# Psychological mechanisms of the relationship between early adversity and psychosis

A thesis submitted to The University of Manchester for the degree of Doctor of Clinical Psychology in the Faculty of Biology, Medicine and Health

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#### Thesis Abstract

The current thesis titled 'Psychological mechanisms of the relationship between early adversity and psychosis' has been prepared by Jessica Williams in the year 2017. The thesis has been submitted to The University of Manchester for the degree of Doctor of Clinical Psychology in the Faculty of Biology, Medicine and Health (School of Health Sciences). The thesis has been prepared in paper based format and comprises three papers. The overall theme of the thesis is the investigation of psychological mechanisms of the relationship between early adversity and psychosis.

Firstly, a systematic literature review regarding the psychological mediators of the relationship between childhood trauma and psychosis is presented. Paper 1 provides a comprehensive review of 30 studies investigating putative psychological mediators of the relationship between childhood trauma and psychosis symptomatology. The review critically synthesises and evaluates the research that has been carried out and published to date. Different traumatic sequalae received some support including post-traumatic symptoms, affective symptoms, emotion regulation, dissociation and insecure attachment; some factors were more tentative, including negative schema and self-esteem. The results are considered in relation to methodological limitations, clinical implications and recommendations for future research.

Secondly, research was carried out to explore dissociation as a potential mediating variable within the fearful attachment and voice-hearing relationship. Paper 2 presents an investigation involving 50 participants with a diagnosis of psychosis. The participants completed a range of self-report measures. Mediation analysis indicated that a fear-based attachment style may predispose an individual to voice-hearing if dissociation is a sequalae of this experience, and highlights the importance of affect regulation in this pathway. The findings are considered in relation to limitations of the study and possible clinical implications and recommendations for future research.

Thirdly, a critical evaluation and reflection of the two papers mentioned above was carried out. Strengths and weaknesses regarding the chosen methodology, directions for theory, clinical practice and future research were considered. Finally, the overall research process was reflected upon.

#### Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning;

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A very special thank you goes to my fiancé Alan, whose patience, support and faith in me helped me to get to the end of this journey. Also to my parents, siblings and friends for their endless understanding, encouragement and confidence in my ability to reach this achievement. Paper 1: Systematic Review

# Psychological mediators of the association between childhood trauma and psychosis: a systematic review

The following paper has been prepared for submission to 'Clinical Psychology Review'. The guidelines for authors can be found in Appendix A.

Word count: 11, 366 (excluding references)

#### Abstract

**Objectives:** This review sought to identify, summarise and critically evaluate studies that examined psychological mediators of the relationship between childhood trauma and psychosis.

**Methods:** An electronic database search of PsychINFO, MEDLINE, Web of Science and CINAHL from 1980 until September 2016 was conducted using keyword search terms synonymous with childhood trauma and psychosis symptomatology.

**Results:** We identified 30 papers, comprising 8,873 participants with a psychotic disorder, and 57, 911 non-clinical participants. The following key mechanisms of the relationship between childhood trauma and psychosis were identified: Attachment; Substance misuse; Dissociation; Depression and anxiety; Emotion regulation; Post-traumatic symptoms; Beliefs and concepts about the self and others; and Miscellaneous (neuroticism and mastery; mindfulness; proximal life stressors). Different traumatic sequalae received some support including post-traumatic symptoms, affective symptoms and emotion regulation, dissociation and insecure attachment; some factors were more tentative, including negative schema and self-esteem.

**Conclusions:** The findings suggest that there are multiple psychological routes to psychosis following experiences of childhood trauma. We recommend future research to include larger samples sizes, longitudinal designs, and more complex modelling techniques to allow for the robust appraisal of different pathways from adversity to psychosis and to better disentangle the contribution of these different processes.

#### Introduction

Risk for psychosis has been linked to a range of adverse life experiences and circumstances, including poverty, discrimination, unemployment and war traumas (Read, Fink, Rudegeair, Felitti, & Whitfield, 2008). However, particular interest has been given to the relationship of childhood trauma to psychosis in an attempt to identify the impact of socio-environmental precursors to psychosis. Childhood trauma covers a range of potentially harmful experiences. The types of adversity that have been most extensively examined in the context of psychosis include physical, sexual or emotional abuse, neglect, the harmful effects of bullying, and parental loss or separation (e.g. Varese, et al., 2012; Matheson et al., 2013; Velthorst et al., 2013; Read et al., 2005; Morgan & Gayer-Anderson, 2016) and have been shown to contribute to both the emergence and maintenance of psychotic symptoms in the general population (Bebbington, 2009) and in the development of psychotic disorders more specifically (Varese et al., 2012; Velthorst et al., 2013; Read et al., 2005).

Several meta-analytic studies suggest that experiencing trauma in childhood increases the risk of developing psychosis (e.g. Varese et al., 2012; Matheson, Shepherd, Pinchbeck, Laurens & Carr, 2013), with an odds ratio of approximately 2.8 (Varese, et al., 2012). There is also evidence of a dose-response relationship, with the more severe the abuse the stronger the relationship with developing psychosis (e.g. Janssen et al. 2004; Shelvin et al., 2007), and evidence of longitudinal associations (e.g. Poulton, Caspi, Moffitt, Cannon, Murray, & Harrington, 2007). However, while these are important indicators of potentially causal relationships, in themselves these factors cannot ascertain causality (Bentall & Varese, 2012). Hill (1965) proposed nine criteria to support evidence of a causal relationship. The criteria (known as the Bradford Hill criteria) include strength, consistency, dose-response, specificity, consideration of alternative explanations, experimental evidence, and plausibility, the latter referring to the identification of a plausible mechanism between cause and effect. Historically, causal inference was approached with the assumption of a single-factor direct relationship (i.e. A causes B). However, researchers now understand that many health and illness outcomes are a result of the interplay between multiple contributing and mediating factors (Fedak, Bernal, Capshaw & Gross, 2015).

With substantial evidence supporting the link between childhood trauma and psychosis, an increasing number of studies have attempted to elucidate potential mediating mechanisms, including psychological processes, which may explain how such adversities exert their influence (Morgan & Gayer-Anderson, 2016). Psychological mechanisms include cognitive process in the domains of attention, memory, imagery, thinking, reasoning and behaviour (Harvey et al, 2004) and affective symptoms (e.g. Garety et al., 2001). Prominent models of psychosis hypothesise different psychological mechanisms proposed to explain the relationship between childhood trauma and psychosis vulnerability or distress maintenance. These include negative schematic models of the self and the world and disrupted affect

(Garety et al., 2001), stress-sensitivity (Myin-Germeys & van Os, 2007), the impact of trauma via the developing brain (Read, Bruce, Perry, Moskowitz & Connolly, 2001), attachment (Barker et al., 2015; Berry & Bucci, 2015), dissociation (Pilton et al, 2015; Longden, Madill & Waterman, 2012; Berry & Bucci, 2015), self-monitoring abnormalities (Feinburg, 1978; Waters et al., 2012), source monitoring difficulties (Bentall, 1990; Brookwell et al., 2013); cognitive appraisals (Chadwick & Birchwood, 1994, 1996; Morrison, 1998, 2001) and peri- and post-traumatic processes (e.g. Steel, 2015; Hardy et al 2016).

Improved statistical techniques have enabled researchers to examine complex pathways where multiple risk factors, confounders, and mediating mechanisms are involved. For example, mediation analysis is a statistical method used to help identify mechanisms by which an exposure influences an outcome of interest. The statistical approach of mediation analysis enables the disentanglement and elucidation of the various pathways of direct and indirect effects that play a role in the relationship between exposures and observable outcomes (Hayes, 2013). Identification of psychological mediators is one of the most widely examined questions in psychological research; however, as yet relatively little is known about the mediators of the link between trauma and psychosis (Read et al., 2008). Identification of psychological mediators can help to ascertain the causal relationship between childhood trauma and psychosis and inform targeted preventative interventions. A review of rigorously tested proposed mechanisms has the potential to support the development of integrated models of psychosis and provide a platform for ensuring that treatment targets the right mechanisms. The Bradford Hill criteria calls for the importance of considering mediation analysis specifically as mediation analysis enables a formal quantification and inferential test of plausible theoretical mechanisms (Hayes, 2013). Formal quantification and inferential tests provide more robust tests of whether an inferential procedure justifies a claim for plausible mechanisms rather than relying on outcomes of a set of hypothesis tests about the relationship between exposures and observable outcomes.

Therefore, the current review aims to provide a systematic review and synthesis of the empirical literature, and an assessment of the quality of the evidence for proposed psychological mechanisms of the childhood trauma-psychosis relationship, taking into account the "robustness" of the statistical mediation methods employed. Specific aims of the current paper are to: 1) provide a comprehensive systematic review of quantitative literature investigating potential psychological mediators examining the link between childhood trauma (i.e. physical, psychological, sexual and emotional abuse, neglect and bullying) and psychosis; 2) evaluate the quality of this evidence, including the relative strength of the statistical mediation analysis used to explain the trauma-psychosis link.

#### Method

#### Search procedure

The current review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). Methods of the analysis and inclusion criteria were specified in advance and documented in a protocol registered with PROSPERO (<u>https://www.crd.york.ac.uk/PROSPERO/</u>; registration number: 42016047842). A systematic search of PsycINFO, MEDLINE, Web of Science and CINAHL was conducted using the following search strings: (voices OR psychosis OR psychotic OR schizo\* OR hallucination OR delusion) AND (child abuse OR physical abuse OR psychological abuse OR emotional abuse OR neglect OR trauma OR advers\* OR maltreat\* OR bully\*). The search terms followed closely those of previously published metaanalyses of the relationship between childhood adversity and severe mental health difficulties (Palmier-Claus, Berry, Bucci, Mansell, & Varese, 2016; Varese et al., 2012). Examination of reference lists of eligible studies was carried out in addition to the database search.

#### Inclusion and exclusion criteria

Eligible studies were empirical studies published in peer reviewed journals from 1980September 2016. The lower limit of our search was selected in line with other reviews of this literature, as the first sufficiently rigorous empirical study on adverse childhood events and psychosis was published in the 1980s (Friedman & Harrison, 1984). Eligible designs were prospective cohort, cross-sectional, and case-control studies that had assessed the association between childhood trauma and psychotic symptoms and/or diagnosis of psychosis and the effect of one or more psychological mediating mechanisms on this relationship. Only reports that utilised mediation analysis to examine whether trauma had an indirect effect on the psychosis outcome via the putative process under study were considered. The term psychological mechanism was adapted from that of Harvey et al. (2004) and was defined in the current review as an aspect of cognition, behaviour, affective symptoms or mood. Both diagnostic (diagnoses in the schizophrenia spectrum) and dimensional measures (clinical presentation classified by quantification of psychosis related attributes) of psychosis were considered eligible since there is evidence that psychotic experiences exist on a continuum with normal experiences (van Os, Linscott, MyinGermeys, Delespaul & Krabbendam, 2009).

Studies were regarded as eligible if the measures used to assess the variables under study (trauma, symptoms/diagnoses and putative mediating mechanisms) were found to be valid and reliable. However, where studies were epidemiological in nature, measures of variables using items created for the study were considered eligible given that population based

studies employ large sample sizes and attempt to test a large number of hypotheses, thus necessitating briefer means of assessing each variable of interest. Measures of childhood trauma were also required to measure exposure prior to the age of 18. Studies that had not differentiated between recent traumatic events and childhood-based trauma were excluded because this would limit the ability to draw specific conclusions about the role of childhood trauma (Shrout & Bolger, 2002). Studies in languages other than English were excluded alongside single case studies, dissertations and conference extracts.

#### Data extraction and analytic plan

JW screened articles in three stages: title, abstract and article levels. JW screened the titles independently. Thirteen percent of abstracts (n=100) were double-rated separately by a postgraduate researcher, with adequate levels of agreement (75%). The majority of discrepancies were due to the secondary coder being overly inclusive and were reviewed and arbitrated by the research team at regular meetings. The whole research team examined full texts to agree the final papers included in the review with excellent levels of agreements found (100%). The analytic plan was to provide a narrative synthesis of the findings of eligible studies, structured around the type of mediator examined.

#### Quality assessment

Following methodological recommendations from PRISMA (Liberati et al., 2009), a component approach to quality assessment was employed. This approach recommends that assessment of quality is investigated on a case-by-case basis rather than employing generic tools, so that only specific methodological features relevant to the topic under study are assessed in detail and contribute to the appraisal of the available evidence. The quality of eligible papers was assessed using a version of the Effective Public Health Practice Project tool (EPHPP; Thomas, 2003) adapted to enable assessment of the specific methodological features of the primary studies pertinent to the research question under scrutiny. Our quality assessment considered the following five domains: (1) Selection bias, (2) Study design, (3) Confounders, (4) Data collection methods and (5) Withdrawals and drop-outs. Analysis was also assessed and each domain was rated as 'strong', 'moderate' or 'weak'. (see Appendix B). The analysis section was amended to allow for specific criteria with which to assess the quality of the mediation analysis used. Regression methods (e.g. Baron & Kenny) where mediational effects are inferred rather than based on direct statistical observation (Hayes, 2009) were rated as weak. A moderate rating was assigned to analyses where regression methods with additional tests of indirect effects, such as the Sobel test, had been used in addition to regression analysis. Explicit analyses estimating direct and indirect effects (e.g.

Preacher & Hayes, 2004; Hayes, 2013) were assigned a strong rating. Table 1 presents the results of the quality assessment.

#### Results

#### Overview of studies

Overall 30 eligible papers were identified. Table 2 provides an overview of the studies reviewed including details regarding the research measures employed. Papers were from the UK (n=15), USA, (n=4), Spain (n= 4), the Netherlands (n= 3), Australia (n= 3) and the Republic of Korea (n=1). The majority of studies used adult samples (k=27); three studies used child samples (Wolke et al, 2013; Murphy, Murphy, & Shelvin, 2015; Fisher et al., 2013). Samples sizes ranged from 60 to 17,337 participants. The total number of participants with a psychotic disorder was 8.873, of which 420 reported a first episode psychosis. Two hundred and thirty-three were classed as ultra high risk (UHR; a state associated with a clinical syndrome that is evident in young adults and typically involves psychotic symptoms and a recent decline in function, Fusar-Poli et al., 2013; Yung et al., 1998), and 547 had identified as having psychotic experiences but had not received a formal diagnosis. A total number of 57,911 non-clinical participants were included. Eleven of the studies employed non-clinical participants, seven of which were student samples (Sheinbaum et al., 2015; Ashford, Ashcroft & Maguire, 2012; Goodall et al., 2015; Varese, Barkus & Bentall, 2012; Sheinbaum, Kwapil & Barrantes-Vidal, 2014; Perona- Garecelán et al., 2014; Evans et al., 2015). Based on data from 20 studies, the mean of the mean ages of the participants was 30.9 years (range of 12.9 - 58 years). No data were provided on the age of participants in 10 studies. Based on the data of 19 studies, 55.9% (n = 20,024) participants were female and 44.9% (n = 15,782) were male. No data regarding gender were provided for 11 studies.

#### Measures

#### Childhood trauma

Nine studies used versions of, or items from, the Childhood Trauma Questionnaire (CTQ; Bernstein and Fink, 1998), which has been validated and shown to reliably detect abuse and neglect histories. Twelve studies used other validated measures with the quality of measures varying among studies. Nine studies used surveys including single items (e.g. Bak et al., 2005), and questionnaires developed for large scale studies (e.g. Whitfield, Dube, Felitti & Anda, 2005). Hardy et al (2016), Sheinbaum et al (2015), Fisher et al. (2012), Wolke, Lereya, Fisher, Lewis and Zammit (2014), Sitko et al., (2014), Berenbaum et al. (2008) and Bebbington et al. (2011) used interview measures to assess experiences of childhood trauma. There is debate regarding whether more veridical childhood historical accounts are achieved from observer-based interviews or from self-report questionnaires (Roy & Perry, 2004). Fink et al. (1995) did find a moderately high convergent validity between an observer-based interview and a self-report questionnaire. The issue remains controversial which adds to the challenge of rating the quality of data collection tools; however, CTQ is currently the most widely used retrospective measure (Tonmyr, Draca, Crain, & MacMillan, 2011) and the information gained from single or limited items will be less detailed when compared with interviews.

#### Psychosis symptomatology

A variety of outcomes related to psychosis were evaluated in the studies reviewed. Twenty studies used symptoms of psychosis as the outcome variable, with three studies examining hallucination-proneness using the Launey-Slade Hallucination Scale-Revised (LSHS-R; Bentall & Slade, 1985) or similar versions of the tool. Most studies used valid and reliable measures of psychotic symptomatology; however, Whitefield, Dube, Felitti and Anda (2005) used a single item to measure hallucinations and Van Neirop et al., (2014) used individual ratings of the frequency, distress and impact of psychotic symptoms. Both studies obtained weak ratings for the measures; however, the studies were epidemiological and the items used had acceptable face validity. Six studies used dimensions of schizotypy such as schizotypal personality disorder traits as outcomes (e.g. Sheinbaum et al., 2015), with all measures being validated. Three studies examined transition to psychosis, with Wolke et al., (2013) and Fisher et al., (2012b) measuring psychotic experiences at 18 using the PLIKSi (Zammit et al., 2013) and Thompson et al., (2016) using various validated measures such as the Brief Psychotic Rating Scale (BPRS; Overall & Gorham, 1962) to capture this.

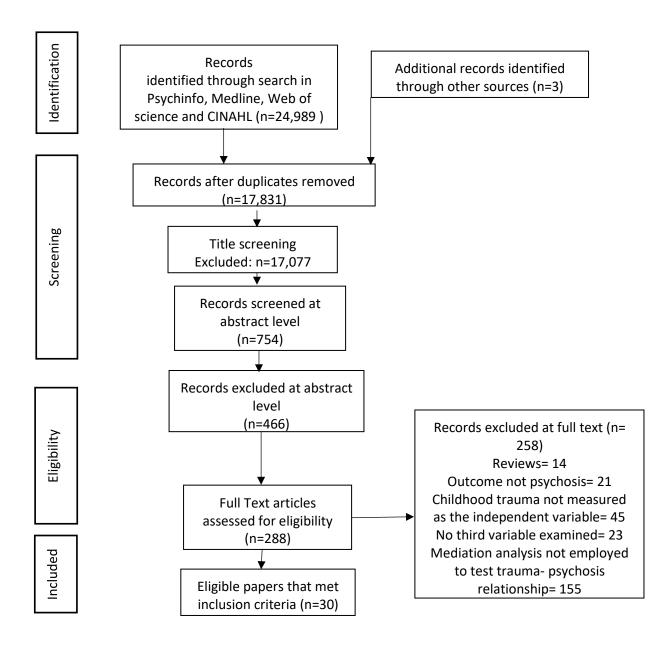


Fig. 1. Paper selection flow chart.

#### Meditators

A range of potential mediators was captured by various measures. Five epidemiological studies obtained weak ratings for measures employed to capture the mediating variable (Whitefield, Dube, Felitti & Anda, 2005; Bebbington et al.,2011; Boyda, McFeeters & Shelvin, 2014; Bak et al., 2005 and Van Neirop et al., 2014). The remaining studies employed valid and reliable measures of the mediators being investigated.

#### **Key findings**

For the purposes of the review we categorised studies according to the type of mediator investigated. Categories were discussed with other members of the team and the following

key mechanisms of the relationship between childhood trauma and psychosis were identified: Attachment; Substance misuse; Dissociation; Depression and anxiety; Emotion regulation; Post-traumatic symptoms; Beliefs and concepts about the self and others; Miscellaneous (neuroticism and mastery; mindfulness; proximal life stressors).

#### Attachment

Five studies presented evidence for attachment as a potential mediator of the link between childhood trauma and dimensions of psychosis. Attachment theory (Bowlby, 1973) proposes that an infant internalises their experience of interactions with a primary caregiver. This representation is carried forward into adulthood and influences expectations about the self and others in interpersonal interactions. Attachment styles develop in the context of the early relational environment- a secure attachment is formed when a primary caregiver is seen as responsive and available, conversely, adverse interactions lead to insecure attachment patterns. Applying Bowlby's ideas about mental representations and internal working models, Bartholomew (1990) proposed a four-category model of adult attachment. Four attachment patterns were conceptualised- secure (a sense of worthiness and an expectation that other people are generally responsive); preoccupied (a sense of unworthiness combined with a positive evaluation of others); dismissive avoidant (a sense of worthiness combined with a negative disposition toward other people); and fearful-avoidant (a sense of unworthiness combined with an expectation that others will be untrustworthy and rejecting). Insecure attachment patterns have been shown to be associated with early adverse experiences (Waters et al., 2000) and psychosis (e.g. Gumley et al., 2013).

The studies converged to show evidence of attachment anxiety and avoidance mediating the relationship between various measures of childhood trauma and positive psychosis symptomatology (Goodall et al., 2015; Sitko et al., 2014; Van Dam et al., 2014; Sheinbaum et al., 2015). However, Sheinbaum et al., (2015) also found that neither withdrawn (difficulty getting close and overly self-reliant; Bifulco & Jacobs, 2008) nor fearful attachment (high mistrust and a high fear of rejection; Bifulco & Jacobs, 2008) acted as mediators, whereas Sheinbaum, Kwapil and Barrantes-Vidal (2014) found that fearful attachment significantly mediated the relationship between physical/emotional trauma and positive and negative non-clinical psychotic phenomena.

