	Recruitment	Control sample	
		<i>N</i> (<i>n</i> males)	Mean age (SD, range)		<i>N</i> (<i>n</i> males)	Mean age (SD)			<i>N</i> (<i>n</i> males)	Mean age (SD, range)
Birrer et al. (2007)	Switzerland	65 (7)	<i>Not reported</i>	Clinical, multiple and community	TED 20 (2) DWT 19 (4)	TED 44 (10) DWT 46 (1)	PTSD	Clinical, multiple and community	26 (1)	39 (10)
Brewin et al. (1996b)	United Kingdom	31 (10)	<i>See depressed</i>	Clinical, multiple	31 (10)	41 (12)	None			

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Newby & Moulds (2010)	Australia	85 (35)	24.26 (6.05)	Community	25 (8)	25.48 (7.22)	RD and ND	Community	RD 30 (12) ND 30 (15)	RD 25.07 (6.55) ND 22.43 (3.80)
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Table 1 continued

Methodological and Sample Characteristics of Included Studies

Study	Country	Overall sample		Recruitment	Depressed sample		Type	Recruitment	Control sample	
		<i>N</i> (<i>n</i> males)	Mean age (SD, range)		<i>N</i> (<i>n</i> males)	Mean age (SD)			<i>N</i> (<i>n</i> males)	Mean age (SD, range)
Parry & O'Kearney (2014)	Australia	87	35.67 (16.42)	Clinical, multiple and community	29 (11)	38 (17.43)	PTSD and HC	Clinical, multiple and community	PTSD 28 (13) HC 30 (13)	PTSD 33 (15.90) HC 36 (15.97)
Patel et al. (2007)	United Kingdom	39 (13)	<i>See depressed</i>	Clinical, multiple	39 (13)	38.36 (8.13)	None			
Reynolds & Brewin (1999)	United Kingdom	105 (40)	41.7 (13.1)	Clinical, multiple	62 (23*)	42.2 (13.9) ^a	PTSD	Clinical, multiple	43 (17)	<i>Not reported</i>
Smets et al. (2014)	Belgium	102	<i>Not reported</i>	Clinical, single	37 (11)	39.32 (12.26)	HC	University students	65 (14)	19.28 (2.33)

Abbreviations: DWT, depression without trauma; HC, healthy controls; ND, never depressed; PTSD, posttraumatic stress disorder; RD, recovered depressed; TED, trauma-exposed depressed.

Note. Clinical, multiple refers to recruitment from more than one clinical setting whilst clinical, single refers to recruitment from a single clinical setting.

^a Data taken from Brewin, Reynolds & Tata (1999), reporting on the same sample.

Table 2

Methodological Quality Ratings

Study	Quality criteria					Overall quality rating
	Clearly defined target population	Representative sample	Consideration of comorbid PTSD	Operationalisation of intrusive memories	Assessment of intrusive memories	
Birrer et al. (2007)	0	2	1	1	1	5
Brewin et al. (1996b)	2	1	0	2	1	6
Newby & Moulds (2010)	2	2	2	0	1	7
Parry & O'Kearney (2014)	2	2	1	2	2	9
Patel et al. (2007)	2	1	1	2	1	7
Reynolds & Brewin (1999)	2	1	2	2	2	9
Smets et al. (2014)	1	0	1	2	2	6

Note. Each article was rated green or '2' (criterion fully met), amber or '1' (criterion partially met) or red or '0' (criterion not met) against each quality criterion, detailed in Supplementary Material A.