Less conclusive evidence was found for negative symptoms. Negative symptoms refer to a loss, typically of emotion, speech or motivation. Attachment style was not found to mediate the relationship between childhood maltreatment and negative symptoms in clinical participants (Van Dam, 2014), and mixed results were found in studies considering nonclinical participants (Sheinbaum et al., 2015; Sheinbaum, Kwapil, & Barrantes-Vidal, 2014). However, Van Dam (2014) did find attachment style to be an important mediator of

the relationship between childhood maltreatment and negative symptoms in siblings of participants with psychosis.

The studies provide evidence of attachment style mediating the relationship between childhood trauma and positive psychosis symptomatology across clinical and non-clinical samples. The discrepancy between the findings of Sheinbaum et al (2015) and Sheninbaum, Kwapil, & Barrantes-Vidal, (2014) may reflect the different measures of childhood trauma used in each study. Sheninbaum, Kwapil, & Barrantes-Vidal, (2014) examined early adverse relational experiences of parental antipathy (the extent to which the parent shows hostility, criticism, rejection and coldness towards the child) and role reversal (the extent to which a child assumes parental responsibility and provides emotional support to the parent), whereas Sheinbaum et al (2015) utilised the CTQ (Bernstien & Fink, 1998) to measure experiences of abuse and neglect. Empirical evidence supports conceptual connections between fearful-avoidant and the disorganised attachment pattern (see Simpson & Rholes, 2002 for a review). Disorganised attachment is hypothesised to develop as a result of conflict between the attachment system and the defence system, which may be understood as early relational trauma arising from interactions with a caregiver who is both the source of, and the solution for, the infant's fear (Liotti, 2004). Therefore, it may be that fearful attachment style is relevant to more severe forms of childhood maltreatment than antipathy and role-reversal, which may explain the discrepancy between the two studies.

All studies except for Van Dam et al., (2014) employed robust mediation methods, which adds strength to the evidence for attachment acting as a mediator. However, the crosssectional nature of all studies limits the conclusions that can be drawn in terms of causality. Further, three studies employed student samples (Sheinbaum, Kwapil, & Barrantes-Vidal, 2014; Goodall et al., 2015; Sheinbaum et al, 2015), which limits the generalisability of the study findings due to the lack of representative samples. All studies used different tools and definitions to measure attachment styles and childhood trauma which makes comparisons across studies difficult, and also makes it difficult to ascertain whether specific attachment styles may be more relevant to the childhood trauma-psychosis relationship.

#### Substance misuse

Three studies examined substance misuse as a potential mediator. There is a well established relationship between substance misuse and psychosis (Moore et al., 2007). Cannabis use more specifically has been found to be more prevalent in individuals who have experienced childhood trauma (Oshri, Rogosch, Burnette & Cicchetti, 2011) and has been found to be a predictor of psychosis onset and relapse (Zammit, et al.,2008).

Two epidemiological studies examined the role of cannabis misuse, but did not find evidence of mediation (Bebbington et al., 2011; Van Neirop et al., 2014). However, Van Neirop et al.,

(2014) did find that cannabis use predicted severity of psychotic experiences for participants with the extended psychosis phenotype (EPP; at least one self-reported psychotic experience, Van Neirop et al., 2014) and participants diagnosed with a psychotic disorder. Neither study employed robust methods of mediation analysis. Bebbington et al., (2011) employed regression methods to tests mediation, and Van Neirop et al., (2014) employed regression and additional tests of indirect effects. For both studies, the tools utilised to measure childhood trauma and cannabis use were rated as weak as they were developed for the study with no evidence of validity or reliability beyond face validity which limits the confidence in the study findings.

Whitfield, Dube, Felitti and Anda (2005) examined the role of substance misuse in the relationship between adverse childhood experiences and hallucinations. Substance abuse was found to slightly reduce the relationship between adverse childhood experiences and hallucinations, and the authors suggested a mediating role for substance misuse based on these findings. However, regression methods were employed to test mediation and the mediator and outcome measures obtained weak ratings as both were created for the study that lacked robust validity and reliability.

Given the methodological issues with the studies, further research with validated and reliable measures and more robust methods of testing mediation may be required to investigate the role of substance use before conclusions can be drawn. However, the studies do consistently show no mediation effect of cannabis use on the relationship between childhood trauma and psychosis. It may be that substance misuse is relevant, but other associations are possible. For example, a history of childhood abuse, may moderate the interaction between cannabis and psychosis (Wilkinson, Radhakrishnan, Deepak & D'Souza, 2014).

#### Dissociation

Six studies examined dissociation as a potential mediating variable. Reliable associations between trauma and dissociation in both clinical and non-clinical samples support the idea that dissociation may be a direct consequence of trauma resulting from a decontextualised representation of the trauma memory (Dalenberg et al., 2012). Further, strong correlations have been found between dissociation and psychotic experiences in both clinical and nonclinical samples (e.g. Kilcommons & Morrison, 2005; Vogel et al., 2011; Pilton, Varese, Berry & Bucci, 2015).

Three studies used similar versions of the Dissociative Experiences Scale (DES; Bernstein & Putnam, 1986), the most commonly employed questionnaire to measure dissociation. The DES assesses three distinct areas of dissociation including absorption (the experience of losing contact with one's current experience and becoming immersed in internal events; Waller, Putnam, & Carlson, 1996), and depersonalisation/derealisation (experiencing a

sense of unreality, detachment or disconnection in relation to one's body and surroundings; Hunter, Sierra, & David, 2004). One study used a between group design, comparing participants with psychosis to a non-clinical student sample (Evans et al., 2015) and two further studies employed clinical samples with psychosis (Varese, Barkus & Bentall, 2012; Perona- Garecelán et al., 2012). From a statistical perspective, four studies utilised recommended bootstrapping analyses (Varese, Barkus & Bentall, 2012; Evans et al., 2015; Perona- Garecelán et al., 2012; Perona- Garecelán et al., 2014), with two studies employing less robust regression techniques and additional tests of indirect effects (Thompson et al., 2016; Berenbaum et al., 2008).

Three studies found evidence of dissociation mediating the relationship between childhood trauma and voice-hearing/hallucination-proneness (Perona- Garecelán et al., 2014; Perona-Garecelán et al., 2012; Varese, Barkus & Bentall, 2012). Varese, Barkus & Bentall, (2012) found a stronger effect for sexual abuse relative to other types of trauma for clinical and nonclinical samples. Perona- Garecelán et al., (2014) found that both depersonalisation and absorption mediated the relationship between childhood trauma and hallucination proneness in a non-clinical sample. However, Perona- Garecelán et al., (2012) found that dissociation did not mediate this relationship for delusions.

Berenbaum et al., (2008) found that absorption mediated the relationship between childhood maltreatment and schizotypal symptoms. Evans et al., (2015) found that dissociation mediated the relationship between physical neglect and psychosis group membership, but not emotional, physical and sexual abuse or emotional neglect. Thompson et al., (2016) also did not find evidence of dissociation mediating the relationship between childhood sexual abuse and transition to psychosis in an Ultra High Risk sample. However, the tool utilised by Thompson et al., (2016) to measure dissociation (CAARMS; Young et al., 2005) provided a relatively rudimentary measure of the construct.

The current evidence base suggests that dissociation may be an important psychological mechanism in the relationship between childhood trauma and psychosis. The findings in support of dissociation mediating the relationship between sexual abuse and hallucinations but not psychosis group membership may suggest that dissociation acts as a mediator for the relationship between childhood sexual abuse and hallucinations specifically, rather than psychosis more generally. However, Evans et al., (2015) acknowledged a rarity of sexual abuse reported by the study sample. The study participants were not drawn from a comprehensive group of the target population, which may explain rarity of sexual abuse and the resulting non-significant finding. Once more, as the studies were cross-sectional, designs more suited to identifying causal relationships will be required for possible causal relationships to be identified. Furthermore, Perona- Garecelán et al., (2012), Berenbaun et

al., (2008) and Thompson et al., (2016) did not control for important covariates, which limits the strength of the findings.

#### Depression and anxiety

Eight studies examined anxiety and depression as potential mediators. Anxiety and depressive disorders have been found to increase risk for psychotic-like experiences (Varghese et al., 2011). Further, major depression and anxiety disorders are frequent in adults with a history of childhood abuse (e.g., Felitti et al 1998; Mullen et al 1996). Seven studies reported evidence for anxiety and depression as mediators. One study examined the relationship in a probable psychosis sample (Bebbington et al., 2011), and seven studies employed non-clinical samples (Sitko et al., 2014; Marwaha & Bebbington, 2015; Fisher et al., 2013; Fisher, Appiah-Kusi & Grant, 2012; Wolke et al., 2013; Berenbaum, Valera & Kerns, 2003; Ashford, Ahscroft & Maguire, 2012).

Three studies looked at early experiences of being bullied and found that depression mediated its relationship to paranoid thinking and persecution (Ashford, Ahscroft & Maguire, 2012), and psychotic experiences more generally (Wolke et al., 2013; Fisher et al., 2013). Sitko et al., (2014) also found that depression mediated the relationship between physical and sexual abuse and paranoia and between witnessing an injury/killing, sexual and physical abuse and hallucinations. Furthermore, some studies suggest the mediating effect of depression might be more robust in the case of particular adverse experiences. For example, Fisher et al., (2013) found a larger effect for depression when exposure to domestic violence and harsh parenting were employed as measures of childhood trauma.

Fisher, Appiah-Kusi & Grant, (2012) found that anxiety mediated the relationship between emotional abuse, but not physical abuse, and paranoia in a student sample. Depression and anxiety were also found to mediate the relationship between sexual abuse and psychosis (Marwaha and Bebbington, 2015; Bebbington et al. 2011). However, Thompson et al., (2016) found that neither depression nor anxiety mediated the link between childhood sexual abuse and transition to psychosis.

Overall, the studies provide consistent evidence for the role of depression and anxiety as mediators in the relationship between childhood trauma and psychosis. In the Thompson et al., (2016) study, only a proportion of the sample completed the anxiety and depression measures and the tool utilised to examine those factors provided relatively crude measures. Thus, the inconsistent findings should be interpreted with caution. Most studies employed relatively robust methods of mediation analysis to examine whether anxiety or depression acted as mediators, apart from Bebbington et al. (2011) who used regression techniques. None of the studies included in the current review utilised samples which strongly represented the target population which limits the generalisability of the findings; however,

Fisher et al., (2013) employed a prospective longitudinal design which adds strength to claims of depression and anxiety acting as mediators.

#### Emotion regulation

Three studies examined the impact of difficulties with regulating mood on the relationship between childhood trauma and psychosis. People with psychosis have been found to attempt to regulate emotions using maladaptive emotional regulation strategies (Livingstone, Harper, & Gillanders, 2009). Furthermore, evidence suggests that emotion regulation difficulties may arise as a result of developmental trauma (Birchwood, 2003).

Two studies utilised clinical participants with psychotic disorders (van Neirop et al., 2014; Marwaha et al., 2014), one study used UHR adults (Thompson et al., 2016) and was the only study that utilised a longitudinal design. Van Neirop et al., (2014) found that affective dysregulation mediated the relationship between childhood trauma and the extended psychosis phenotype (EPP) but not psychotic disorder. Marwaha et al., (2014) found evidence of mediation by mood instability in the relationship between sexual abuse and diagnosis of psychosis, persecutory ideation and hallucinations. However, Thompson et al. (2016) found no evidence of mediation by mood swings, lability or mania for sexual abuse and transition to psychosis. Both Van Neirop et al., (2014) and Marwaha et al., (2014) utilised measures created for the study resulting in less valid tools. However, the studies were epidemiological, using large sample sizes, and employed relatively robust methods of mediation analysis providing more confidence in the findings. While a strength of the study by Thompson et al., (2016) lies in the longitudinal design, the study employed crude measures of the mediator variables.

The results suggest a possible role of mood regulation difficulties acting as a mediator in the relationship between childhood trauma and psychosis; however, the variable definitions and tools used to capture the concepts make comparisons between studies difficult.

#### Post-traumatic symptoms

Six studies examined post-traumatic symptoms as potential mediating variable. All studies used different but valid measures of post-traumatic symptoms. Research has shown that there is a high incidence of post-traumatic stress disorder (PTSD) in individuals with a primary psychosis-related diagnosis (Kilcommons & Morrison, 2005).

Post-traumatic symptoms were found to mediate the relationship between various measures of childhood trauma and psychosis symptomatology in both clinical (Choi et al., 2015; Hardy et al., 2016) and non-clinical samples (Murphy, Murphy, and Shevlin, 2015; Berenbaum et al., 2008; Powers, Thomas, Ressler and Bradley, 2011). Berenbaum, Valera & and Kerns,

(2003) investigated whether psychological dysfunction (measured using PTSD symptoms, depression, dissociation and difficulties identifying one's own feelings) acted as a mediator and found evidence for neglect and schizotypal personality disorder, but not for physical or sexual abuse. However, the study did not examine post-traumatic symptoms in isolation and the sample consisted only of women, which limits the generalisability of the findings.

All studies employed a cross sectional design and so corroboration is required from longitudinal studies to determine directional and causal relationships, and all studies except for Hardy et al (2016) showed evidence of selection bias. Furthermore, two studies (Murphy, Murphy, and Shevlin, 2015; Choi et al., 2015) scored weak ratings for selection bias and two obtained moderate ratings (Powers, Thomas, Ressler and Bradley 2011; Berenbaum et al. 2008) which limits the generalisability of the findings. However, the results suggest the posttraumatic symptoms may represent a mediating mechanism in the childhood trauma psychosis relationship.

#### Beliefs or concepts about self and others

Nine studies examined the role of beliefs or concepts about the self and/or others in the relationship between childhood trauma and psychosis. A range of concepts were examined across different studies, namely; self-concept clarity, self-esteem, social defeat, and negative schema.

#### Self-concept clarity

Self-concept refers to the 'totality of an individual's thoughts and feelings with reference to himself and an object' (Rosenburg, 1979). It has been suggested that a damaged selfconcept may confer risk of psychosis (Bell & Wittkowski, 2009). Evans et al, (2015) examined the role of self-concept clarity in the relationship between childhood trauma and psychosis. Self-concept clarity has been defined as 'the extent to which the contents of the self-concept are clearly and consistently defined, internally consistent, and temporally stable' (Campbell et al., 1996). Evans et al. (2015) found that self-concept clarity mediated the relationship between childhood trauma, emotional abuse, physical abuse, emotional neglect and physical neglect and psychosis group membership. An effect was not found for sexual abuse; however, the study obtained a weak rating for selection bias as the participants were not drawn from a comprehensive group of the target population, which may explain the rarity of sexual abuse reported by the samples.

#### Self-esteem

It has been suggested that childhood trauma may contribute to low self-esteem. Furthermore, individuals with psychosis have been found to have low self-esteem (Freeman, Garety, Fowler, et al., 1998). Fisher et al., (2013) examined the role of self-esteem and found that it mediated the association between harsh parenting, exposure to domestic violence and bullying and symptoms of psychosis. Fisher et al., (2013) employed a prospective longitudinal design and utilised valid and reliable measures, which adds strength to the study findings. Morgan et al., (2012) also examined the role of self-esteem in the trauma-psychosis relationship. However, the mediation model examined paths leading from parental separation to psychosis via education and adult disadvantage and so the results cannot be used as direct support for self-esteem as a mediator of the trauma-psychosis relationship.

#### Social defeat

Social defeat refers to feelings of outsider status and reduced value. It has been suggested that experiences of childhood abuse may lead to social defeat (Cantor-Graae & Selten, 2005). Van Nierop et al., (2014) showed evidence that social defeat mediated the relationship between childhood trauma and the extended psychosis phenotype (EPP) but not a clinical diagnosis of a psychotic disorder. Relatedly, Murphy, Murphy and Shelvin (2015) investigated negative social comparisons as a potential mediator and failed to find a significant relationship between negative social comparisons and psychotic experiences. Murphy, Murphy and Shelvin (2015) utilised a primary school sample, which may explain the discrepancy between their findings and those of Van Nierop et al., (2014) as it may be that adolescence is too early in cognitive development for early experiences of threat to be attributed to feelings of subordination. The measure of social defeat utilised by Van Neirop et al., (2014) received a weak quality rating as items were created for the study; however, the study was epidemiological in nature, with a large sample size, which increases the strength of the study findings.

#### Negative schema

Traumatic experiences have been shown contribute to the development of faulty self and social knowledge (Kilcommons & Morrison, 2005). Three studies examined whether negative beliefs about self and others mediated the relationship between childhood trauma and psychosis. Ashford, Ashcroft and Maguire (2012) found that negative beliefs about the self and others mediated the relationship between bullying experiences and paranoia and persecution. Hardy et al., (2016) found that negative other beliefs mediated the relationship between emotional abuse and persecutory delusions. However, Fisher, Appiah and Grant (2012) did not find evidence of negative self or other beliefs mediating the relationship

between emotional and physical abuse and paranoia. Further, Hardy et al., (2016) did not find evidence of negative other beliefs mediating the relationship between childhood sexual abuse and auditory hallucinations or between emotional abuse and referential delusions. Ashford, Ashcroft and Maguire (2012) and Fisher, Appiah and Grant (2012) obtained weak ratings for the samples utilised as both recruited via universities and neither study controlled for potential confounders, whereas Hardy et al (2016) employed a more representative clinical sample and controlled for important covariates which adds strength to the study findings. The results suggest mixed evidence for the role of negative schema in the relationship between childhood trauma and psychosis, although the mixed findings may also reflect a degree of symptom specificity for the role of beliefs in the trauma-psychosis relationship.

#### Miscellaneous

Five studies examined other potential psychological mediators of the relationship between childhood trauma and psychosis.

#### Neuroticism and mastery

Bak, et al., (2005) found neither neuroticism nor mastery mediated the relationship between trauma and perception of distress caused by psychosis symptoms. The instruments used to measure neuroticism and mastery were valid; however, the authors acknowledged that they may not have been sensitive enough to capture the constructs. Further, regression methods were used to test mediation and childhood trauma was measures using items created for the study, which further limits the strength of the study.

#### Mindfulness

Perona- Garecelán et al., (2014) employed robust statistical mediation methods to examine whether dispositional mindfulness acted as a mediating factor between childhood trauma and hallucination proneness and did not find an effect.

#### Proximal life stressors

Two studies used path analysis to examine the role of proximal life stressors in the relationship between childhood trauma and vulnerability to delusions (Goldstone, Farhall and Ong, 2011) and hallucinations (Goldstone, Farhall and Ong, 2012) in both clinical and nonclinical samples. For the non-clinical sample, life hassles were found to mediate the

relationship between emotional abuse and hallucinations (Goldstone, Farhall and Ong, 2012), and delusions (Goldstone, Farhall and Ong, 2011). For the clinical sample, childhood sexual trauma predicted delusions and auditory hallucinations when combined with life hassles. Robust methods of mediation analysis were employed; however, important confounding variables were not controlled for and both studies obtained weak ratings for selection bias.

#### Loneliness

Boyda McFeeters & Shevlin (2015) utilised an epidemiolocal design and found that loneliness did not mediate the relationship between childhood sexual abuse and psychosis. However, the measurement of loneliness was a single item and childhood sexual abuse items were also created for the study, which limits the strength of the findings.

#### Discussion

#### Summary of findings

The aims of this paper were to provide a comprehensive systematic review of quantitative literature investigating potential psychological mediators of the association between childhood trauma and dimensional and categorical psychosis symptoms. A further aim was to evaluate the quality of this evidence, including the relative strength of the statistical mediation analysis used to explain the trauma-psychosis link. The results suggest that attachment style, dissociation, self-concept clarity, social defeat, depression and anxiety, post-traumatic symptoms, life hassles, negative self and other beliefs, and, more tentatively, self-esteem, may be important psychological mediators of the relationship between childhood trauma and psychosis symptomatology across clinical and non-clinical samples. However, there is currently not enough evidence to support substance misuse, neuroticism and mastery, dispositional mindfulness and loneliness as mediating mechanisms. The findings that mediation held for both dimensional and categorical outcomes in psychosis may provide further support for a psychosis continuum, with the degree and severity of environmental risk factors potentially determining whether symptoms remain subclinical or develop into a diagnosable psychotic disorder (van Os et al., 2009).

There appeared to be a degree of specificity both in terms of the type of childhood trauma and the psychosis symptomatology investigated with regards to the role of some psychological mechanisms. For example, there was some evidence to suggest that the mediating effect of dissociation was more pronounced for the relationship between sexual abuse and hallucinations rather than psychosis in general (Varese, Barkus & Bental, 2012; Evans et al., 2015). Furthermore, negative other beliefs appeared to mediate the relationship between bullying experiences and paranoia and persecution (Ashford, Ashcroft and Maguire, 2012) and between emotional abuse and persecutory delusions (Hardy et al., 2016) but not sexual abuse and auditory hallucinations (Hardy et al., 2016). It has been suggested that negative expectations of others may be a core process in paranoid delusions specifically (Bentall & Fernyhough, 2008), which may explain these findings. However, further empirical scrutiny of claims of specificity is required before conclusions can be drawn.

The findings of the current review support conclusions reached by Morgan and GayerAnderson (2016) who conducted a narrative review exploring potential mechanisms involved in explaining the childhood adversity and psychosis link. Whilst helpful in summarising much of the literature around childhood adversity and psychosis, the literature was not systematically searched. More importantly, one particular issue when evaluating psychological mechanisms is the robustness of the study design employed and statistical analytic methods used to examine the mechanisms. These factors were not assessed in the previous review. Congruent with the present review, Morgan and Gayer-Anderson (2016) identified evidence for dissociation, negative beliefs about the self, reasoning biases, selfesteem and affect as mediators of the childhood trauma-psychosis link. However, there are a number of discrepancies between the findings of Morgan and Gayer-Anderson (2016) and those of the present review. The previous review reported source monitoring biases (Varese, Barkus & Bentall, 2012) and sleep disturbances (Freeman & Garety, 2014) as potential psychological mechanisms; however, robust mediation analysis was not employed to test these links. The current review also identified a number of mechanisms that were not included in the previous review, including self-concept clarity, loneliness, attachment, posttraumatic symptoms and dispositional mindfulness.

Significant evidence shows that childhood trauma contributes towards the development of an increased vulnerability to psychosis (Varese, et al., 2012; Matheson et al., 2013; Read et al., 2005). The findings of the current review show that several causal partners appear to be involved in this relationship and provide support for several models of psychosis. For example, the putative mechanisms identified support a role for negative schematic models of the self and the world and disrupted affect (Garety et al., 2001), the impact of trauma via the developing brain (Read et al., 2001), attachment (Barker et al., 2015; Berry & Bucci, 2015), dissociation (Pilton et al, 2015; Longden Madill & Waterman, 2012; Berry & Bucci, 2015), appraisals (Chadwick & Birchwood, 1994, 1996; Morrison, 1998, 2001) and peri- and posttraumatic processes (e.g. Steel, 2015; Hardy et al 2016).

Consistent evidence was found for attachment style mediating the trauma-psychosis link. Evidence suggests that insecure attachment styles are associated with difficulties such as dissociation (Longden, Madill, & Waterman, 2012), negative beliefs about the self and others, and difficulties in regulating affect (Mikulincer & Shaver, 2012), which were also found to mediate the relationship between childhood trauma and psychosis in the present review. Consistent positive findings were also reported for dissociation as an important mechanism in the relationship between early trauma and hallucinations specifically and psychosis in general. However, dissociation was conceptualised across the included studies as a unitary construct, whereas evidence suggests that there may be different kinds of dissociation (Brown, 2006). Therefore, current measures and conceptualisations of dissociation may not be able to detect important mechanisms, which may explain the trauma-psychosis link.

Our findings also showed that faulty self and other knowledge such as poor self-concept clarity, social defeat, low self-esteem and negative self and other beliefs acted as mediators. It is possible that early trauma contributes to the development of faulty self and social knowledge, with this knowledge increasing a person's vulnerability to interpreting unusual experiences in a culturally unacceptable way (Morrison, 2001; Birchwood et al., 2000). The current review also found good evidence to suggest that depression, anxiety and affect regulation difficulties were important mechanisms in the trauma-psychosis relationship. The findings fit with the cognitive model of positive symptoms developed by Garety et al., (2011), which postulates that emotional changes, such as depression and anxiety, in response to a triggering event may impact the processing of anomalous experiences and influence their content.

The Bradford Hill criteria tells us that an association is likely to be causal if the association is strong and specific; if the data are consistent and the cause always precedes the effect; if there is a dose-response effect; if the effects are reversible; if alternative possibilities can be excluded; and if there is a plausible mechanism. While previous reviews (e.g. Varese, et al., 2012; Matheson et al., 2013; Read et al., 2005) have established that the link between trauma and psychosis is consistent, graded and temporally ordered, they lacked the appraisal of plausible mechanisms provided by the current review, which is required to identify causality (Bradford-Hill Criteria; Hill, 1965). The findings of the current review add to the overall evidence for a potential causal association between childhood trauma and psychological routes to psychosis following the experience of trauma. It is clear from the findings of the present review that different traumatic sequalae have received some support including posttraumatic symptoms, affective symptoms and emotion regulation, dissociation and insecure attachment; whilst some findings are more tentative, including negative schema and self-esteem.

#### Limitations

Findings should be considered in light of some limitations. First, the majority of identified studies were cross sectional in nature, which limits the conclusions that can be drawn regards causality (Kraemer, Kiernan, Essex & Kupfer, 2008). Further, based on the quality assessment tool used, several studies obtained weak scores for selection bias (Perona-Garecelán et al., 2014; Perona- Garecelán et al., 2012; Evans et al., 2015; Fisher, Appiah-Kusi & Grant, 2012; Boyda, McFeeters & Shevlin, 2015; Goodall et al., 2015; Wolke et al., 2013; Berenbuam, Valera & Kerns, 2003; Choi et al., 2015; Sitko et al., 2014; Murphy, Murphy & Shelvin, 2015; Ashford, Ahscroft & Maguire, 2012; Fisher et al., 2013). Therefore, samples may not have been representative of the target population and sample biases may exist whereby data reported failed to capture the true variability in childhood trauma, psychosis symptomatology and the mediating variable under investigation. A number of studies did not control for potential confounders (Perona- Garecelán et al., 2012; Boyda, McFeeters & Shelvin, 2015; Goodall et al., 2015; Berenbuam, Valera & Kerns, 2003; Choi et al., 2015; Murphy, Murphy & Shelvin, 2015; Ashford, Ahscroft & Maguire, 2012; Sheinbaum, Kwapil, and Barrantes-Vidal, 2014; Goldstone, Farhall & Ong, 2011; Goldstone, Farhall and Ong, 2012; Thompson et al., 2016) and so caution is required in the interpretation of the relative contribution of the mediators examined in these studies on the trauma-psychosis relationship.

There were also some limitations to the review itself. Included articles were restricted to those published in peer-reviewed journals, and written in English, which may have resulted in relevant evidence being overlooked. A potential source of bias in the current review is a failure to retrieve a comprehensive sample of studies. While the search strategy was sensitive, it may have missed studies, particularly unpublished studies, which may impact on the current findings. It is also possible that many other mediators have been considered in the unpublished literature, which may not have been captured here as researchers may be less likely to submit non-significant findings for publication. Therefore, caution is recommended in the interpretation of the current findings, and future evidence syntheses could either minimise the occurrence of such biases when appraising the literature by including grey literature, or estimate the extent to which these biases affect the findings of the review. A further limitation is that studies that had not employed mediation analysis to examine relationships between variables were excluded (e.g. Berry, Barrowclough & Wearden 2009). This inclusion criterion was considered pertinent to ensure that claims of plausible mechanisms were based on inferential tests. Studies which had not employed mediation analysis had not statistically tested putative mechanisms and therefore could not be taken to provide evidence for mediation. However, the causal steps approach to mediation analysis is still widely employed by authors, despite its limitations. Therefore, it is possible that research projects have been terminated early in a research program, or

rejected by journals because the data did not conform to Baron and Kenny's (1986) criteria. This approach would have the impact of impeding theoretical development and biasing the findings of the current review. Furthermore, the current review focused solely on psychological mechanisms and did not include social factors. However, the review does investigate the role of social factors in the cause of psychosis.

#### Clinical implications and future research

On the basis of the evidence presented in the current review, a number of risk factors appear to be involved in the process leading from early trauma to the emergence of psychotic symptoms, and several pathways are possible. Further exploration of the pathways between childhood adversity and psychosis is warranted to test these postulated mechanisms and has the potential to support the development of more effective interventions by enabling a focus on the right mechanisms. Given the lack of clarity regarding the extent to which these processes are relatively independent from each other, or their relative contribution to explain risk for psychosis in survivors of childhood trauma, future research is needed to better disentangle the contribution of these different processes, and whether certain experiences are particularly likely to "trigger" certain processes (see Bentall et al., 2014). This research will require larger samples sizes, longitudinal design, and more complex modelling techniques to allow for the robust appraisal of different pathways from adversity to psychosis. The causes of psychosis are likely to be multifactorial, with genetic, neurobiological, environmental and psychological factors interacting to increase risk for psychosis. Therefore, future research aimed at illuminating the pathways that lead from childhood trauma to psychosis may benefit from the integration of biological and psychosocial research, avoiding ideological biases and developing coherent and integrated models of psychosis. Furthermore, several included studies examined diagnosic groups such as depression (e.g. Sitko et al., 2014) and anxiety (e.g. Fisher, Appiah-Kusi & Grant, 2012) as putative mechanisms. Future research would benefit from the utilisation of more transdiagnostic measures, as the pursuit of disorder-specific processes may de-emphasise and limit our understanding of substantial commonalities that exist across putative mechanisms (McEvoy, Nathan & Norton, 2009). More transdiagnostic measures would enable a clearer delineation of commonalities across the proposed mechanisms.

Another important factor to consider is that the majority of the studies included in the present review have focused on the presence of psychotic symptoms, but it is possible that the mediators of distress and need for care might either overlap or be distinct from those captured from these studies. This is perhaps a neglected area of research, which could provide great benefit in terms of informing psychological interventions for psychosis. The findings of the present review highlight several important traumatic sequalae including post-traumatic symptoms, affective symptoms and emotion regulation, dissociation and insecure attachment. The findings support NICE (2014) recommendations for assessing trauma, post-traumatic stress symptoms, anxiety, depression and substance misuse in all clients with psychosis, and suggest that assessment should also consider additional psychological processes so that these processes can be included in psychological formulations. Appropriate psychological interventions considering these processes should in turn be offered. Evidence suggests that psychotherapy can move people from insecure attachment to more secure attachment styles (Taylor, Rietzschel, Danquah, & Berry, 2015) and the findings of the current review suggest that interventions which focus on moving people to more secure ways of relating could improve outcomes for individuals experiencing psychosis. Furthermore, insecure attachment styles have been implicated in difficulties regulating affect (Mikulincer & Florian, 1998) and it may be that a shift towards a more secure attachment style could lead to improvements in regulating emotions. There is a limited evidence base for effective interventions which target dissociative process in psychosis (Newman-Taylor & Sambrook, 2013). However, where dissociative process become active in therapy, techniques such as grounding may be required. Future research employing larger samples sizes, longitudinal design, and more complex modelling techniques could contribute towards the development of more effective treatment through supporting a better understanding of the causal pathway from early trauma to the development of psychosis.

#### Conclusions

In summary, the present review has aimed to summarise and critically evaluate a broad and varied range of mechanisms proposed to explain the relationship between childhood trauma and dimensional and categorical outcomes in psychosis. We outline a number of methodological issues that may have biased the literature in this area. Nonetheless, the evidence synthesised in the present review suggest that several causal mechanisms may be involved in the link between exposure to childhood trauma and the both dimensional and categorical outcomes in psychosis.

Author	Selection bias	Confounders		Data collection	Withdrawals and	Analysis	
			IV	DV	М	drop outs	
Hardy et al.	S	S	S	S	S	N/A	S
(2016)							
Sheinbaum et al.	М	М	S	S	S	N/A	S
(2015)							
Boyda,	W	W	W	W	S	N/A	S
McFeeters &							
Shelvin (2014)							
Bak et al. (2005)	М	М	W	Neuroticism=W	S	N/A	W
				Mastery=S			
Murphy, Murphy	W	W	S	S	S	N/A	S
& Shelvin (2015)							
Ashford,	W	W	S	S	S	N/A	S
Ashcroft &							
Maguire (2012)							
Thompson et al.	М	W	S	S	S	N/A	
(2016)							
Goodall et al.	W	W	S	S	S	N/A	S
(2015)							
Wolke et al.	W	S	М	S	S	W	S
(2013)							

#### Table 1. Quality assessment tool ratings.

Whitfield et al. (2005)	М	S	M	W	W	N/A	W
Varese, Barkus &	Clinical=M	S	S	S	S	N/A	S
Bentall (2012)	Non-clinical=M						
Perona-Garcelán	W	W	S	S	S	N/A	S
et al. (2012)							
Morgan et al	Clinical=M	S	М	М	S	N/A	S
(2014)	Non-clinical=M						
Marwaha &	М	S	М	М	М	N/A	М
Bebbington							
(2015)							
Marwaha et al.	М	S	W	S	S	N/A	М
(2014)							
Van Neirop et al.	Case= S	М	W	W	W	N/A	М
(2014)	Control=S						
Sitko et al. (2014)	М	S	S	S	М	N/A	S
Sheinbaum,	W	W	S	S	S	N/A	S
Kwapil &							
Barrantes-Vidal							
(2014)							

Powers Thomas,	М	М	S	S	S	N/A	М
Ressler &							
Bradley (2011)							
Perona-Garcelán	W	S	S	S	S	N/A	S
et al. (2014)							
Goldstone,	Clinical=W	W	М	M	М	N/A	S
Farhall & Ong	Non-clinical=W						
(2012)							
Goldstone,	Clinical=W	W	М	М	М	N/A	S
Farhall & Ong	Non-clinical=W						
(2011)							
Fisher, Appiah-	W	S	М	S	S	W	S
Kusi & Grant							
(2012)							
Evans et al	Clinical=W	S	S	S	S	N/A	S
(2015)	Non-clinical=W						
Choi et al (2015)	W	W	S	S	S	N/A	S
Berenbaum,	W	W	S	S	S	N/A	S
Valera & Kerns							
(2003)							
Berenbaum et al.	М	W	S	S	S	N/A	М
(2008)							

Bebbington et al (2011)	М	S	W	Anxiety=S cannabis=W	S		
Van Dam et al. (2014)	Case=M Control=M	М	S	S	S	N/A	W
	Siblings=M						
Fisher et al. (2013)	W	S	S	S	S	N/A	S

S= strong, M= moderate, W= weak

 Table 2. Overview of studies included in review.

Author, Date, Country	Design	Sample	<u>Measures</u> Childhood trauma	Mediator(s)	Psychosis	<u>Analysis</u>	Main (relevant) findings
Hardy et al. (2016) UK	Crosssect	tional 228 adults with relapsed psychosis, 165 male, 63 female (M=38.24 years, SD= 11.11)	THQ	SRS-PTSD BCSS BDI-II	Scales for the Assessme -nt of Positive Symptoms (Andrease n,1984)	Mediation analysis using Valeri & Vanderwee le (2013) approach	<ul> <li>Posttraumatic avoidance, numbing (OR= 1.48) and hyperarousal (OR= 1.44) mediated the relationship between childhood sexual abuse and auditory hallucinations. Negative other beliefs mediated the relationship between childhood emotional abuse and persecutory delusions (OR= 1.34). No evidence was found of mediation through negative other beliefs for childhood sexual abuse and auditory hallucinations or childhood emotional abuse on referential delusions. Intrusive trauma memory was not found to mediate the relationship between childhood sexual abuse and auditory hallucinations.</li> </ul>

Sheinbaum et.al. (2015) Spain	Crosssectional	214 students, 78% women (M= 21.4 years, SD= 2.4) 123 with elevated psychosis-	CECA	ASI	CAARMS; Structured Clinical Interview for DSM- IV Axis II	Hayes (2013) approach to mediation	Angry-dismissive attachment was found to mediate the relationship between antipathy and subclinical positive symptoms ( <i>b</i> = 0.126). Antipathy was found to have an indirect effect on paranoid and schizotypal PD traits through both
		proneness scores, 91 with scores below 1.0.			Disorders		angry-dismissive and enmeshed attachment. The relationship between role reversal and subclinical positive and negative symptoms was not mediated by any of the attachment styles. Enmeshed attachment was found to mediate the relationship between role reversal and paranoid ( $b$ = 0.11) and schizotypal ( $b$ = 0.12) PD traits.
Boyda, McFeeters & Shelvin. (2014) UK	Crosssectional/ populatio n based study	<ul> <li>7403 adults,</li> <li>3197 men, 4206</li> <li>women (Age</li> <li>over 16, means</li> <li>not reported)</li> </ul>	Yes/no to item Sexual abuse before 16 years of age	Single item from Social Functioning section of survey	PSQ	Mediation model for dichotomou s outcomes (Muthén, 2011)	Childhood sexual abuse (CSA) predicted loneliness, however, CSA did not predict psychosis and loneliness failed to mediate the relationship between CSA and psychosis

Bak et al., (2005) The Netherlands	Crosssectional, populatio n based study	<ul> <li>163 adults age</li> <li>16-64 years</li> <li>identified as</li> <li>having psychotic</li> <li>experience.</li> <li>(Mean age not</li> <li>provided)</li> </ul>	Yes/no to survey item asking whether experience abuse before 16 and rating of frequency	Groningen Neuroticism Scale Five item mastery scale	MACS	Regression	The measures of neuroticism and mastery did not affect the association between trauma and perception of distress. The association between childhood trauma and coping related control was only slightly reduced neuroticism ( $b$ = -1.8) and mastery ( $b$ = -1.9).
Murphy, Murphy,& Shelvin. (2015) UK	Crosssectional	785 pupils, 345 male, 440 female (M= 16.20 years, SD= 1.06).	ELES	SCS PTCI IPSM	PSS	Conditional process analysis (Hayes, 2012)	The conditional indirect effects of traumatic cognitions on relationship between childhood threat and psychotic experiences was found to be significant ( $b$ =0.21). Negative social comparisons were associated with feelings of childhood threat; however, this relationship did not extend to psychotic experiences.

Ashford, Ashcroft &	Crosssectional	135 students, 123 female, 12	Modified DIAS	IPSM	GPTS	Mediation analysis using	Depression and negative beliefs about the self significantly
Maguire. (2012) UK		male (M= 19.8 years, SD not provided).		HADS BCSS		Preacher & Hayes (2008) approach	mediated the effect of indirect aggression on paranoid thinking (PE= 0.11 and 0.16 respectively and persecution PE= 0.1 and 0.18 respectively). Negative beliefs about others mediated the effect of direct verbal aggression on paranoid thinking (PE= 0.24). Negative beliefs about others mediated the effect of direct verbal aggression on persecution (PE=0.11).
Thompson, et al. (2016) Australia	Follow-up	233 UHR for psychosis. Adults aged 1530 years, mean and SD not provided.	CTQ	The Hamilton Anxiety rating scale and Hamilton Depression Rating Scale.	CAARMS BPRS CASH	Mediation using Karlson Holm Breen command (Breen et al., 2013)	No significant mediation by depression (OR=1.00), anxiety (OR= 1.00), dissociation (OR=0.99), mood instability OR=1.00) or mania (OR=1.01) found.
				CAARMS			

Goodall, et al. (2015) UK	Cross- Sectional	283 non-clinical (58% students, 72% female) (M= 26 years, SD= 9.28)	CTQ	ECR-R	SPQ-B	Parallel multiple mediator model using conditional process modelling (Hayes, 2013)	Both attachment anxiety and attachment avoidance mediated the relationship between emotional abuse and schizotypy (PE= 0.06 and PE= 0.04 respectively), with anxiety having the greater effect.
Wolke et al. (2013) UK	Longitudinal	4720 children followed up to age 18	Child reported bullying- Bullying and Friendship Interview Schedule	Short Mood and Feelings Questionnai - re (Angold et al., 1995) PLIKSi completed at age 12.9	PLIKSi completed at age 18	Path analysis	The association between child reported peer victimization in childhood and psychotic experiences at age 18 was mediated by depression ( $B$ = 0.03) and previous psychotic experiences ( $B$ = 0.07).
Whitfield, Dube, Felitti & Anda. (2005) USA	Crosssectional/ epidemiol ogical	17,337 adults, 9367 women, 7970 men (M= 57 years, SD= 15.3)	ACE questionna -ire	Substance abuse items from ACE study questionnaire	Yes/no in response to item "have you had or do you have hallucinations"	Regression	Substance abuse slightly reduced the relationship between adverse childhood experience and hallucinations (OR reduced from 3.0 to 2.5), suggesting a mediating role for substance abuse.

Varese, Barkus & Bentall. (2012) UK	Crosssectional/ casecontrol	45 patients with schizophrenia spectrum diagnoses (Hallucinating 15, M=45.6 years, SD= 12.2, males=6;	CATS	DES	LSHS-R	Mediation using Imai et al.,'s (2010) general approach	mediated between of and hallud (b= 0.12), effect for s relative to trauma in	on positively the relationship childhood trauma cination-proneness with a stronger sexual abuse other types of both the ed ( $b$ = 0.65) and
PeronaGarce et al. (2012)	yea Crosssection	ars, SD= 14.6, male nal 71 patients diagnosed with psychosis (M= 39.08 years,	s= 11) and 20 TQ	0 healthy con		.4 years, males= 7; ars, SD= 14.6, male PANSS	s= 11) Mediation analysis using Preacher	Simple mediation analysis showed that dissociation significantly mediated the relationship between childhood
Spain		SD= 8.98)					and Hayes, (2004) approach	trauma and hallucinations ( $b$ = 0.21) but not delusions ( $b$ = 0.07). Multiple mediation models showed that only depersonalisation mediated the relationship between childhood trauma and hallucinations ( $b$ = 0.19).