Table 3

Assessment of Depression in Included Studies

Study	Instrument for depression diagnosis	Instrument for assessment of depression severity	Depression severity Mean (SD)			Between groups comparison of depressive symptom severity
			Depressed	PTSD	Healthy controls	
Birrer et al. (2007)	DID \geq 15	DID and BDI	TED	BDI 19 (9.6)		No significant group differences
	and BDI \geq 11		BDI 24 (8.5) DID 27 (9.2)	DID 22 (9.2)		
Brewin et al. (1996b)	DSM-III-R interview	HADS	DWT			
			and Report of low mood or anhedonia	BDI 20 (6.7) DID 23 (7.2)		
Newby & Moulds (2010)	SCID-I (DSM-IV criteria)	BDI-II	13.9 (<i>not reported</i>)		RD 12.23 (7.06)	Depressed > RD** Depressed > ND** RD > ND*
			28.60 (8.61)		ND 6.03 (3.72)	
Parry & O’Kearney (2014)	SCID (DSM-IV criteria)	CES-D	29.52 (12.25)	27.71 (11.53)	10.17 (7.64)	Depressed = PTSD Depressed > HC*** PTSD > HC***
	and CES-D \geq 16					

Table 3 continued

Assessment of Depression in Included Studies

Study	Instrument for depression diagnosis	Instrument for assessment of depression severity	Depression severity Mean (SD)			Between groups comparison of depressive symptom severity
			Depressed	PTSD	Healthy controls	
Patel et al. (2007)	SCID (DSM-IV criteria)	BDI	33.68 (7.94)			
Reynolds & Brewin (1999)	SCID (DSM-IV criteria)	BDI	27.8 (10.1)	<i>Not reported</i>		Depressed = PTSD ^a
Smets et al. (2014)	Psychiatrist diagnosis and BDI-II ≥ 20 and MDQ (DSM-IV criteria)	BDI-II	33.8 (10.0)		11.2 (7.7)	Depressed > HC*** ^b

Abbreviations: BDI, Beck Depression Inventory; CES-D, Centre for Epidemiological Depression Scale; DID, Diagnostic Inventory for Depression; DSM, Diagnostic and Statistical Manual of Mental Disorders; DWT, depression without trauma; HADS, Hospital Anxiety and Depression Scale; HC, healthy controls; MDQ, Major Depression Questionnaire; ND, never depressed; PTSD, posttraumatic stress disorder; SCID, Structured Clinical Interview for DSM-IV-TR for Axis I Disorders; RD, recovered depressed; TED, trauma-exposed depressed.

Note: * $p < .05$, ** $p < .01$, *** $p < .001$.

^a Mean reported for overall sample = 26.9 (10.9) but not reported for PTSD group.

^b Calculated as not reported

Table 4

Assessment of Intrusive Memories and Measures of Prevalence in Included Studies

Study	Method of assessment of intrusive memories	Timeframe for prevalence	Prevalence of intrusive memories		
			Depressed	PTSD	Healthy controls
Birrer et al. (2007)	Intrusion Questionnaire, adapted from Intrusion Interview (Michael et al., 2007)	Current experience, timeframe not stated	TED	26 (100%)	
			DWT	17 (90%)	
			Combined	37 (94.9%)	
Brewin et al. (1996b)	Semi-structured interview	Current experience, timeframe not stated	27 (87.1%)		
Newby & Moulds (2010)	Semi-structured interview	Previous week with prompt for 'most recent' if none reported. Intrusive memories experienced more than a year ago excluded.	24 (96.0%)	RD	
				24 (80.0%)	
				ND	
				22 (73.3%)	
				Combined	
				46 (76.7%)	

Table 4 continued

Assessment of Intrusive Memories and Measures of Prevalence in Included Studies

Study	Method of assessment of intrusive memories	Timeframe for prevalence	Prevalence of intrusive memories		
			Depressed	PTSD	Healthy controls
Parry & O’Kearney (2014)	Intrusive Memory Questionnaire, adapted from Intrusive Memory Interview (Hackmann et al., 2004)	Previous week	14 (48.3%)	22 (78.6)	7 (23.3%)
Patel et al. (2007)	Semi-structured interview	Previous week with prompt for experience during a ‘ <i>typical week</i> ’ or during last depressive episode if none reported.	17 (43.6%)		
Reynolds & Brewin (1999)	Semi-structured interview	Previous week	45 (72.6%)	42 (97.7%)	
Smets et al. (2014)	Semi-structured interview	Previous week	27 (73.0%)		34 (52.3%)

Abbreviations: DWT, depression without trauma; ND, never depressed; PTSD, posttraumatic stress disorder; RD, recovered depressed; TED, trauma-exposed depressed.