Morgan et al. (2014) UK	Crosssection Case- control	al/ 391 cases with a first episode psychosis, 161 males, 230 females (M= 37.3 years, SD= 12.5), 390 populationbased controls, 218 male, 172		; odemographic edule	Rosenberg Self-Esteem Scale MRC Sociodemographic Schedule	Diagnosis of psychosis	Mediation analysis using Preacher and Hayes (2008) approach	Self-esteem had a weak effect on the pathway from separati psychosis via education disadvantage (OR= 1.02).	
		nale (M= 30.5 ars, SD= 8)							
Marwaha & Bebbington. (2015) UK	epidemiol ogical	5689 adults aged 16 and above (mean and SD not provided)	Detailed sexual abuse history	CIS-R	Diagnosis of psychosis or score on PSQ	Mediation using Karlson Holm Breen command (Karlson, Holm & Breen, 2011) and Sobel test	between bot sexual interc of contact al and unwante and psychos 1.60 respect	e relationship th non-consensual course and all forms buse (intercourse ed sexual touching) sis (OR= 2.41 and tively), with accounting for a	

Marwaha et al. (2014) UK	Populatio n- based study	7403 adults with psychosis over age 16 (mean and SD not provided)	Items from British national survey of psychiatric morbidity 2007	Structured Clinical Interview for DSM-IV (SCID-II)	Diagnosis of psychosis or score on PSQ Score on continuous dimension of paranoia	Mediation analysis using Karlson Holm Breen command (Karlson, Holm & Breen, 2011)	Mood instability mediated the relationship between child sexual abuse and psychosis (OR difference= 2.30), paranoid ideation (OR difference= 1.63) and hallucinations (OR difference= 1.41).
Van Neirop et al. (2014) The Netherlands	Epidemiol ogical/ casecontrol	5868 controls, 46% male (M= 44 years, SD= 12.4), 384 extended psychosis phenotype; 36% male (M= 43	Questionn aire based on the NEMESIS- 1 trauma questionn aire	Social defeat- various questions indexing selfdevaluation Substance	Ratings of frequency, distress and impact of psychotic experience	Regressio -n and tests of indirect effects	Affective dysregulation mediated the relationship $\beta$ between childhood trauma and EEP (= 0.04) but not PD ( $\beta$ = .01). Social defeat mediated the relationship between childhood trauma and both EEP ( $\beta$ =0.03) but not PD ( $\beta$ =0.04). Cannabis use did not appear to mediate these
		years, SD= 13.1), 43 psychotic disorder (M= 41 years, SD= 12.9)		Use section of the CIDI 3.0. Various questions indexing general affective symptoms			relationships.

Sitko, et al.	Epidemio-	5877 adults	UM-CIDI	Adult	Beliefs	Muthen	Paranoia-
(2014) UK (data from	logical	aged 15-54 (mean and SD		Attachment Questionnaire	and Experiences	and Muthen	Avoidant and anxious attachment
USA)		not provided).		Quoononnano	module of	(19982011)	fully mediated the relationship between neglect and paranoia (β=
				Sadness	the UM-	approach	0.047)
				module of the UM-CIDI	CIDI	to mediation	Avoidant attachment mediated the
						mediation	relationship between being held captive/threatened with a weapon
							and paranoia
							Rape had an indirect relationship with
							paranoid thoughts through anxious attachment
							Depression mediated the relationship
							between physical abuse and
							paranoia Sexual molestation had an indirect
							relationship with paranoia through
							depression
							Hallucinations-
							Anxious attachment mediated the
							relationship between rape and hallucinations
							Avoidant attachment mediated the relationship
							between being held

							captive/threatened with a weapon and hallucinations Neglect had an indirect relationship with hallucinations through avoidant and anxious attachment Depression mediated the relationship between witnessing an injury/killing and hallucinations, the relationship between sexual molestation and hallucinations and the relationship between physical abuse and hallucinations.
Sheinbaum, Kwapil & BarrantesVidal (2014) Spain	Crosssectional	546 students, 83.2% female, (M= 20.6 years, SD= 4.1)	СТQ	RQ	CAPE SPQ WSS	Mediation analysis using Hayes (2013) method	Fearful attachment significantly mediated the relationship between physical/emotional trauma and positive (B= 0.063 (PLE); 0.056 (suspiciousness); 0.010 (positive schizotypy) and negative (B= 0.019) non-clinical psychotic phenomena. Dismissing and preoccupied attachment did not mediate this link.
Powers, Thomas, Ressler & Bradley (2011) USA	Cross- Sectional	541 adults, mean (SD) age in the sample was 38.4 (13.3) years (range, 18-81 years).	СТQ	CAPS	SNAP	Mediation analysis using Baron & Kenny (1986) model and Sobel test	Intensity of lifetime PTSD symptoms mediated the relationship between childhood emotional abuse and schizotypal personality pathology (β= .27).

Perona- Garcelán, et al. (2014) Spain	Crosssectiona	al 329 students, 21% male, 79% female (M= 21.41 years, SD= 5.78)	TQ	Southampton Mindfulness Questionnaire TAS	LSHS-R	Mediation analysis using Preacher and Hayes	Only depersonalization ( $\beta$ = 0.16) and absorption ( $\beta$ = 0.38) significantly mediated the relationship between childhood traumas and hallucination proneness.
				CDS		(2008) method	Mindfulness did not mediate this relationship.
Goldstone, Farhall & Ong. (2012) Australia	control (~ 1 1 w d n	33 non-clinical, 9% female 45% aged 825. 00 diagnosed vith a psychotic lisorder, 56% nale (33% aged 6-35)	Early Trauma Inventory- Self Report	Cannabis use scale Survey of recent life experience Acceptance and Action Questionnaire II Metacognitions Questionnaire	LSHS-R	Path analysis	Non-clinical: The path from emotional trauma to sub-clinical hallucinations via life hassles was one of the strongest pathways ( $\beta$ = -0.32). Clinical- The non-clinical model did not provide a good fit with the clinical sample. Replacing childhood emotional trauma with sexual trauma improved the fit. The ability of life hassles to predict hallucinations was reduced for the clinical sample. Sexual trauma did not appear to work with life hassles to predict symptom severity.

Goldstone,	Crosssectional	/133 non-clinical,	Early	Survey of	PDI	Path	Non-clinical- Emotional trauma was
Farhall & Ong (2011) Australia	Case- control	59% female (45% aged 18- 25) 100 diagnosed with a psychotic disorder, 56% male (33% aged 26-35)	Trauma Inventory- Self Report	Recent Life Experience Acceptance and Action Questionnair e II		analysis	the only trauma measure to be significantly correlated with delusions. The pathway from emotional trauma to life hassles was one of the strongest predictors of subclinical delusions ( $\beta$ = 0.34). Clinical- The non-clinical model did not provide a good fit with the data. Findings indicated that experiences of childhood sexual trauma predicted delusions when combined with life hassles.
Fisher, Appiah-Kusi & Grant (2012) UK	Crosssectional	212 non-clinical adults, 65.4% female. Mean age 27 (8.4)	CTQ	BAI Brief Core Schema Scales BDI	PSQ	Binary mediation	Anxiety and negative self-schemas formed the strongest indirect pathways between emotional abuse and paranoia, however only anxiety reached statistical significance (OR=1.05). The proposed mediators did not significantly mediate the relationship between physical abuse and paranoia.

Evans et al. (2015) UK	Crosssectional/ casecontrol	29 diagnosed first-episode	CTQ	SCCS	PANSS	Preacher Hayes	Dissociation positively mediated the
		psychosis, 34.5% female (Aged between 18-38) 31 non-clinical, 38.7% female (Aged between 18-38)		DES-II	PSQ	(2008) approach to mediation	relationship between physical neglect and group membership (B= -0.101). The indirect effects for emotional, physical and sexual abuse and emotional neglect were not significant. Self-concept clarity mediated the relationship between psychosis group membership and total childhood trauma (B= 0.057), emotional abuse (B= 0.144), physical abuse (B= 0.195), emotional neglect (B= 0.130) and physical neglect (B= 0.210). The indirect effect of sexual abuse did not reach statistical significance (B= 0.294).
Choi et al. (2015) Republic of Korea	Crosssectional	126 adult psychiatric inpatients with symptoms of psychosis, 70 female, 56 male (M= 36.14, years SD=	CTQ	Korean version of the Impact of Events ScaleRevised	PSYCH subscale of the PSY-5 Factor Scale of the Minnesota Multiphasic Personality	Structural equation modelling	Posttraumatic stress symptoms mediated the relationship between child abuse and self-reported psychotic symptoms ( $\beta$ = 0.172).
		13.79)			Inventory-2		

Berenbaum, Valera & Kerns (2003) USA	Crosssectional	75 non-clinical women (M= 38.7 years, SD= 14.2	CTQ Interview pre- and post-teen sexual abuse	Various measures of psychological dysfunction	SIDP IV SPQ	Structural equation modelling	Psychological dysfunction mediated the relationship between neglect (but not physical or sexual abuse) and schizotypal personality disorder
			SelfReport of Childhood Abuse				
Berenbaum et al. (2008) USA	Crosssectional	303 non- clinical adults 53.1% female (M= 43.2, SD= 17.6)	SelfReport of Childhood Abuse Physical interview procedure CTQ	DPS CES SCID-D; DES-T CAPS	PDI-IV	Baron and Kenny (1986) approach and Sobel test.	For women, absorption ( $\beta$ =0.15) and current ( $\beta$ = 0.16) and lifetime ( $\beta$ =0.20) PTSD symptoms mediated the relationship between childhood maltreatment and schizotypal symptoms. For men, only absorption ( $\beta$ = 0.39) and current PTSD symptoms ( $\beta$ = 0.39) were significant mediators.

Bebbington et al. (2011) UK	Crosssectional/ epidemiol -ogcial	43 adults with probable psychosis aged 16 and over (mean and SD not provided)	Items asking about different levels of sexual abuse experienc	Items asking about different levels of sexual abuse experienced after age 16	SCAN or meeting least 2 criteria of psychosis screening criteria items from	at	Baron and Kenny (1986) approach.	Cannabis use was not associated with childhood sexual abuse or probable psychosis. Both anxiety and depression were found to mediate the relationship between non-consensual childhood sexual intercourse and psychosis
			ed before age 16	e CIS-R Use of cannabis over 100 times	survey			reduced OR from 10 to 5.8 ad 4.1 respectively).

Van Dam et al. (2014) The Netherlands	Crosssectional; Case- control, case- sibling, siblingcontrol	131 adults meeting criteria for psychotic disorder, 84% male (M= 31.19 years, SD= 10.58) 123 relatives, 47.2% male (M= 58 years, SD= 47.2) 72 controls, 63.9 % male (M= 30.89 years, SD= 7.47)	CTQ	ΡΑΜ	CASH SCAN CAPE	Hierarchic al multiple regression	Attachment style mediated the relationship between childhood maltreatment and positive symptoms for siblings (B= 0.197 for anxiety and B= 0.201 for avoidance) with a reduced effect for patients (B= 0.140 for anxiety and B= -0.066 for avoidance). In siblings, attachment style was also found to mediate the relationship between childhood maltreatment and negative symptoms (B= 0.430 for anxiety and B= 0.29 for avoidance), however this was not the case for patients.
Fisher et al., (2013) UK	Longitudi nal	6692 children who completed the PLIKSi at an average age of 12.9 years	Mother reported victimisation Bullying and Friendship Interview Schedule	NSIE Harter's Self Perception Profile for Children	SCAN PLIKSi	Multiple mediation analysis using Hayes (2013) approach	Harsh parenting was indirectly associated with both broadly and narrowly defined PLIKSi symptoms through clinically relevant depressive symptoms (OR= 1.03 and 1.01 respectively), and to a lesser extent via low self-esteem (OR= 1.01 for both), and level of anxiety (OR= 1.01
				DAWB SMFQ			for both). Indirect pathways between bullying

victimization and psychotic symptoms were apparent via low self-esteem (OR= 1.02), depressive symptoms (OR= 1.01), and level of anxiety (OR= 1.00). The results were largely unchanged when confounders were included in these models.

THQ= Trauma History Questionnaire; SRS-PTSD= Self-report Scale for Posttraumatic Stress Disorder; BCSS= Brief Core Schema Scale; BDI-II= Beck Depression Inventory II: CECA= Childhood Experience of care and Abuse: ASI= Attachment Style Interview; CAARMS= Comprehensive Assessment of At-Risk Mental States; PSQ= Psychosis Screening Questionnaire; MACS= Maastrict Assessment of Coping Strategies; ELES= Early Life Experiences Scale; SCS= Social Comparison Scale; PTCI= Posttraumatic Cognitions Inventory; IPSM=Interpersonal Sensitivity Measure; PSS= Adolescent Psychotic-like Symptom Screener; DIAS= Direct and Indirect Aggression Scales; HADS= Hospital Anxiety and Depression Scale; BCSS= Brief Core Schema Scales; GPTS= Green et al., Paranoid Thoughts Scales; CTQ= Childhood Trauma Questionnaire; BPRS= Brief Psychiatric Rating Scale; CASH= Comprehensive Assessment of Symptoms and History; ECR-R= Experiences in Close Relationships Questionnaire- Revised; SPQ-B= Schizotypal Personality QuestionnaireBrief; SDQ= Strengths and Difficulties Questionnaire; PLISKi= Semi-Structured Psychosis interview; ACE= Adverse Childhood Experiences study guestionnaire; CATS= Child Abuse and Trauma Scale; DES= Dissociative Experiences Scale; LSHS-R= Launey-Slade Hallucination Scale-Revised; PANNS= Positive and Negative Syndrome Scale; CIS-R= Clinical Interview Schedule-Revised; PSQ= Psychosis Screening Questionnaire; SCID= Structured Clinical Interview for DSM-IV; UM-CIDI= University of Michigan Diagnostic Interview; RQ= Relationship Questionnaire; CAPR= Community Assessment of Psychic Experiences; WSS= Wisconsin Schizotypy Scale; CAPS= Clinician Administered PTSD Scale; SNAP= Schedule for Non-adaptive Personality; TAS= Tellegen Absorption Scale; CDS= Cambridge Depersonalization Scale; PDI= Peter's Delusional Inventory; BAI= Beck Anxiety Inventory; BDI= Beck Depression Inventory; SCCS= Self-Concept Clarity Scale; DPS= Dissociative Processes Scale; CES= Creative Experiences Scale; DES-T= Dissociative Experiences Scale-Taxon; PDI-IV= Personality Disorder Interview-iv; CIS-R= Clinical Interview Schedule-Revised; CTQ-SF= Childhood Trauma Questionnaire-Short Form; PAM= Psychosis Attachment Measure; CASH= Comprehensive Assessment of Symptoms and History; NSIE= Nowicki-Strickland External Scale; DAWBA= Development and Well-being Assessment; SMFQ= Short Moods and Feelings Questionnaire.

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Paper 2: Empirical Study

# Does dissociation mediate the relationship between fearful attachment and voice-hearing in psychosis?

The following paper has been prepared for submission to Psychological Medicine. The guidelines for authors can be found in Appendix C

Word count: 5,648 (excluding references)

## Abstract

**BACKGROUND** Dissociation represents an important mechanism in the development of voices in individuals exposed to early trauma. The present study extends existing research by exploring the mediating role of dissociation in the relationship between fear-based attachment style and auditory hallucinations.

**METHOD** Participants with schizophrenia spectrum disorders (n=50) comprising current voice-hearers (n=23), a psychosis control group who had not experienced voices (n=15) and a remitted group who were not currently hearing voices (n=12) completed questionnaire measures of hallucination proneness, dissociative tendencies and attachment style.

**RESULTS** Compared to non-hallucinating controls, current voice-hearers reported significantly higher dissociative tendencies. Fearful attachment and hallucination proneness were both significantly associated with dissociation. Dissociation positively mediated the relationship between fearful attachment and voice-hearing proneness. However, this effect did not remain when depression was controlled for.

**CONCLUSIONS** The findings are consistent with proposals that a fear-based attachment style may predispose an individual to voice-hearing if dissociation is a sequalae of this experience, and highlight the importance of affect regulation in this pathway. The findings highlight the need to consider attachment and dissociation in the assessment and formulation of voice-hearing.

### Introduction.

Auditory verbal hallucinations (voices) occur in approximately 70% of people with a schizophrenia-spectrum diagnosis, but they also occur in non-clinical samples in association with factors such as sensory deprivation, bereavement and near-death experiences (Watkins, 2008). The way a voice-hearer relates to their voice has been likened to an interpersonal relationship, whereby interaction with voices reflect voice-hearers general pattern of relating to others (Hayward, Overton, Dorey & Denney, 2009). As attachment theory (Bowlby, 1973) is a key theory of interpersonal relationships, attachment style is being increasingly considered as a putative underlying mechanism to explain the development and maintenance of voices.

Attachment theory (Bowlby, 1973) proposes that the infant's experience of interactions with a primary caregiver becomes internalised and is carried forward into adulthood to produce expectations about the self and others in interpersonal interactions. These implicit relational schemata, or 'internal working models', are thought to form the prototype for interpersonal relationships across the life span. Infant attachment research has shown that infants develop different patterns of attachment behaviour towards their caregiver by 12 months (Ainsworth, Blehar, Walters & Wall, 1978). These attachment behaviours develop as a result of the caregiver's response to the infant's requests for comfort, protection and soothing. Where the infant can predict a caregiver's response to their requests for care, attachment behaviours become organised in a way that secures the best care available. Infants who fail to develop any organised attachment is hypothesised to develop as a result of conflict between the attachment and defence systems. This experience of conflict may be understood as early relational trauma arising from interactions with a caregiver who is both the source of, and the solution for, the infant's fear (Liotti, 2004).

Applying Bowlby's ideas about mental representations and internal working models, Bartholomew (1990) proposed a four-category model of adult attachment: secure (a sense of worthiness and an expectation that others are generally responsive); preoccupied (a sense of unworthiness combined with a positive evaluation of others); dismissive avoidant (a sense of worthiness combined with a negative disposition toward other people); and fearfulavoidant (a sense of unworthiness combined with an expectation that others will be untrustworthy and rejecting). Empirical evidence supports conceptual connections between fearful-avoidant and the disorganised attachment pattern (see Simpson & Rholes, 2002 for a review). For example, both are characterised by a lack of interpersonal soothing resulting from an approach-avoidance conflict with significant others (Anderson & Alexander, 1996). Furthermore, both disorganised (Liotti & Gumley, 2008) and fearful (Anderson & Alexander, 1996; Sandberg, 2010) attachment have been suggested to increase vulnerability to dissociative psychopathology, which supports contentions by Liotti (1992) that dissociation is a manifestation of a fear-based, disorganised attachment pattern.

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At a general level, dissociation has been described as the failure to integrate information regarding psychological functioning, such as thoughts, feelings and experiences (Bernstein & Putnam, 1986). More specifically, some researchers describe two distinct categories of dissociation: "detachment" and "compartmentalization". Detachment is conceptualised as an altered state of consciousness characterised by a sense of detachment from every day experiences (Holmes et. al., 2005). Compartmentalization is defined as a deficit in the ability to deliberately control processes such as bringing information into conscious awareness that would normally be amenable to such control (Brown, 2002). Dissociative experiences are core components of both dissociative disorders and trauma-related presentations included in the DSM-5 (American Psychiatric Association, 2013), and are reported to be the result of an integrative failure and a defence mechanism that serves to reduce the effects of traumatic events. Voices have been understood by some researchers as a dissociative experience resulting from factors such as early relational trauma, which are experienced as external and current rather than intrusive memories (Longden, Madill & Waterman, 2012). Evidence supports a large association between dissociation and voice-hearing (Pilton, Varese, Berry & Bucci, 2015), and that dissociation is related to hallucinations in particular rather than psychosis in general (Kilcommons & Morrison, 2005; Varese, Barkus & Bental, 2012).

In line with evidence supporting associations between voice-hearing, dissociation and attachment, Berry and Bucci (2015) developed the Cognitive Attachment model of Voicehearing (CAV). The model draws on cognitive, attachment and dissociative process to account for the development and maintenance of distressing voice-hearing. It predicts that a disorganised attachment style may predispose an individual to voice-hearing by creating vulnerabilities to dissociation. A key hypothesis of the model is that disorganised attachment style increases vulnerability to experiencing dissociation. Research by Ogawa, Sroufe, Weinfield, Carlson and Egeland (1997) and Anderson and Alexander (1996) provide support for the hypothesis that dissociative psychopathology is the outcome of infant disorganised and adult fearful attachment facilitating dissociative responses to trauma. Ogawa et al. (1997) found that infants with disorganised attachment showed higher mean dissociation scores as young adults than those with organised attachment patterns. Furthermore, Anderson and Alexander (1996) found fearful attachment to be significantly correlated with dissociation in a sample of adult incest survivors.

Evidence suggests that dissociation may represent an important mediating mechanism involved in the development of voices in individuals exposed to early adversity (Pilton, Varese, Berry & Bucci, 2015). However, despite much research noting links between trauma, dissociation and voices, and evidence that disorganised and the overlapping concept of fearful attachment have been suggested to increase vulnerability to dissociative psychopathology (Liotti & Gumley, 2008; Sandberg, 2010; Anderson & Alexander, 1996), no studies to date have examined the role of fear-based attachment patterns in the relationship between dissociation and voice-hearing. Therefore, the overarching objective of the current study was to examine whether dissociation mediates the relationship between a fear-based attachment style and voice-hearing. As a self-report measure of disorganised attachment validated in a psychosis sample does not currently exist, a measure of fearful attachment was used as a proxy measure of disorganised attachment in the current study. This decision is based on the strong conceptual overlap between fearful and disorganised attachment (Bartholomew, 1994; Simpson & Rholes, 2002). Specifically, we had four hypotheses. Firstly, we sought to examine whether dissociation acts as a vulnerability factor for voices more specifically rather than psychotic experiences more generally. Furthermore, we sought to examine whether dissociation was related to current voice-hearing specifically or vulnerability to voice-hearing more generally. As such, we divided our sample into three groups: current voice hearers with psychosis; remitted voice-hearers with psychosis; a psychosis group who reported never hearing voices. We hypothesised that participants who were currently hearing voices would report higher levels of dissociation than those who had never heard voices and remitted voice-hears, who would further report significantly higher levels of dissociation compared to those who had never heard voices (Dissociation: currently hearing voices>remitted voices>never heard voices). Secondly, we hypothesised that there would be a significant positive association between fearful attachment and voice-hearing proneness in the sample as a whole. Thirdly, we hypothesised that there would be a significant positive association between fearful attachment and dissociation. Lastly, a model was tested whereby dissociation was examined as a mediator in the relationship between fearful attachment and voice-hearing in the sample as a whole.

## Method

#### Sample

Participants were recruited from Mental Health Trusts and the voluntary sector (e.g. Hearing Voices Network) across the North West of England. Eligibility criteria included: participants who had received a schizophrenia-spectrum diagnosis as confirmed by the referring clinician or key worker, aged over 18 and capacity to consent to the research. Exclusion criteria were: organic psychosis, not fluent in English, being unable to provide informed consent, and known moderate to severe learning disability that would affect taking part in the research. All procedures were approved by the relevant local research ethics committee (see Appendix D).

# Procedure and Measures

Members of the individual's care team initially screened potential participants from inpatient and community mental health teams to confirm eligibility status. Potential participants from service user groups (e.g. The Hearing Voices Network) were provided with information about the study and contact details for the researchers should they wish to take part. Consent was sought to inform potential participants' key workers of their involvement in the study and to confirm study eligibility. Individuals willing to take part met with the researcher to discuss the study and obtain informed consent. Participants completed the measures in the order presented below. Participants were screened for voice-hearing status to determine whether they would be assigned to the current, remitted, or never heard voices group.

#### Demographic information

Age, gender, years of education, diagnosis, ethnicity, marital status and employment status were recorded (see Appendix E). Sociodemographic characteristics of the sample are reported in Table 1.

Dissociative Experiences Scale- Second Revision (DES-II; Carlson & Putnam, 1993). The DES-II is a self-report measure of dissociative symptoms. Participants are asked to determine to what degree each experience described in the questionnaire applies to them, and select a number from 0 to 100 to rate the percentage of time they have the experience. It contains 28 questions and returns an overall score as well as three sub-scale results-absorption (the experience of losing contact with one's current experience and becoming immersed in internal events; Waller, Putnam, & Carlson, 1996), amnesia (the inability to intentionally recall autobiographical information that would normally be accessible; Spiegel et al., 2011), and depersonalisation (experiencing a sense of unreality, detachment or disconnection in relation to one's body and surroundings; Hunter, Sierra, & David, 2004). (see Appendix H). Internal consistency of the scale was good (Cronbach's alpha  $\propto = .94$ ).

Revised Launay-Slade Hallucination Scale: Auditory Subscale (LSHS-R (AH); Morrison, Wells & Northard, 2000). The Launay-Slade Hallucination Scale is a commonly used measure of hallucination proneness (see Appendix F). The revised version used in this study was developed to separate factors relating to auditory and visual hallucinations. Five items relating specifically to experiences of auditory hallucinations were used following their use in previous studies examining auditory hallucinations (e.g. McCarthy-Jones and Fernyhough, 2011; Alderson-Day et al., 2014), with good internal reliability reported (Cronbach's alpha  $\propto$ = .73). Items are scored on a four- point scale ranging from "Never" (1) to "Almost always" (4). Good internal consistency for the LSHS-R was demonstrated in this study (Cronbach's alpha  $\propto$  = .71). The revised version was used here because the hypotheses were related to auditory hallucinations specifically rather than hallucinations in general. A proneness measure of voice-hearing was employed as this would have greater sensitivity relative to a dichotomous definition of voice-hearing.

*Relationship questionnaire (RQ; Bartholomew and Horowitz, 1991).* The Relationship Questionnaire yields continuous ratings of the four aforementioned attachment styles (see Appendix G). The measure consists of four short paragraphs describing attitudes towards relationships in general: secure, preoccupied, dismissive-avoidance and fearful-avoidance.

Each respondent is asked to make ratings on a 7-point scale regards the degree to which they as individuals resemble each of the four styles.

*Calgary Depression Scale for Schizophrenia (CDSS, Addington, Addington & MatickaTyndale, 1993*). Evidence suggests that depressive symptoms are associated with poor childhood care, insecure attachment styles, and psychotic phenomena (Harris, & Curtin, 2002; Smith et al., 2006; Roberts, Gotlibl, & Kassel,1996). Therefore, a measure of depression was employed so that this variable could be controlled for in the mediation analysis. The Calgary Depression Scale for Schizophrenia is a short, semi-structured interview assessing depression in psychosis (see Appendix I). The CDSS has been found to have good internal and inter-rater reliability and good validity. In the current study, the CDSS had good internal consistency (Cronbach's Alpha: 0.85).

## Data analysis

A power calculation was carried out using G\*power. With 50 participants, analysis of variance (ANOVA) had 80% power to detect an effect size of 0.45 or greater with a 0.05 twotailed significance. Mediation analysis using bias-corrected bootstrapping had 80% power to detect an indirect effect size of 0.35 or greater with a 0.05 two-sided significance level (Fritz & MacKinnon, 2007).

Variables were examined for skewness and kurtosis. DES-II amnesia and depersonalisation showed high skew and kurtosis and were transformed using square root transformations. As parametric assumptions were met following transformations, parametric analyses were used. All analyses involving the DES-II were carried out after excluding the DES-II hallucination item to avoid any confound arising from the overlapping content with auditory hallucinations. For the purpose of the between group analyses, participants were divided into three groups: i) current voice-hearers, comprised participants who reported experiencing voices at the time of testing; ii) remitted voice-hearers, comprised participants who had not heard voices in the past six months; iii) non-voice-hearers, comprised participants who reported never hearing voices.

Between group differences on the clinical and demographic variables were tested using ANOVA and chi-squared (X<sup>2</sup>) test. To test hypothesis 1, ANOVA was used to test for differences in dissociation scores between groups. Post-hoc comparisons were conducted using Tukey's test. For hypotheses 2 and 3, Pearson's correlation coefficient was conducted to analyse the relationships between fearful attachment and auditory hallucination proneness, and between fearful attachment and dissociative tendencies, in the sample as a whole. For hypothesis 4, the mediating role of dissociation in the relationship between fearful attachment and auditory hallucination between fearful attachment and auditory hallucination proneness was tested using the approach to mediation analysis developed by Preacher and Hayes (2008). Statistical analyses were

performed using the Statistical Package for Social Sciences (SPSS; v. 22) and PROCESS (Hayes, 2013). A bias corrected bootstrapping procedure was used and mediation was investigated by directly testing significance of the indirect effect of the independent variable (fearful attachment scores) on the dependent variable (LSHS-R AH score) through the mediator variable (DES-II scores). This indirect effect was quantified as the product of the effects of the IV on the mediator (a) and of the mediator on the DV (b), partialling out the direct effects of the IV (c'). This is outlined in Figure 1. Age, gender, and ethnicity have been found to be associated with psychosis (e.g. Fisher et al, 2009; Fisher et al., 2011) as has depression (Harris, & Curtin, 2002; Smith et al., 2006; Roberts, Gotlibl, & Kassel,1996). Therefore, a further analysis was run with depression and demographic variables (age, gender, and ethnicity) controlled for in the model. A statistically significant indirect effect provides evidence of mediation (Preacher & Hayes, 2008). Indirect effects were deemed statistically significant when the bias corrected confidence intervals did not include zero, and bootstrapping with 1,000 replications was used (Preacher & Hayes, 2008).

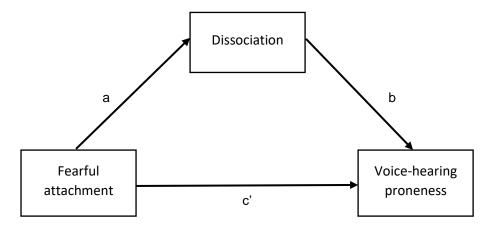


Fig. 1. Mediation model showing direct and indirect effects of IV on DV.

### Results

#### Sample characteristics

Table 1 presents the characteristics of the sample. Fifty people participated in the study, with 23 current voice-hearers, 15 remitted voice-hearers and 12 participants who had never heard voices. The majority of participants were White British males, unemployed, recruited from inpatient services with a diagnosis of schizophrenia. The mean age of the sample was 41.6 years (SD= 13.41).

	Aggregate sample (n=50)	Current voicehearers (n= 23)	Remitted voicehearers (n=15)	Non- voicehearers (n=12)	F/X2
Age	41.36 (13.41)	43.22 (13.34)	41.13 (10.90)	38.08 (16.57)	F(2, 49)= .571; p= .569
Gender	Female: 16 Male: 34	Female: 9 Male: 14	Female: 3 Male: 12	Female: 4 Male: 8	X² (2)= 1.54; p=.463
Status	Inpatient: 38	Inpatient: 13	Inpatient: 13	Inpatient: 12	X² (2)= 9.51, p .009
Years of education	11.24 (2.22)	11.13 (2.58)	11.67 (1.35)	10.92 (2.43)	F(2,49) = .423; p=.658
Employment	Unemployed: 42, Other: 8	Unemployed: 18, Other: 5	Unemployed: 14, Other: 1	Unemployed: 10, Other: 2	X² (4)= 2.46; p .651
Diagnosis	Schizophrenia: 36 Schizoaffective : 7 Depression with psychotic features:3 Delusional disorder: 2 Psychosis not otherwise specified (NOS): 2	Schizophrenia:1 6 Schizoaffective: 5 Depression with psychotic features:1 Delusional disorder:1 Psychosis (NOS):0	Schizophrenia:1 5 Schizoaffective: 0 Depression with psychotic features:0 Delusional disorder: 0 Psychosis (NOS):0	Schizophrenia:5 Schizoaffective: 2 Depression with psychotic features:2 Delusional disorder: 1 Psychosis (NOS):2	X <sup>2</sup> (8)= 17.12 µ .029
Ethnicity	White:34 Non-white: 16	White:19 Non-white: 4	White:7 Non-white: 8	White:8 Non-white: 4	X² (2)= 5.40; p= .067
Marital status	Married/living as if married: 7 Separated/ Divorced: 11 Widowed: 1 Never married: 31	Married/living as if married: 4 Separated/ Divorced: 5 Widowed: 0 Never married: 14	Married/living as if married: 2 Separated/ Divorced: 4 Widowed: 0 Never married: 9	Married/living as if married: 1 Separated/ Divorced: 2 Widowed: 1 Never married: 8	X² (8)= 4.50; p .810

**Table 1**. Means (S.D.) and observed frequencies for the demographic characteristics of the sample.

**Hypothesis 1.** The analyses on the total dissociation scores revealed significant group differences (F(2, 49) = 4.99, p=.011). Current voice-hearers scored significantly higher than those who had never heard voices (p=.011); however, the difference between current voicehearers and remitted voice-hearers was non-significant (p=.132) as was the difference between remitted voice-hearers and those who had never heard voices (p=.520). The

analyses on the DES-II subscales revealed similar group differences, except for

depersonalisation. Hypothesis 1 was therefore partially supported (see Table 2).

	Aggregate	Current voice-	Remitted	Non-	ANOVA
	sample	hearers	voice-hearers	voicehearers	
Fearful attachment	4.58 (2.45)	4.52 (2.27)	4.40 (2.97)	4.92 (2.23)	F(2,49)= .155 <i>, p</i> =.857
LSHS-R (AH)	9.72 (3.58)	11.74 (3.31)	8.87 (3.34)	6.92 (1.73)	F(2,49)= 10.90, <i>p</i> =.000
DES total	25.61 (19.70)	33.91 (21.53)	22.00 (16.79)	14.23 (11.81)	F(2,49)= 4.99, <i>p</i> =.011
DES absorp.	37.20 (25.76)	47.46 (15.82)	33.44 (23.95)	22.22 (18.74)	F(2,49)= 4.60, <i>p</i> =.015
DES amnesia*	3.07 (2.70)	4.04 (2.85)	2.86 (2.47)	1.47 (1.93)	F(2,49)= 4.09, <i>p</i> =.023
DES depers*	3.28 (2.85)	4.14 (12.92)	2.70 (2.50)	2.36 (2.78)	F(2,49)= 2.12, <i>p</i> =.133
Depression	6.33 (5.94)	8.73 (6.70)	3.13 (2.70)	5.92 (5.76)	F(2, 48)= 4.60, p= .015

**Table 2**. Means (S.D) for the DES-II, LSHS-R (AH), depression and fearful attachment measures.

LSHS-R (VH), Revised Launay Slade Hallucination Scale (auditory hallucinations subscale); DES-II, Dissociative Experiences Scale version 2. \* Transformed variable

**Hypothesis 2.** Fearful attachment was not associated with auditory hallucination proneness (r= .124, p= .393). Our hypothesis therefore was not supported (see Table 3).

**Hypothesis 3.** There was a significant positive association between fearful attachment and total dissociation (r= .327, p= .021), with similar results for the DES-II subscales. Our hypothesis was therefore supported (see Table 3). Furthermore, preoccupied and dismissing attachment were both not significantly associated with dissociation and secure attachment was negatively correlated with total dissociation score (r= -0.353, p= 0.012) (See Table 6, Appendix J).

<b>Table 3</b> . Correlations between auditory hallucination proneness, dissociation, fearful
attachment and depression measures for aggregate sample.

	Fearful attachment	LSHS- R (AH)	DES-II total	DES-II amnesia	DES-II absorption	DES-II depers
SHS-R (VH)	0.124, (p= .393)	-				
ES-II total	0.327, (p= .021)	0.728, (p=.000)	-			
DES-II Imnesia	0.295, (p=.037)	0.693, (p=.000)	0.873 (p=.000)	-		
DES-II bsorption	0.289, (p=.045)	0.653, (p=.000)	0.869 (p=.000)	.0.723 (p=000)	-	
ES-II depers. Depression	0 .363, (p=.010) 0.305 (p=.033)	0.613, (p=.000) 0.370 (p=.009)	0.762 (p=.000) 0.456 (p=000)	0.943 (p=.000) 0.497 (p=0000	0.657 (p=.000) 0.521 (p=.000)	- 0.480 (p=000)

LSHS-R (AH), Revised Launay Slade Hallucination Scale (Auditory Hallucinations subscale); DES-II, Dissociative Experiences Scale version 2.

**Hypothesis 4.** A correlation matrix of the main variables of interest is presented in Table 3. As reported, fearful attachment and voice-hearing proneness were not significantly correlated; however, mediation analysis does not impose evidence of simple association between the independent and outcome variable as a precondition (Hayes, 2013). Therefore, mediation analysis was employed to test whether dissociation mediated the relationship between fearful attachment and LSHS-R (AH) scores. We present the results for unadjusted analyses and analyses adjusted for confounding factors, including depression, gender, ethnicity and age.

As can be seen in Table 4, the relationship between fearful attachment and auditory hallucination proneness was positively mediated by dissociation. When focusing on subscales of the DES, similar findings were obtained except for absorption, which was approaching significance. However, these effects were no longer significant when age, gender, ethnicity and depression were entered as covariates (see Table 5.). The effects did remain significant, however, when only age, gender and ethnicity were included as covariates (b = 0.38, 95% CI= 0.06 to 0.71).

Table 4. Point estimates (95% CI) for the total, direct and indirect (i.e. mediated via
dissociative tendencies) effects of fearful attachment on auditory hallucination proneness.

Mediator variable	Indirect effect	Direct effect	Total effect	P Value (indirect effect)
DES-II total	0.37 (0.07 to 0.68)	-0.19 (-0.49 to 0.12)	0.18 (-0.24 to 0.60)	0.024
DES absorption	0.28 (0.02 to 0.58)	-0.10 (-0.44 to 0.24)	0.18 (-0.24 to 0.60	0.056
DES amnesia	0.31(0.00 to 0.63)	-0.13 (-0.45 to 0.20)	0.18 (-0.24 to 0.60)	0.044
DES depers.	0.35 (0.10 to 0.65)	-0.17 (-0.53 to 0.20)	0.18 (-0.24 to 0.60)	0.017

**Table 5.** Point estimates (95% CI) for the total, direct and indirect (i.e. mediated via dissociative tendencies) effects of fearful attachment on auditory hallucination proneness controlling for age, gender, ethnicity and depression.

Mediator variable	Indirect effect	Direct effect	Total effect	P Value (indirect effect)
DES-II total	0.19 (-0.10 to 0.53)	-0.16 (-0.49 to 0.18)	0.04 (-0.42 to 0.49)	0.226
DES absorption	0.11 (-0.14 to 0.42)	-0.07 (-0.44 to 0.29)	0.04 (-0.41 to 0.49)	0.437
DES amnesia	0.16 (-0.14 to 0.52)	-0.13 (-0.48 to 0.22)	0.04 (-0.41 to 0.49)	0.340
DES depers.	0.19 (-0.04 to 0.47)	-0.16 (-0.55 to 0.22)	0.04 (-0.41 to 0.49)	0.156

#### Discussion

The aims of the current study were to explore associations between fearful attachment, dissociation and voice-hearing, and to examine dissociation as a mediator between fearful attachment and voice-hearing in the context of psychosis.

Specific to dissociation, current voice-hearers scored significantly higher than participants with psychosis who had never heard voices; however, no other group differences were significant. The non-significant findings are inconsistent with previous findings by Varese, Barkus and Bentall (2012) who found significant differences in terms of dissociation across current voice-hearing, remitted voice-hearing, never hallucinated and healthy controls, with a similar sample size in all groups to the current study. However, the dissociation scores in the current study followed the expected trajectory, with current voice-hearers showing higher levels of dissociation than both remitted and participants who had never heard voices, and remitted voice-hearers obtaining higher scores than the latter group. Thus, although cautionary, the results suggest that dissociation is a vulnerability factor for voices more specifically rather than psychotic experiences more generally.

Fearful attachment was not found to be significantly associated with voice-hearing proneness. These findings are inconsistent with previous findings by Korver-Nieberg, Berry, Meijera, de Haana, and Ponizovskyc, (2015) who found a statistically significant relationship between fearful attachment style and hallucinations in a sample of 500 psychiatric patients. The size of the correlation in Korver-Nieberg et al. (2015) was of a similar magnitude to the correlation in the current study, suggesting that our null findings may be reflective of the smaller sample size, which limited the power of the study. Fearful attachment was found to be related to dissociation which provides some corroboration for fear-based attachment patterns providing a diathesis for dissociation (Longden, Madill & Waterman, 2012; Berry & Bucci, 2015; Liotti, 2008). Importantly, the finding that fearful attachment was not associated with voice-hearing proneness suggests that the development of fear-based attachment patterns alone cannot account for vulnerability to voice-hearing. Yet, when dissociation is the sequalae of this experience, its key relationship to voice hearing emerges. However, an unexpected finding was that secure attachment was negatively correlated with dissociation, with a stronger association than was found for the relationship between fearful attachment and dissociation. The attachment system is active across the life-span (Bowlby, 1988), in situations where awareness of the need for safeness or the presence of threat is indicated. A lack of secure attachment may facilitate a focus on the threat posed by others, particularly where there is a lack of feeling of safeness in interpersonal situations (MacBeth, Schwannauer, & Gumley, 2008). This may result in the employment of strategies such as dissociation to deal with the absence of safeness in such threat-based situations. Further research is required to elucidate the contributions of both disorganised attachment styles and a lack of secure attachment and attempt to delineate the effect of both on the development and maintenance of voice-hearing in the context of psychosis.

An indirect effect of dissociation on the relationship between fearful attachment and voicehearing proneness was found. The findings provide support for contentions by Longden, Madill & Waterman (2012) that voice-hearing may be understood as a dissociative experience. The findings also provide some support for the cognitive attachment model of voices (Berry & Bucci, 2015), which suggests that a disorganised attachment style, which we know to conceptually overlap with fearful attachment, may predispose an individual to voicehearing if dissociation is a sequalae of the early interpersonal conflict (Berry & Bucci, 2015).

Specific to the DES subscales, depersonalisation showed the largest indirect effect, whilst the effects of absorption and amnesia appeared non-significant and verging on nonsignificance respectively. This finding is congruent with research by Perona- Garcelán et al., (2012) who found that depersonalisation alone mediated the relationship between childhood trauma and hallucinations in a psychosis sample, and provides some support for an understanding of depersonalisation as the dissociative variable that distinguishes clinical voice-hearing (Perona- Garecelán et al., 2011). This interpretation is, however cautionary, given the limited power of the study.

In the current study, when depression was controlled for, dissociation no longer significantly mediated the relationship between fearful attachment style and voice-hearing proneness. Attachment styles have been conceptualised as relating to different methods of regulating affect (Mikulincer & Florian, 1998). Therefore, individuals with fear-based attachment patterns may struggle to regulate their emotions. Individuals who are fearfully attached are more likely to be depressed than individuals who are characterised by either a secure or dismissing attachment style (Murphy and Bates, 1997), and difficulties with affect regulation may be exacerbated if individuals come to rely on sub-optimal strategies such as dissociation to cope with traumatic stressors (Liotti, 2004). Furthermore, studies have shown depression to mediate the relationship between early trauma and hallucinations (Sitko, Bentall, Shelvin, O'Sullivan & Sellwood, 2014). Therefore, while attachment and dissociation appear to play an important role in the development of voice-hearing, depression may also be an important mechanism in this pathway. Arguably paranoia may also be an important mechanism to assess and control for in research investigating associations between attachment and voice-hearing due to the high co-morbidity of paranoia and voice-hearing and previous research suggesting insecure attachment is related to paranoia but not voicehearing when paranoia is controlled (Pickering, Simpson & Bentall, 2008). As the sample size in the current study was relatively small, larger samples are needed to reliably explore and disentangle the role of these potential putative mechanisms. Measures of paranoia would also useful to examine their potential confounding effect, and enable more robust tests of hypotheses regarding symptom specificity.