Table 5

Assessment of PTSD and Trauma Exposure in Included Studies

Study	Instrument for PTSD diagnosis	Exclusion of PTSD	Trauma exposure	PTSD severity Mean (SD)			Between groups comparison of PTSD symptom severity
				Depressed	PTSD	HC	
Birrer et al. (2007)	PDS (DSM-IV criteria) \geq 15, including persistent re-experiencing of a traumatic event with avoidance, arousal and interference in functioning.	Control group	TED $n = 20$ (51%)	TED 21 (10.9) DWT 21 (7.0)	31 (6.3)		PTSD > TED* PTSD > DWT* TED = DWT
Brewin et al. (1996b)	<i>Not assessed</i>		<i>Not assessed</i>				
Newby & Moulds (2010)	SCID-I (DSM-IV criteria)	Excluded	<i>Not assessed</i>				
Parry & O'Kearney (2014)	PDS (DSM-IV criteria)	Control group	TED $n = 12$ (41%) Trauma-exposed healthy controls $n = 17$ (57%)	21.48 (12.97)	28.32 (12.04)	6.05 (5.64)	PTSD > Depressed* PTSD > HC*** Depressed > HC***

Table 5 continued

Assessment of PTSD and Trauma Exposure in Included Studies

Study	Instrument for PTSD diagnosis	Exclusion of PTSD	Trauma exposure	PTSD severity Mean (SD)		Between groups comparison of PTSD symptom severity
				Depressed	PTSD HC	
Patel et al. (2007)	SCID (DSM-IV criteria)	Included	<i>Not assessed</i>	33.68 (7.94)		
Reynolds & Brewin (1999)	SCID (DSM-IV criteria) and Posttraumatic symptom scale	Depression with PTSD <i>n</i> = 3 Control group	<i>Not assessed</i>	<i>Not reported</i>		
Smets et al. (2014)	Psychiatrist diagnosis	Included TED <i>n</i> = 1	<i>Not assessed</i>			

Abbreviations: DSM, Diagnostic and Statistical Manual of Mental Disorders; DWT, depression without trauma; HC, healthy controls; PDS, Post-traumatic Diagnostic Scale; PTSD, posttraumatic stress disorder; SCID, Structured Clinical Interview for DSM-IV-TR for Axis I Disorders; TED, trauma-exposed depressed.

Note: * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 6

Leave One Out Analysis

Study omitted	Meta-analysis		Heterogeneity	
	Prevalence estimate (95% CI)	Standard error	I^2 (95% CI)	Q (df)
Birrer et al. (2007)	71.8% (54.7 – 86.3%)	0.088	85.3 (70.0 – 92.8)	34.13*** (5)
Brewin et al. (1996b)	74.0% (54.8 – 89.5%)	0.100	89.0 (78.7 – 94.3)	45.48*** (5)
Newby & Moulds (2010)	71.9% (54.3 – 86.7%)	0.091	87.18 (74.4 – 93.6)	38.99*** (5)
Parry & O’Kearney (2014)	79.8% (63.2 – 92.6%)	0.092	87.08 (74.2 – 93.5)	38.71*** (5)
Patel et al. (2007)	80.7% (66.0 – 92.2%)	0.082	83.20 (64.7 – 92.0)	29.76*** (5)

Reynolds & Brewin (1999)	76.6% (55.8 – 92.5%)	0.109	89.65 (80.2 – 94.6)	48.33*** (5)
Smets et al. (2014)	76.5% (56.8 – 91.8%)	0.104	89.68 (80.2 – 94.6)	48.44*** (5)

Note: * $p < .05$, ** $p < .01$, *** $p < .001$.