#### Limitations

The cross-sectional nature of the design means that conclusions cannot be made in terms of causation. Also, longitudinal evidence suggests that children categorised as disorganised may develop dismissing attachment strategies in adulthood to protect themselves from future relational trauma (Main, Hesse, & Kaplan, 2005). This limits the ability to robustly conclude that fear-based attachment styles in adulthood are the developmental trajectory of disorganised patterns in childhood. Existing findings are congruent with the possibility that infant disorganised attachment may lead to continued unintegrated states of mind in adulthood (Ogawa, et al., 1997); however, the findings of the current study are limited in their ability to make claims that fear-based, disorganised attachment patterns identified in our adult sample reflect life-long patterns of relating to others. The findings do at least point to a fear-based attachment pattern maintaining voice-hearing through increasing vulnerability to dealing with distress with dissociation, and suggest an important role for depression in this pathway.

A further limitation was that the sample might not be representative. For example, individuals with fearful attachment patterns have been described as passive and socially insecure (Bartholomew & Horowitz, 1991), which may have resulted in fewer people with this attachment style agreeing to take part in the current study. Also, the relatively small number of participants may have limited the power of the study. For example, the effect of depression rendering the mediating role of dissociation non-significant, the failure to find a relationship between fearful attachment and voice-hearing proneness, and the nonsignificant group comparisons of dissociation scores may be related to the limited power of the study.

Importantly, the measure of fearful attachment was employed as a proxy measure of disorganised attachment. Support for disorganised attachment as conceptually similar to fearful attachment comes from Mikulincer & Shaver (2007) and Simpson and Rholes (2002) who have argued that individuals who are categorised as fearfully attached appear to both fear intimacy with a partner because of the possibility of rejection, yet also desire to have an intimate relationship with attachment figures. It is argued that this mixed attachment strategy could lead to confusion, disorientation, and chaotic behaviours with partners, resembling the disorganised attachment pattern characterised by Main and Hesse (1990). However, it has not yet been empirically established that the Relationship Questionnaire measure of fearful attachment Interview (AAI; George, Kaplan & Main, 1997) provides a measure of 'unresolved' attachment style, which is analogous to a disorganised attachment style and has been used with psychosis samples (Gumley, Taylor, Schwannauer & MacBeth, 2014). However, the AAI is resource and time intensive, which rendered it not feasible for use in the current study.

Furthermore, the self-report measures for fearful attachment and auditory hallucination proneness consisted of relatively brief Likert-scales and therefore may not have been sensitive enough to detect subtle associations between fearful attachment and voicehearing. Therefore, future research may be required to develop reliable and valid self-report measures of disorganised attachment (e.g. Paetzold, Rholes & Kohn, 2015). However, while self-report measures of attachment have been found to be reliable and valid in psychosis samples (Gumley, Taylor, Schwannauer, & MacBeth, 2014) and the domain of social psychology (Bartholomew & Shaver, 1998), they rely on a person's conscious selfevaluation and do not necessarily correspond to unconscious attachment representations that are activated and assessed by measures such as the Adult Attachment Interview (George, West, & Pettem, 1999). Combing self-report with informant report measures may provide a useful means of overcoming this potential difficulty.

### Future Research

Future research should include longitudinal studies to further investigate the potential causal role of early attachment experiences on dissociation and voice-hearing. This study should also be replicated using larger sample sizes to improve the generalisability of the findings and provide greater power to detect effects, should they be present. Furthermore, a self - report measure of disorganised attachment validated in psychosis is needed so that models implicating a mechanistic role for disorganised attachment in the development of voice hearing can be more robustly examined.

The attachment system is fundamentally activated during times of stress (Bartholomew, 1990). The current study did not employ a measure of voice-related distress, and attachment style has been found to be related to voice-related distress and various dimensions of voice hearing such as omnipotence and intrusiveness (Pilton et al., 2016). Future research should include measures of voice-related distress and examine its relationship to an activated attachment system to determine if disorganised, fear-based attachment and dissociative tendencies vary with level of distress. Also, it is likely that disorganised attachment is not the only etiological factor in dissociation (Liotti, 1992); the pathway from early relational trauma to voice-hearing is likely to be multifactorial. Therefore, future research should look at other important factors which have been implicated in this pathway, such as source-monitoring (Varese, Barkus & Bentall, 2011) and depression (Sitko, et al., 2014), and employ complex modelling techniques to allow for the robust appraisal of different pathways from early relational trauma to voice-hearing.

### Clinical Implications

The findings of the present study add to an existing literature supporting the role of dissociation in voice-hearing (Longden, Madill & Waterman, 2012; Berry & Bucci, 2015; Pilton et al., 2016). Although cautionary, support was also found regarding the role of dissociation as a possible mediator of the relationship between fear-based attachment and voice-hearing. These findings warrant further investigation and highlight the importance of considering dissociation and the quality of early attachments to inform formulations and therapeutic work with voice-hearers with psychosis.

There is good evidence that individuals insecurely attached can move to more secure patterns of relating following corrective experiences with responsive and supportive partners, and that the therapeutic relationship can provide this corrective experience and move people from insecure to more secure patterns of relating (Mikulincer, Shaver, & Berant, 2013; Taylor, Rietzschel, Danguah, & Berry, 2015). Therefore, therapeutic models focusing on the client-therapist relationship may be useful in providing the safe-base and corrective experience required to shift attachment styles and produce positive therapeutic outcomes (e.g. Fonagy et al, 1996; Bucci, Seymour-Hyde, Harris, & Berry, 2016). In a review by Taylor, Rietzschel, Danguah and Berry (2015) some evidence was found for particular therapeutic interventions reducing attachment anxiety such as Transference-Focused psychotherapy and Psychodynamic Interpersonal Psychotherapy. However, this evidence was not found in the case of attachment avoidance, and disorganised attachment specifically was not investigated. Therefore, future research will be required to identify and evaluate models that are able to move individuals from avoidant and disorganised attachment styles to more secure patterns of relating. Furthermore, given evidence supporting that the way voice-hearers relate to their voice is associated with distress (Hayward, Denny, Vaughn & Fowler, 2008; Vaughan & Fowler, 2004; Sorrell, Hayward & Meddings, 2010), therapeutic approaches should consider the influence of relational factors, such as attachment style, upon voice-hearer's perceptions of distress and control (Hayward, Overton, Dorey & Denney, 2009).

Although tentative, the findings of the current study also highlight the role of dissociation in the development and maintenance of voice-hearing. Currently, there is limited research examining effective psychological interventions that target dissociation in individuals experiencing psychosis (Newman-Taylor & Sambrook, 2013). However, techniques shown to be beneficial for individuals with primary dissociative disorders, for example grounding techniques, may be helpful. Therefore, therapists should be vigilant for dissociative processes becoming active in therapy and utilise grounding to enable the essential safe base for effective therapeutic outcomes. Moreover, associations between fear-based attachment, dissociation and voice-hearing highlight the importance of focusing on preventative interventions so that disorganisation of attachment style, and its developmental sequalae can be reduced.

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# Paper 3. Critical refection

# Word count: 4,706 (excluding references)

# Introduction

The following paper presents a critical appraisal of the research conducted within the current thesis. Consideration of the planning, implementation and interpretation of the systematic review and empirical study will be discussed. The strengths and limitations of the research will also be discussed. Further, personal reflections on the research process will be offered.

### Systematic literature review (Paper 1)

### Rationale for topic choice

There is a plethora of research suggesting that childhood trauma increases risk for psychosis (e.g. Varese et al., 2012; Matheson et al., 2013) and so recent research has begun to elucidate this pathway and look at putative mediating mechanisms. Gaining an understanding of the potential mechanisms involved in this pathway has the potential to support evidence of a causal relationship between childhood trauma and psychosis, and to support the development of more integrated models and targeted interventions. A further motivation for conducting a review of the vast and varied putative mechanisms examined in the literature was the sense that researchers tended to focus on their area of interest and not necessarily integrate their findings with those of different backgrounds, which has the risk of leading to ideological biases. It was felt that by synthesising the literature, a framework could be provided for more integrative research to study potential pathways from childhood trauma to psychosis. Narrative reviews of potential mechanisms had been conducted (e.g. Morgan & Gayer-Anderson, 2016; Bentall et al., 2014); however, the literature was not systematically searched and, importantly, the reviews failed to assess the quality of the studies included in the reviews. It was agreed that it would be important to conduct a systematic review and evaluation of the empirical literature to date that had examined putative psychological mechanisms of the childhood-trauma-psychosis relationship.

It was decided that an important consideration for the review would be the statistical methodology used to test mediation in the included papers. This decision was made based on recent literature comparing and evaluating statistical methods used to tests mediation models (e.g. Hayes, 2013; MacKinnon et al., 2002), which highlights the importance of employing methods which test indirect effects rather than inferring mediation based on a series of regression analyses (e.g. Baron & Kenny, 1986). Tests of intervening variable effects are crucial for establishing the plausibility of causal relationships implied by the theories being tested (MacKinnon et al., 2002) and so it was agreed that the use of mediation analysis would be an important inclusion criteria in order to enable a comprehensive review and appraisal of the literature examining psychological mediators of the trauma-psychosis relationship.

### Search terms

The process of deciding specifically which search terms to utilise for the search was done through discussion with supervisors. The search terms were selected based on those used by previously published meta-analyses of the relationship between childhood adversity and severe mental health difficulties (e.g. Varese et al., 2012; Matheson et al., 2013). It was likely that studies examining mediators of this relationship did not include key words relating to mediation in the titles of the study, therefore the search was carried out without 'mediator'

as a search term so that the search would be more sensitive to producing relevant papers. This resulted in over 17,000 titles being captured by the search terms for psychosis and trauma, after the exclusion of duplicates.

### Inclusion and exclusion criteria

It was agreed that the focus of the review would be on psychological mechanisms. A literature search was conducted and advise sought from previous ClinPsyD trainees who had also examined psychological mechanisms. Following this process, it was agreed that the definition of a psychological mechanism would be based on that of Harvey et al. (2004) who employed a transdiagnostic approach to identify the psychological mechanisms involved in the maintenance of psychological disorders. While social mechanisms such as migration and ethnicity appear to have an important role in the development of psychosis (e.g. Morgan, Charalambides, Hutchinson, & Murray, 2010), it was agreed that for the purpose of the systematic review the topic would be limited to psychological mechanisms. If broader mechanism were to be considered it would be too broad to be feasible for a ClinPsyD review, furthermore, it would add to the challenge of synthesising a broad and varied body of literature. However, the definition of childhood trauma utilised covered social factors such as physical neglect, although there are obviously other social causal and mediating factors.

There was a great deal of discussion regarding the reliability and validity of tools employed by included studies. After deliberation, it was decided that only articles utilising a validated measures of psychosis symptomatology, childhood trauma and the putative mechanism under study would be included. The reasoning behind this was that if only validated measures were included, assurances could be made regarding their construct validity, which is a vital component of the research process (O'Leary-Kelly & Vokurka, 1998). However, as briefly discussed in the methods section of the systematic review, where epidemiological studies had employed surveys and items created for the study, these were included in the review given the methodological issues of including lengthy measures with large populations. It was agreed that it would be important that epidemiological studies were not excluded on the basis of measures only showing face validity, given that studies employing large numbers of subjects are likely to be more valid than smaller studies. Therefore, the inclusion criteria were adapted so that where whole measures had been used which were shown to be valid and reliable a strong rating would be given. A moderate rating would be given where a previously valid and reliable measure had been changed for the purpose of the study (e.g. items taken from the measure). A weak rating would be assigned where it was unclear if the measure has been validated and tested for reliability but the measure had shown content and face validity. It was also agreed that measures of trauma had to measure exposure prior to the age of 18. This decision was made to enable clear conclusions about

the role of childhood trauma. One example of when an article was excluded due to the trauma measure not differentiating between childhood trauma and later life events was when trauma was measured by lifetime trauma (Freeman & Fowler, 2009). Studies that had not employed mediation analysis to examine relationships between variables were excluded (e.g. Berry, Barrowclough & Wearden 2009) as mediation could not be inferred. However, the causal steps approach to mediation analysis is still widely employed by authors, despite its limitations. Therefore, it is possible that research projects have been terminated early in a research program, or rejected by journals because the data did not conform to Baron and Kenny's (1986) criteria. This approach would have the impact of impeding theoretical development and biasing the findings of the current review.

#### Quality assessment

Quality assessments are a key component of systematic reviews and the use of structured assessment tools appropriate to the studies included in the review is essential to ensure systematic rigour (Jadad et al., 2000). It was, therefore, important to choose the most suitable measure. However, a variety of designs had been employed by the included studies and most tools are designed for reviews of randomised control trials. Following a review of quality assessment tools, two tools were highlighted as being more suitable than others: the 'Quality Assessment Tool for Studies with Diverse Designs' (Sirriveh, et al., 2012) and the Effective Public Health Practice Project tool (EPHPP; Thomas, Ciliska, Dobbins, & Micucci, 2004). The EPHPP was eventually decided upon as the content appeared to fit best with the review question; however, given Sanderson et al.'s (2007) recommendation that tools should be as specific as possible to the particular study design, the tool was adapted to ensure that only specific methodological features relevant to the review topic were assessed. Following recommendations by PRISMA (Liberati et al., 2009), a component approach was employed. This approach highlights that risk of bias items may be topic or even study specific. It is recommended that risk of bias items are investigated on a case-by case basis, based on clinical and methodological insight. Thus, rather than a general recipe, it is recommended that reviewers consider what aspects of study quality may have a bearing on the results. This was considered to be the most appropriate for the current review given the pertinence given to factors such as analysis and the requirement to adapt assessment of data collection tools to enable assessment of data collection tools which could accurately and fairly assess those employed by epidemiological studies.

The criteria were amended through regular meetings and through an iterative process. For example, an earlier version of the tool did not have different criteria for assessing the selection bias of studies that had employed either clinical or non-clinical samples. It was highlighted that for non-clinical studies, a key issue would be whether the participants were likely to represent the general population, whereas for clinical participants, it would need to

be demonstrated that they represented the diagnostic population under study. Therefore, the tool was adapted to more clearly delineate separate criteria to enable clear criteria on which the rater could base their scoring. When considering criteria against which to rate data analysis, decisions were made based on recent literature comparing and evaluating statistical methods used to tests mediation models (e.g. Hayes, 203; MacKinnon et al., 2002). A high degree of reliability was obtained ( $\Box$ =0.81) and it was felt that this was reflective of the time invested in developing a tool that was clear and reliable.

### Synthesising data

Due to the lack of homogeneity of designs in the studies identified for the review, a metaanalysis was not deemed to be appropriate (Blundell, 2014). Therefore, a narrative synthesis was presented. Due to the heterogeneity of the designs and putative mediators examined in the studies, a key challenge was to present the findings in a coherent and concise way. It was decided that presenting the results according to the mediators under study, rather than psychosis symptomatology, would be the most meaningful way of presenting the findings, because of the wide variety of outcomes examined. A challenge that was encountered when attempting to coherently present the findings was the heterogeneity of the mediators examined; for example, only one study examined mindfulness as a potential mediator (Perona- Garecelán et al., 2014). It was therefore decided to include a heading of 'miscellaneous' as a way of summarising discrete mediators examined.

### Personal reflections

Overall, identifying, synthesising and evaluating the large body of evidence for the review was a challenging and time intensive process. The topic chosen was an area of interest rather than an area of expertise; however, through immersion of the literature a greater understanding of the area was developed. Furthermore, the empirical paper also examined mediating mechanisms, and an understanding and interpretation of mediation analysis employed by studies in the review was greatly enhanced following conducting this analysis in the empirical paper. The decision to present the findings in terms of the putative mechanisms under study was felt to be the most effective means of synthesising a vast and heterogenic body of research. However, organising the results according to the psychosis symptomatology outcome examined may have enabled a clearer examination of symptom specificity hypotheses. Given the broad range of outcomes examined, including schizotypy (Sheinbaum et al., 2015), diagnosis of psychosis related disorder (Goldstone, Farhall & Ong 2012) and hallucination proneness (Varese, Barkus & Bentall, 2012) it was felt that focusing on the mediating mechanisms did allow the review to tell a more coherent story.

A key aim of the review was to provide a systematic and objective evaluation of studies that examined psychological mediators of the relationship between childhood trauma and psychosis. However, while the review presented an evaluation of the evidence presented for putative mediating mechanisms, the issue remains regarding how to evaluate each mechanism objectively. This is an issue for evaluating causal pictures in general (Bentall & Varese, 2012). By evaluating the quality of the evidence the review went some way to addressing this issue; however, a meta-analysis of studies which have examined psychological mediators of the relationship between childhood trauma and psychosis would allow further scrutiny of the evidence available.

#### **Empirical Paper (Paper 2)**

#### Development of the research question

The empirical study presented in paper two was carried out to improve knowledge of the relationships between disorganised attachment, dissociation and voice-hearing in psychosis and to assess whether dissociation mediated the relationship between disorganised attachment and voice-hearing. Evidence suggests a pervasiveness of childhood trauma in psychosis (Varese et al., 2012). Furthermore, research suggests links between trauma, dissociation and auditory hallucinations (Longden, Madill & Waterman, 2012) and a relationship between disorganised attachment and dissociative psychopathology (Liotti, 2004). However, less is known about the role of disorganised attachment in the relationship between dissociation and voice-hearing.

#### Measures

One of the challenges of the empirical study was identifying an appropriate measure of disorganised attachment. As mentioned in the limitations section of the empirical paper, at present a self-report measure of disorganised attachment validated in clinical samples does not exist. The Adult Attachment Interview (AAI; George, Kaplan & Main, 1997), does provide a measure of unresolved attachment style, which is considered to mirror disorganised attachment patterns. Furthermore, the AAI has been found to be reliable within psychosis populations (MacBeth, Gumley, Schwannauer & Fisher, 2010). However, the tool uses a semi-structured interview to measure attachment, which is then transcribed and rated in terms of attachment categories, and requires extensive training to obtain reliability in the measure. Therefore, the tool was not chosen due to the time-consuming nature and potential burden to participants given the considerable number of questionnaires already being administered. However, given the evidence pointing towards a disorganised attachment style having an important role in the developmental sequalae leading to

voicehearing, it was decided that it would be important to examine these concepts with the data collection tools currently available. To identify which measure was most appropriate, literature was reviewed. As highlighted in the introduction and discussions sections of the empirical paper, evidence suggest that the fearful attachment style identified by Bartholomew (1990) has important conceptual overlaps with an adult disorganised pattern (Mikulincer & Shaver, 2007). Fearful and disorganised attachment are both described as employing strategies that reflect both anxiety and avoidance (Bartholomew & Horrowwitz 1991; Main & Solomon, 1990). Furthermore, attachment disorganisation in adulthood is linked to simultaneous attitudes of hostility and helplessness, adult psychopathology and dissociation (Liotti, & Gumley, 2008); fearful attachment is also conceptualised as a negative evaluation of self and other, and has been found to be related to trauma and conflict (George & West, 1999), interpersonal difficulties (Bartholomew & Horrowitz, 1991) and dissociation (Anderson & Alexander, 1996). The decision to use fearful attachment as a proxy for disorganised attachment was based on the aforementioned evidence in support of conceptual overlaps between the two attachment styles. However, as it has not yet been empirically established that the measure of fearful attachment is equivalent to disorganisation, the evidence presented in the empirical paper cannot provide robust evidence for a role of disorganised attachment in the development of voice-hearing. Moreover, the measure of fearful attachment was not found to be associated with voicehearing proneness. This might be an issue with the sensitivity of the measure, given that fearful attachment is only measured by a rating on a single item.

In terms of the measure of voice-hearing, a proneness measure was chosen as it was considered to be most sensitive to detecting differences in auditory hallucination experiences, as opposed to a categorical approach, given the small n of the study. The original version of the measure developed by Launay and Slade (1981) measured predisposition towards hallucinations in general. However, as the hypotheses of the empirical paper were related to auditory hallucinations in particular rather than hallucinations in general, a literature review was conducted to identify a tool. Morrison Wells, and Northard (2000) found a two-factor structure including auditory and visual hallucinations when they administered a modified LSHS to a normal sample; however, Morrison Wells, and Northard's (2000) scale had reported low internal reliability (McCarthy-Jones & Fernyhough, 2011). McCarthy-Jones and Fernyhough (2011) revised the Morrison et al version and found good levels of internal reliability. Therefore, the authors were contacted and a copy of the revised questionnaires was requested and received.

### **Confounding variables**

A strength of the study was the use of depression as a confounding variable. The significant indirect effect of dissociative tendencies on the relationship between fearful attachment and

voice-hearing did not remain when depression was entered as a covariate. It became apparent in the undertaking of the systematic review that many studies did not control for confounders when utilising mediation analysis. This trend may result in important putative mechanisms of the pathway from early adversity to psychosis symptomatology being missed and highlights the importance of non-significant results to help understand the processes and pathways implicated.

A potential weakness of the study could be that a measure of paranoia was not included. A previous study which employed a non-clinical sample found that the relationship between insecure attachment and voice-hearing did not remain significant when controlling for paranoia (Pickering, Simpson & Bentall, 2008). Measures of paranoia, negative symptoms and delusions would have been useful to examine their potential confounding effect, and enable more robust tests of hypotheses regarding symptom specificity.

#### Recruitment and contribution to the research

The original recruitment target was 90 participants. Given the large numbers required it was decided that combining recruitment and measure administration with another trainee's research project would be the most efficient and effective approach. Each trainee designed their individual study and generated a list of research measures required to answer their research question. In addition, further measures were included so that the data could form part of a larger body of research which aimed to test the Cognitive Attachment model of Voice-hearing (Berry & Bucci, 2015) and included guestionnaires which asked about childhood abuse. The overall measure administration time was between one hour and two hours, depending on whether the participant currently heard voices as this would involve additional measures, which asked about their voice-hearing experience. Therefore, it was felt important to consult with members of the Community Liaison Group (CLG) to ensure that the project was feasible and acceptable. The CLG consists of current and ex-service users of mental health services who provide consultation on research projects carried out as part of the ClinPsyD programme. A pilot run of the measures was conducted and the CLG member made recommendations regarding the study, such as ensuring that participants were debriefed about the content of the interview and that participants should be offered a break every 30 minutes, with a break timed to follow completion of the trauma questionnaire. Recruitment was shared equally, with the present trainee recruiting twenty-five of the fifty participants recruited.

The length of the study and the number of participants required made the recruitment process time intensive. A great amount of time was invested in attending team and allocation meetings across community mental health teams (CMHT's) to present the study and emphasise the potential benefits for services and service users. However, only seven participants were recruited from CMHT's, with issues regarding staff being limited in terms of

time to approach potential participants and a lack of clients on caseloads who would meet eligibility criteria being cited as key reasons for the services not being fruitful. This experience is in line with findings by Bucci et al. (2015) who examined the barriers to carecoordinators referring mental health service users to research trials. Steps were taken to in an attempt to maximise successful recruitment from community teams, such as engaging care-coordinators though face-to-face meetings. However, this did not have a significant effect on the number of referrals received. Consequently, recruitment became focused on services where more recruitment success was evident, which was predominantly inpatient services. The larger proportion of participants recruited form inpatient services than community services may have resulted selection bias and limit the generalisability of the study findings.

On occasion, services expressed concerns about the potential of our study to destabilise participants. Advising clinicians that evidence shows that the majority of participants who take part in trauma focussed research report their participation as positive, rewarding, and do not experience distress (e.g. Legerski & Bunnell, 2010) was able to alleviate some concerns. Furthermore, a robust risk protocol was developed and employed. Also, the majority of participants opted to complete the measures with the researcher and a large proportion fed back that they found the experience of sharing their experiences rewarding and valuable. This was helpful feedback to pass on to staff to further alleviate concerns.

### Analysis

Findings from the empirical study showed a significant indirect effect of dissociation on the relationship between fearful attachment and voice-hearing proneness when depression was not included as a covariate. This result was found despite fearful attachment and voice-hearing not being significantly correlated, and a significant total effect was not found in the mediation analysis.

Historically, it has been argued that mediation analysis should only be undertaken when an association between the DV and IV has been demonstrated (Baron & Kenny, 1986). However, more recent developments have demonstrated that this is not a necessary precondition (Hayes, 2013). This argument is based on several factors, including the claim that correlation is neither necessary nor sufficient to establish causation, and the likelihood that the data available is collected at a single time point without the use of experimental manipulation, leaving theory as the more solid ground on which to base causal claims. Given evidence supporting relationships between disorganised attachment and dissociation (Liotti, 2004) and between dissociation and voice-hearing (Pilton, Varese, Berry & Bucci, 2015), it was felt that there was a strong theoretical ground on which to base an interpretation of the data as showing evidence of dissociation being causally located between fearful attachment and voice-hearing. Furthermore, a popular method of mediation analysis, the casual steps approach (Baron & Kenny, 1986), has as a requirement that particular steps must be established to state mediation has occurred. One requirement is that there should be a significant direct effect, that is, X must predict Y in the absence of the mediator. However, more recent developments in mediation analysis suggest that a direct effect of X on Y should not be a pre-requisite for examining evidence of indirect effects (e.g. Hayes, 2013; Shrout & Bolger, 2002). Again, there are several reasons for the claim that the direct effect is not necessarily the best estimator of the effect of X on Y. For example, where the relationship between X and Y is likely to be subtle or distal the effect size of the relationship is typically reduced (Shrout and Bolger, 2002). The size of the effect typically gets smaller because the more distal an effect becomes, the more likely it is to be transmitted through additional links in the causal chain, or be affected by other random factors. Given that attachment patterns are formed early in life (Bowlby, 1973), it is arguable that the relationship between fearful attachment and voice-hearing is a distal one, requiring large samples sizes and more powerful studies to detect effects, should they exist. An alternative, or complementary, interpretation may be that, as fearful attachment has been implicated in mental ill health in general (e.g. Dutton, Starzomski, Saunders, & Bartholomew, 1994), its relationship to voicehearing specifically may be a subtle one. As mediation analysis provides higher statistical power to detect an indirect effect than a total or direct effect (Shrout & Bolger, 2002), this may explain why only the indirect effects in the empirical paper were significant, given the small sample size, which limited the power of the study. Furthermore, the total effect of X on Y, which is the sum of the direct and indirect effect, is also no longer considered a good estimator of the effect of X on Y (Haye's, 2013). This is demonstrated in the empirical paper, where a non-significant total effect was found. This can be the result of issues such as X being unrelated to Y among some people but positively related to Y among others- if there is a larger proportion of the first group in the sample then the association between X and Y will be diluted and a large sample would be required to detect an effect. In the current study, it could have been the result of the negative (although non-significant) relationship of fearful attachment to voice-hearing summing to zero.

Where the effect of X on Y can be experimentally induced, is proximal and is likely to show a large effect, analysis should be able to demonstrate this by a significant direct effect (Shrout & Bolger, 2002). However, where the effect of X on Y is more distal, is expected to be small, and cannot be experimentally manipulated, setting requirements of significant direct and total effects before interpreting evidence of mediation runs the risk of researchers under analysing their data and risking a Type II error for the entire mediation system (Shrout & Bolger, 2002; Hayes, 2013). Therefore, it is argued and that tests of indirect effects are all that are required (Hayes, 2013). Of course, there are caveats to the causal claims of the empirical paper due to the small sample size, the lack of experimental manipulation and cross-sectional nature of the study design. More robust tests of the paper's hypothesis are required before any strong conclusions can be drawn.

### Personal reflections

Through the research process, the researcher experienced a transition from identifying more closely with the concept of a therapist to identifying strongly with the concept of a scientist practitioner. With a limited background in research and the research topic being one of interest rather than expertise, it was a daunting journey to commence. As a result, a significant amount of time and effort was invested in developing an understanding of the research area and the methods employed. Through immersion in the research literature and conducting the research project, a greater understanding of the importance of conducting high quality research to inform practice was developed. Furthermore, on commencement of the research process, the trainee held reservations regarding their ability to complete a doctoral level piece of research and utilise and interpret complex statistical methodologies. A proactive approach was taken to address those initial doubts by investing time in understanding the process and requirements of clinical research, and through consultation with research supervisors and other colleagues who possessed knowledge and expertise of research in general and the topic area of the thesis more specifically. This approach enabled the trainee to become more confident in their ability and greatly enhanced their competence in research methodology and mediation methods.

Adopting the role of a researcher brought its own challenges, particularly when participants were discussing traumatic experiences. As a clinician, time would have been spent normalising and attempting to reduce distress associated with these experiences; however, this was not appropriate for the role of the researcher. As a consequence, it was important to develop an understanding of the need to adhere to the boundaries of the researcher, and the use of supervision and reflection aided this process. A balance was found and the skills developed through clinical experience, such as the expression of empathy and compassion, were found to be effective in ensuring that participants were not left in distress following participation in the research. As stated, this approach resulted in a number of participants expressing that, while the experience could be challenging, they found taking part in the research a valuable and meaningful experience. This reported experience mirrors that of the researcher.

#### Dissemination

Paper one will be submitted to Clinical Psychology Review for publication. Paper Two will be submitted to Psychological Medicine for publication. The presentation of this information at psychology and inter-disciplinary research seminars may be of value and current plans for dissemination include a presentation of the findings at a complex-cases psychology service professionals meeting, and dissemination to participants who took part in the research and

requested feedback of the findings. It is hoped that dissemination of the research findings will inform the development of knowledge across mental health services. Furthermore, the researcher acknowledges a responsibility to disseminate the findings given the time and efforts invested by the participants who took part in the research.

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Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

## Acknowledgements

Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

## Formatting of funding sources

List funding sources in this standard way to facilitate compliance to funder's requirements: Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa]. It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding. If no funding has been provided for the research, please include the following sentence:

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281-304). New York: E-Publishing Inc.

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Appendix B: Quality rating tool

## **Review Title: Psychological mediators of the link between CT and dimensional outcomes in psychosis**

## Effective Public Health Practice Project (EPHPP) QUALITY ASSESSMENT TOOL FOR QUANTITATIVE STUDIES (ADAPTED BY AMY DENGAN\* FURTHER ADAPTED BY JESSICA WILLIAMS 10.03.17)

*Common types of design include: (A) non-randomized controlled trials, and (B-C-D) observational analytic study or component where the intervention/exposure is defined/assessed, but not assigned by researchers.* 

#### A. Non-randomized controlled trials

The intervention is assigned by researchers, but there is no randomization, e.g., a pseudo-randomization. A non-random method of allocation is not reliable in producing alone similar groups.

## B. Cohort study

Subsets of a defined population are assessed as exposed, not exposed, or exposed at different degrees to factors of interest. Participants are followed over time to determine if an outcome occurs (prospective longitudinal).

## C. Case-control study

Cases, e.g., patients, associated with a certain outcome are selected, alongside a corresponding group of controls. Data is collected on whether cases and controls were exposed to the factor under study (retrospective).

## D. Cross-sectional analytic study

At one particular time, the relationship between health-related characteristics (outcome) and other factors (intervention/exposure) is examined. E.g., the frequency of outcomes is compared in different population sub-groups according to the presence/absence (or level) of the intervention/exposure.

## \*This measure has been adapted for use in a review of studies including crosssectional and cohort (prospective, longitudinal) analytical designs

## \*The following subscales have been omitted:

- B STUDY DESIGN
- D BLINDING Q1 AND Q2
- G INTERVENTION INTEGRITY Q1, Q2 AND Q3
- H ANALYSES Q1, Q2, AND Q4

## **COMPONENT RATINGS**

## A.1.) SELECTION BIAS CLINCIAL

(Q1) Are the individuals selected to participate in the study likely to be representative of the target population?

Very likely

Somewhat likely

Not likely

Can't tell

## (Q2) What percentage of selected individuals agreed to participate?

- 1. 80 100%
- 2. 60 79%
- 3. Less than 60% agreement
- 4. Not applicable
- 5. Can't tell

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

## A.2.) SELECTION BIAS NON-CLINCIAL

# (Q1) Are the individuals selected to participate in the study likely to be representative of the target population?

Very likely Somewhat likely Not likely

Can't tell

(Q2) What percentage of selected individuals agreed to participate? 6.

- 80 100%
- 7. 60 79%
- 8. Less than 60% agreement
- 9. Not applicable
- 10. Can't tell

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

## **DICTIONARY: SELECTION BIAS**

(Q1) Participants are more likely to be representative of the target population if they are randomly selected from a comprehensive list of individuals in the target population (score very likely). They may not be representative if they are referred from a source (e.g. clinic) in a systematic manner (score somewhat likely) or selfreferred (score not likely).

(Q2) Refers to the % of subjects in the control and intervention groups that agreed to participate in the study before they were assigned to intervention or control groups.

## STUDY SPECIFIC NOTES: SELECTION BIAS

## A1. CLINCIAL PARTICIPANTS

(Q1) They may not be representative if they are referred from a source (e.g. clinic) in a non-systematic manner (e.g. convenience sample approached based on service such as Early Intervention Services) or subsample selected from an earlier study (score not likely).

(Q2) This includes declines only and does not include those who were approached but do not meet inclusion criteria.\*When papers did not give details of selection procedures, but direct you to another paper/provide reference for further details then rate based on this info but do make a note for discussion.

## A2. NON CLINCIAL PARTICIPANTS

(Q1)For non-clinical samples, participants are considered in terms of whether they are likely to represent the general population. Participants are more likely to be representative of the target population if they are randomly selected from a comprehensive list of individuals in the general population (score very likely). They may not be representative if they are referred from a source (e.g. university) (score somewhat likely) or self-referred (score not likely).

(Q2) This includes declines only and does not include those who were approached but do not meet inclusion criteria.\*When papers did not give details of selection procedures, but direct you to another paper/provide reference for further details then rate based on this info but do make a note for discussion.

## **SELECTION BIAS SCORING**

**Strong:** The selected individuals are very likely to be representative of the target population (Q1 is 1) and there is greater than 80% participation (Q2 is 1). **Moderate:** The selected individuals are at least somewhat likely to be representative of the target population (Q1 is 1 or 2); and there is 60 - 79% participation (Q2 is 2). 'Moderate' may also be assigned if Q1 is 1 or 2 and Q2 is 5 (can't tell). **Weak:** The selected individuals are not likely to be representative of the target population (Q1 is 3); or there is less than 60% participation (Q2 is 3) or selection is not described (Q1 is 4); and the level of participation is not described (Q2 is 5).

## **B) CONFOUNDERS**

(Q1) Were important differences between groups or important covariates taken into account (controlled for) in the analysis <u>(or design</u>)?

Yes

No Can't tell

## STUDY SPECIFIC NOTES: CONFOUNDERS

The following are examples of confounders in the relationship between childhood trauma and outcomes of interest (i.e. voice-hearing, paranoia, severity/frequency, psychosis, risk status)

Ethnic group; Gender; Age; Education/employment; Marital status; Social class/socioeconomic factors/financial strain; Living status/residence Diagnosis; Service (inpatient/outpatient, acute/rehab, community care/CMHT/CPN); Medication use; Substance misuse; Duration/severity of mental health problem General psychopathology factors (e.g. depression, anxiety); Outcomes of interest (e.g. positive (e.g controlling for paranoia if outcome of interest in voice-hearing; negative symptoms)

## (Q2) If yes, indicate the percentage of relevant confounders that were controlled - either in the design (e.g. stratification, matching) or analysis?

Rating of 80-100% (most) = 2+ confounders controlled for in analysis or design (where applicable) Rating 60-79% (some) = 1+ confounders controlled for in analysis or design (where applicable) Rating less than 60% (few or none) = No attempt to control for confounders in analysis or design (where applicable)

Can't Tell Not applicable

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

## **DICTIONARY: CONFOUNDERS**

By definition, a confounder is a variable that is associated with both the independent variable and the dependent variable. The authors should indicate if confounders were controlled in the design [by stratification or matching] or in the analysis. There should be no obvious dissimilarities between groups or important covariates that may account for differences in outcomes.

# \*Please note question 1 includes in analysis but we have changed this to also include research design

Examples of controlling for confounders in analysis include comparing groups (e.g. t-test) to check for differences if one group not included in analysis; partial correlation; controlling for variables in regression; covariates in ANCOVAs; Examples of controlling for confounders in design include restriction (e.g. control for gender and age by including all males over 60 years) and matching (e.g. for age and gender – also have to control for this in analysis as use different stats to unmatched studies) and randomisation (i.e. equal chance of being in each group, so

*likely similar distribution of confounding factors – success can be examined via statistical comparison of baseline characteristics)* 

(Q1) If some attempt to control for confounders in either analysis or design rate as 'yes' (NB., where there are more than two analyses in one paper, if control for confounders in only one still rate yes – can rate the extent via percentage rating in Q2).

(Q2). Where there are two or more relevant analyses, the rating for percentage of confounders will be analysed across all relevant analyses (e.g. if there are two relevant analyses and a number of confounds are adjusted for but only in one out of the two analyses, then rate across both and reduce the final percentage rating – cannot score higher than '60-79%')

- *Rating of 80-100% (most) = 2+ confounders controlled for in analysis or design (where applicable)*
- *Rating* 60-79% (some) = 1+ confounders controlled for in analysis or design (where applicable)
- Rating less than 60% (few or none) = No attempt to control for confounders in analysis or design (where applicable) \*Where Q1 is no, Q2 is not applicable.

## **CONFOUNDERS SCORING**

**Strong:** will be assigned to those articles that controlled for at least 80% of relevant confounders (Q1 is 2); or (Q2 is 1).

**Moderate:** will be given to those studies that controlled for 60 - 79% of relevant confounders (Q1 is 1) and (Q2 is 2).

**Weak:** will be assigned when less than 60% of relevant confounders were controlled (Q1 is 1) and (Q2 is 3) or control of confounders was not described (Q1 is 3) and (Q2 is 4).

## C.1) DATA COLLECTION METHODS- Mediator measures

## (Q1) Were data collection tools for outcome measures shown to be valid?

Yes

No

Can't tell

## (Q2) Were data collection tools for outcome measures shown to be reliable?

No

Can't tell

Yes

## C.2) DATA COLLECTION METHODS – CT measure

- (Q1) Were data collection tools for outcome measures shown to be valid? Yes
- No

Can't tell

## (Q2) Were data collection tools for outcome measures shown to be reliable? Yes

No

Can't tell

## C.2) DATA COLLECTION METHODS – Outcome measure

(Q1) Were data collection tools for outcome measures shown to be valid? Yes

No

Can't tell

(Q2) Were data collection tools for outcome measures shown to be reliable? Yes

No

Can't tell

Mediator measure

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

Childhood trauma measure

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

Outcome measure

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

## **DICTIONARY: DATA COLLECTION METHODS**

Tools for primary outcome measures must be described as reliable and valid. If 'face' validity or 'content' validity has been demonstrated, this is acceptable. Some sources from which data may be collected are described below:

<u>Self- reported data</u> includes data that is collected from participants in the study (e.g. completing a questionnaire, survey, answering questions during an interview, etc.). <u>Assessment/Screening</u> includes objective data that is retrieved by the researchers. (e.g. observations by investigators).

<u>Medical Records/Vital Statistics</u> refers to the types of formal records used for the extraction of the data.

Reliability and validity can be reported in the study or in a separate study. For example, some standard assessment tools have known reliability and validity.

## STUDY SPECIFIC NOTES: DATA COLLECTION METHODS

\*Data collection ratings will be made for measures relevant to the review question. Therefore, this rating will be conducted in relation to the childhood trauma measures(s), mediator variable measure and the outcome(s) of interest only (and not in relation to other reported measures).

\* Measures which have shown test-retest reliability will score 'yes' on Q2. \*Where one measure is valid/reliable and the other is not valid/reliable, rate 'no'. All measures have to have some indication of validity/reliability to rate 'yes either in the actual paper or in a paper referenced by the authors.

\*All studies must have utilised measures for the variables of interest that show content and face validity. Where whole measures have been used which have been shown to be valid and reliable a strong rating will be given. A moderate rating will be given where a previously valid and reliable measure ahs been changed for the purpose of the study (e.g. items taken from the measure). A weak rating will be given where it is unclear if the measure has been validated and tested for reliability but the measure shown content and face validity.

\*If papers have used reliable and validated measures but have translated these into another language, they will still be valid/reliable if they have used forwardbackward procedures. If not, rate not valid/reliable.

## **DATA COLLECTION METHODS SCORING**

**Strong:** The data collection tools have been shown to be valid (Q1 is 1); **and** the data collection tools have been shown to be reliable (Q2 is 1).

**Moderate:** The data collection tools have been shown to be valid (Q1 is 1); and the data collection tools have not been shown to be reliable (Q2 is 2) or reliability is not described (Q2 is 3).

**Weak:** The data collection tools have not been shown to be valid (Q1 is 2) **or** both reliability and validity are not described (Q1 is 3 and Q2 is 3).

## D) WITHDRAWALS AND DROP-OUTS (if applicable)

(Q1) Were withdrawals and drop-outs reported in terms of numbers and/or reasons per group?

Yes

No

Can't tell

Not Applicable (i.e. one time surveys or interviews)

(Q2) Indicate the percentage of participants completing the study. (If the percentage differs by groups, record the lowest).

80 -100% 60 - 79% less than 60%

> Can't tell Not Applicable (i.e. Retrospective case-control)

RATE THIS SECTION	STRONG	MODERATE	WEAK	
See dictionary	1	2	3	Not Applicabl e

## DICTIONARY: WITHDRAWALS AND DROP-OUTS

(Q1) Score YES if the authors describe BOTH the <u>numbers and reasons</u> for withdrawals and drop-outs.

Score **NO** if either the numbers or reasons for withdrawals and drop-outs are not reported.

(Q2) The percentage of participants completing the study refers to the % of subjects remaining in the study at the final data collection period.

## STUDY SPECIFIC NOTES: WITHDRAWALS AND DROP-OUTS

<u>\*Rating not applicable for one time point cross-sectional studies – only rate for</u> longitudinal studies

(Q1) If withdrawals are not referred to in the paper, and the 'n' included in the analysis is the same as the 'n' for the original sample, presume there are no drop outs.

\*Consider how many were included in the analysis. If the 'n' in the reported results (e.g. tables) is different to the original 'n' but the authors do not explicitly report the withdrawals/drop-outs/missing data in the text then rate as 'no'. If they report the numbers but do not give reasons then also report as 'no'. <u>Must report both for a rating of 'yes'.</u>

## WITHDRAWALS AND DROP-OUTS SCORING

**Strong:** will be assigned when the follow-up rate is 80% or greater (Q2 is 1). **Moderate:** will be assigned when the follow-up rate is 60 - 79% (Q2 is 2) **OR** Q2 is 5 (N/A).

**Weak:** will be assigned when a follow-up rate is less than 60% (Q2 is 3) or if the withdrawals and drop-outs were not described (Q2 is 4).

**Not applicable =** no follow up (not longitudinal)

(E) ANALYSES

(Q1) Was the analysis appropriate to the research question and the statistical methods appropriate for the study design?

Yes No Can't tell

## STUDY SPECIFIC NOTES: ANALYSES

## \*Consider this rating for the mediation analysis only

\* Consider this rating in terms of whether the analysis was appropriate and reported in a way that it is clear how it illuminates the research questions.

\*Consider whether the authors report analysis clearly – Is the analysis clearly reported? (I.e. is there an analysis section in the methods or is the analysis sufficiently described in the results?) Are relevant statistics presented?

## ANALYSES SCORING

**Strong:** will be assigned when the analysis is appropriate and reported in a way that it is clear how it illuminates the research questions (Q1 is *yes*). *The authors use methods to test direct and indirect effects (e.g. Hayes & Preacher method)* 

**Moderate:** will be assigned when the analysis is appropriate but is not reported in a way that it is clear how it illuminates the research questions (*Q1 is yes or can't tell*). *Regression analysis has been used to test mediation however additional inferential methods have also been used (e.g. Sobel Test)* 

**Weak:** will be assigned when the analysis is not appropriate, or it is not clear (*Q1 is no or can't tell*). The analysis may be appropriate however only regression analysis has been used to test mediation (e.g. Baron & Kenny methodology).

<u>\*NB in the original version of the tool, the analysis section was omitted from the global</u> scoring but it is included in our adapted version<u>\*</u>

\*Additional guidance (italicised text) has been added to the anchor points to aid scoring

## SCORING

## **COMPONENT RATINGS**

Please transcribe the information from the gray boxes on pages 1-4 onto this page. See dictionary on how to rate this section.

Α	Selection bias	Strong	Moderate	Weak
		1	2	3
В	Confounders	Strong	Moderate	Weak
		1	2	3
С	Data collection method	Strong	Moderate	Weak
		1	2	3
D	Withdrawals and dropouts	Strong	Moderate	Weak
		1	2	3
Ε	Analysis	Strong	Moderate	Weak
		1	2	3

## **GLOBAL RATING FOR THIS PAPER (circle one):**

1 STRONG (no WEAK ratings)

2 MODERATE (one WEAK rating)

3 WEAK (two or more WEAK ratings)

With both reviewers discussing the ratings:

Is there a discrepancy between the two reviewers with respect to the component (AD) ratings?

If yes, indicate the reason for the discrepancy

1 Oversight

2 Differences in interpretation of criteria

3 Differences in interpretation of study

## Final decision of both reviewers (circle one):

1 STRONG 2 MODERATE 3 WEAK

## **Component Ratings of Study:**

For each of the six components A - E, use the following descriptions as a roadmap.

## **A) SELECTION BIAS**

**Strong:** The selected individuals are very likely to be representative of the target population (Q1 is 1) and there is greater than 80% participation (Q2 is 1). **Moderate:** The selected individuals are at least somewhat likely to be representative of the target population (Q1 is 1 or 2); and there is 60 - 79% participation (Q2 is 2). 'Moderate' may also be assigned if Q1 is 1 or 2 and Q2 is 5 (can't tell). **Weak:** The selected individuals are not likely to be representative of the target population (Q1 is 3); or there is less than 60% participation (Q2 is 3) or selection is not described (Q1 is 4); and the level of participation is not described (Q2 is 5).

## **B) CONFOUNDERS**

**Strong:** will be assigned to those articles that controlled for at least 80% of relevant confounders (Q1 is 2); or (Q2 is 1).

**Moderate:** will be given to those studies that controlled for 60 - 79% of relevant confounders (Q1 is 1) and (Q2 is 2).

**Weak:** will be assigned when less than 60% of relevant confounders were controlled (Q1 is 1) and (Q2 is 3) or control of confounders was not described (Q1 is 3) and (Q2 is 4).

## C) DATA COLLECTION METHODS

**Strong:** The data collection tools have been shown to be valid (Q1 is 1); **and** the data collection tools have been shown to be reliable (Q2 is 1).

**Moderate:** The data collection tools have been shown to be valid (Q1 is 1); and the data collection tools have not been shown to be reliable (Q2 is 2) or reliability is not described (Q2 is 3).

**Weak:** The data collection tools have not been shown to be valid (Q1 is 2) or both reliability and validity are not described (Q1 is 3 and Q2 is 3).

## D) WITHDRAWALS AND DROP-OUTS - a rating of:

**Strong:** will be assigned when the follow-up rate is 80% or greater (Q2 is 1). **Moderate:** will be assigned when the follow-up rate is 60 - 79% (Q2 is 2) **OR** Q2 is 5 (N/A).

**Weak:** will be assigned when a follow-up rate is less than 60% (Q2 is 3) or if the withdrawals and drop-outs were not described (Q2 is 4).

**Not applicable =** no follow up (not longitudinal)

## E) ANALYSES

**Strong:** will be assigned when the analysis is appropriate and reported in a way that it is clear how it illuminates the research questions (Q1 is 1).

**Moderate:** will be assigned when the analysis is appropriate but is not reported in a way that it is clear how it illuminates the research questions. **Weak:** will be assigned when the analysis is not appropriate, or it is not clear.

<u>\*NB in the original version of the tool, the analysis section was omitted from the global scoring but it is included in our adapted version</u>\*

Appendix C: Instructions to authors: Psychological Medicine

## **Psychological Medicine**

## **Editorial Policy**

**Psychological Medicine** is a journal aimed primarily for the publication of original research in clinical psychiatry and the basic sciences related to it. These include relevant fields of biological, psychological and social sciences. Review articles, editorials and letters to the Editor discussing published papers are also published. Contributions must be in English.

#### Submission of manuscripts

Manuscripts should be submitted online via our manuscript submission and tracking site, <u>http://www.editorialmanager.com/psm/</u>. Full instructions for electronic submission are available directly from this site. To facilitate rapid reviewing, communications for peer review will be electronic and authors will need to supply a current e-mail address when registering to use the system.

Papers for publication from Europe, (except those on genetic topics, irrespective of country), and all papers on imaging topics, should submitted to the UK Office.

Papers from the Americas, Asia, Africa, Australasia and the Middle East, (except those dealing with imaging topics), and all papers dealing with genetic topics, irrespective of country, should be sent to US Office.

All enquiries should be directed to the Editorial Office at psychmed@cambridge.org.

#### Please see the below table for the types of papers accepted:

Article Type	Usual Max Word count*	Abstract	References	Tables/figures**	Suppleme material onl
Original article	4500	250 words, structured, using subheadings Background, Methods, Results, Conclusions	Harvard style – see elsewhere in this document for full details	Usually up to 5 total	Ye:
Review article	4500	250 words, not structured	Harvard style	Usually up to 5 total	Ye
Editorial	3500	No	Harvard style	Usually up to 5 total	Ye
Correspondence	1500	Νο	max 20 Harvard style	Max 1	Nc
Commentary	2000 By invitation of editor	No	max 20 Harvard style	Not usually	Ye:

\* Editors may request shortening or permit additional length at their discretion in individual cases \*\* May be adjusted in individual cases at Editors' discretion

NOTE:

- 1. Figures should be submitted as discrete files, not embedded in the text of the main document.
- Supplementary material for online only should be submitted as discrete files, not as part of the main text.

Generally papers should not have text more than 4500 words in length (excluding abstract, tables/figures and references) and should not have more than a combined total of 5 tables and/or figures. Papers shorter than these limits are encouraged. For papers of unusual importance the editors may waive these requirements. Articles require a structured abstract of no more than 250 words including the headings: Background; Methods; Results; Conclusions. Review Articles require an unstructured abstract of no more than 250 words. The name of an author to whom correspondence should be sent must be indicated and a full postal address given in the footnote. Any acknowledgements should be placed at the end of the text (before the References section).

Contributors should also note the following:

- 1. S.I. units should be used throughout in text, figures and tables.
- 2. Authors should spell out in full any abbreviations used in their manuscripts.
- 3. Foreign quotations and phrases should be followed by a translation.
- If necessary, guidelines for statistical presentation may be found in: Altman DG., Gore SM, Gardner, MJ. Pocock SJ. (1983). Statistical guidelines for contributors to medical journals. *British Medical Journal* 286, 1489-1493.

#### **Neuroscience-based Nomenclature**

For papers concerning neuropsychopharmacological treatments, *Psychological Medicine* encourages authors to utilize the 'Neuroscience-based Nomenclature' developed by the ECNP Taskforce on Nomenclature. The need for such a change arose to address a longstanding concern within the neuropsychopharmacological community that the nomenclature of psychotropic drugs did not properly reflect the underlying neuroscience of these compounds, as well as being unhelpful to clinicians and confusing to patients (e.g. the prescription of 'antipsychotics' for depression).

More information about the nomenclature can be found on the <u>ECNP website here</u>, and in the <u>paper here</u>. The Neuroscience-based Nomenclature (NbN) itself is available free of charge as a mobile app (for both <u>Android</u> and <u>iOS</u> devices).

#### Combination artwork (line/tone)

Format: tif or eps Colour mode: grayscale (also known as 8-bit) Size: please size to final publication size Resolution: 800 dpi

#### Black and white halftone artwork

Format: tif Colour mode: grayscale (also known as 8-bit) Size: please size to final publication size Resolution: 300 dpi

#### Colour halftone artwork

Format: tif Colour mode: CMYK colour Size: please size to final publication size Resolution: 300 dpi

If you require any further guidance on creating suitable electronic figures, please visit the <u>Cambridge</u> <u>Journals Artwork Guide</u>.

All graphs and diagrams should be referred to as figures and should be numbered consecutively in Arabic numerals. Captions for figures should be typed double-spaced on separate sheets. Tables should be numbered consecutively in the text in Arabic numerals and each typed on a separate sheet after the References section. Titles should be typed above the table.

#### **Online Supplementary Material**

Relevant material which is not suitable for print production, such as movies or simulations/animations, can be uploaded as part of the initial submission. Movies should be designated as 'Movie' and each individual file must be accompanied by a separate caption and a suitable title (e.g., Movie 1). Accepted formats are .mov, .mpg, .mp4, and .avi, though they should be archived as a .zip or .tar file before uploading. Each movie should be no more than 10MB. Upon publication these materials will then be hosted online alongside the final published article. Likewise, should there be detailed tables or figures which are likely to take up excessive space in the printed journal, these can also be published online as supplementary material [designated as `Other supplementary material']. Note that supplementary material is published 'as is', with no further production performed.

#### **Required Statements**

#### Acknowledgements

You may acknowledge individuals or organisations that provided advice, support (non-financial). Formal financial support and funding should be listed in the following section.

#### **Financial support**

Please provide details of the sources of financial support for all authors, including grant numbers. For example, "*This work was supported by the Medical research Council (grant number XXXXXX)*". Multiple grant numbers should be separated by a comma and space, and where research was funded by more than one agency the different agencies should be separated by a semi-colon, with "and" before the final funder. Grants held by different authors should be identified as belonging to individual authors by the authors' initials. For example, "*This work was supported by the Wellcome Trust (A.B., grant number XXXX, YYYY), (C.D., grant number ZZZZ); the Natural Environment Research Council (E.F., grant number FFFF); and the National Institutes of Health (A.B., grant number GGGG), (E.F., grant number HHHH)*". Where no specific funding has been provided for research, please provide the following statement: "*This research received no specific grant from any funding agency, commercial or not-for-profit sectors.*"

#### **Conflict of interest**

Please provide details of all known financial, professional and personal relationships with the potential to bias the work. Where no known conflicts of interest exist, please include the following statement: "None."

#### **Ethical standards**

Where research involves human and/or animal experimentation, the following statements should be included (as applicable): "The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008." and "The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation is procedures contributing to this work comply with the ethical standards of the relevant national and institutional guides on the care and use of laboratory animals."

#### **Proofs and offprints**

Page proofs will be sent to the author designated to receive correspondence. Corrections other than to printer's errors may be charged to the author. Authors will automatically receive a PDF of their article as soon as the issue in which it appears is published.

#### **Open Access**

Authors in *Psychological Medicine* have the option to publish their paper under a fully Open Access agreement, upon payment of a one-off Article Processing Charge. In this case, the final published Version of Record will be made freely available to all in perpetuity under a creative commons license, enabling its reuse and re-distribution. This Open Access option is only offered to authors upon acceptance of an article for publication.

Authors choosing the Open Access option are required to complete the <u>Open Access License to Publish form</u>. More information about Open Access in *Psychological Medicine*, including the current Article Processing Charge, can be found <u>on our website</u>.

#### AuthorAID

<u>AuthorAID</u> is a global network that provides free support, mentoring, resources and training to help researchers in developing countries to write, publish and otherwise communicate their work.

Key features of AuthorAID are:

- a community space for <u>discussion and questions</u> where researchers can benefit from advice and insights from members across the globe
- access to a range of documents and presentations on best practice in writing and publication
- world-wide training workshops and MOOCs on scientific writing
- a chance to network with other researchers
- personal mentoring by highly published researchers and professional editors

For any authors new to publishing research articles, we encourage you to make use of the AuthorAID resources before submitting your paper to *Psychological Medicine*. Through the AuthorAID network, guidance can be found to help researchers through the process of writing and submitting scientific papers, advice about responding to reviewer comments, as well as research design and grant applications.

Please note that seeking support through AuthorAID will not guarantee acceptance for publication in *Psychological Medicine*, or affect the editorial process in any way.

#### References

- (1) The Harvard (author-date) system should be used in the text and a complete list of References cited given at the end of the article. In a text citation of a work by more than two authors cite the first author's name followed by *et al.* (but the names of all of the authors should be given in the References section). Where several references are cited together they should be listed in rising date order.
- (2) The References section should be in alphabetical order. Examples follow:

**Brown GW** (1974). Meaning, measurement and stress of life events. In *Stressful Life Events: Their Nature and Effects* (ed. B. S. Dohrenwend and B. P. Dohrenwend), pp. 217-244. John Wiley: New York.

Brown J. (1970). Psychiatric Research. Smith: Glasgow.

Brown J, Williams E, Wright H (1970). Treatment of heroin addiction. *Psychological Medicine* 1, 134-136.

Note: authors' names should be in **bold** font; journal titles should always be given in full.

(3) References to material published online should follow a similar style, with the URL included at the end of the reference, with the accession date, if known. Authors are requested to print out and keep a copy of any online-only information, in case the URL changes or is no longer maintained. Examples follow:

Acute Health Care, Rehabilitation and Disability Prevention Research - National Center for Injury Prevention and Control. (<u>http://www.cdc.gov/ncipc/profiles/acutecare/default.htm</u>). Accessed 7 June 2004.

British Psychological Society Research Digest, Issue 12. (http://lists.bps.org.uk/read/messages?id=1423). Accessed 17 February 2004.

#### **Figures and tables**

Only essential figures and tables should be included and should be provided in black and white except in exceptional circumstances, eg PET scan images etc. If you request colour figures in the printed version, you will be contacted by CCC-Rightslink who are acting on our behalf to collect Author Charges. Please follow their instructions in order to avoid any delay in the publication of your article. Further tables, figures, photographs and appendices, may be included with the online version on the journal website.

All wording within submitted figures must be Arial, point size 8. To ensure that your figures are reproduced to the highest possible standards and your article is published as quickly and efficiently as possible, Cambridge Journals recommends the following formats and resolutions for supplying electronic figures. Please note that submitting low quality figures may result in a delay in publishing your valuable research

Please ensure that your figures are saved at final publication size (please see the latest issue of the journal for column widths) and are in our recommended file formats. Following these guidelines will result in high quality images being reproduced in both the print and the online versions of the journal.

#### Line artwork

Format: tif or eps Colour mode: black and white (also known as 1-bit) Size: please size to final publication size Resolution: 1200 dpi Appendix D: NHS ethical approval

## **NHS** Health Research Authority

Email: hra.approval@nhs.net

iss Samantha Bull ainee Clinical Psychologist anchester Mental Health and Social Care Trust norlton House ) Manchester Road norton-Cum-Hardy 21 9UN

! August 2016

ear Samantha Bull

Letter of HRA Approval

udy title:

AS project ID: EC reference: consor Testing the Cognitive Attachment Model of Voice-Hearing: The role of source-monitoring, disorganised attachment and dissociation in voice-hearing. 196897 16/NW/0398 University of Manchester

Im pleased to confirm that <u>HRA Approval</u> has been given for the above referenced study, on the isis described in the application form, protocol, supporting documentation and any clarifications ited in this letter.

#### articipation of NHS Organisations in England

ie sponsor should now provide a copy of this letter to all participating NHS organisations in England.

*ppendix B* provides important information for sponsors and participating NHS organisations in Igland for arranging and confirming capacity and capability. **Please read** *Appendix B* carefully, in Inticular the following sections:

- Participating NHS organisations in England this clarifies the types of participating
  organisations in the study and whether or not all organisations will be undertaking the same
  activities
- Confirmation of capacity and capability this confirms whether or not each type of participating
  NHS organisation in England is expected to give formal confirmation of capacity and capability.
  Where formal confirmation is not expected, the section also provides details on the time limit
  given to participating organisations to opt out of the study, or request additional time, before
  their participation is assumed.
- Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria) this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

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IRAS project ID 196897

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

#### Appendices

The HRA Approval letter contains the following appendices:

- A List of documents reviewed during HRA assessment
- B Summary of HRA assessment

#### After HRA Approval

The document *"After Ethical Review – guidance for sponsors and investigators"*, issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the After Ethical Review document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the <u>HRA website</u>, and emailed to <u>hra.amendments@nhs.net</u>.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation
  of continued HRA Approval. Further details can be found on the <u>HRA website</u>.

#### Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at <a href="http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/">http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/</a>.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

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IRAS project ID 196897

#### **User Feedback**

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please email the HRA at <u>hra.approval@nhs.net</u>. Additionally, one of our staff would be happy to call and discuss your experience of HRA Approval.

#### **HRA Training**

We are pleased to welcome researchers and research management staff at our training days – see details at <u>http://www.hra.nhs.uk/hra-training/</u>

Your IRAS project ID is 196897. Please quote this on all correspondence.

Yours sincerely

Nicola Gilzeane Assessor

Email: hra.approval@nhs.net

Copy to: Ms Lynne Macrae, University of Manchester, Sponsor Contact

Julia Foster, Manchester Mental Health and Social Care Trust, Lead NHS R&D Contact

Jessica Williams, Student

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## Appendix A - List of Documents

## The final document set assessed and approved by HRA Approval is listed below.

Document	Version	Date
Copies of advertisement materials for research participants [R]	1	
Covering letter on headed paper [Letter to committee]		
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Public, Employers and Product]		03 June 2015
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Professional Indemnity ]		31 May 2015
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Employers Liability ]		01 June 2015
GP/consultant information sheets or letters [Letter to GP Participant in Study]	1	20 February 2016
GP/consultant information sheets or letters [Letter to prescribing physician]	1	03 June 2016
IRAS Application Form [IRAS_Form_21042016]		21 April 2016
Letter from sponsor [Letter from sponsor]		14 March 2016
Other [Response to committee]	1	06 June 2016
Other [Demographic questions]	1	26 March 2016
Other [Schedule fo Events GP ]	1	22 August 2016
Other [Statement of Activities GP]	1	22 August 2016
Other [Statement of Activities Hospitalss]	2	22 August 2016
Other [Schedule of Events Hospitals]	2	22 August 2016
Other [Notification of minor amendment to PIS and adding sites]		22 August 2016
Participant consent form [Participant consent form]	1	26 March 2016
Participant information sheet (PIS) [PIS ]	4	22 August 2016
Research protocol or project proposal [Study Protocol V1 26.03.2016]	1	26 March 2016
Summary CV for Chief Investigator (CI) [Samantha Bull CV]	1	06 April 2016
Summary CV for student [CV Jessica Williams]	1	06 April 2016
Summary CV for supervisor (student research) [KB CV]	1	06 April 2016
Validated questionnaire [Validated questionnaires]		
Validated questionnaire [Creative Experiences Scale]		
Validated questionnaire [BAVQ-R]		
Validated questionnaire [Calgary Depression Scale for Schizophrenia]		
Validated questionnaire [Community Assessment of Psychotic Experiences]		
Validated questionnaire [Childhood Trauma Questionnaire]		
Validated questionnaire [Dissociative Experiences Scale-II]		
Validated questionnaire [GAD-7]		
Validated questionnaire [Hamilton Program Schizophrenia Voices Questionnaire]		
Validated questionnaire [Launey Slade Hallucination Scale- Revised]		
Validated questionnaire [Psychosis Attachment Measure]		
Validated questionnaire [PSYRATS- Auditory Hallucinations only]		
Validated questionnaire [Relationship Questionnaire]		
Validated questionnaire [Brief Betrayal Trauma Survey]		

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#### Appendix B - Summary of HRA Assessment

This appendix provides assurance to you, the sponsor and the NHS in England that the study, as reviewed for HRA Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England to assist in assessing and arranging capacity and capability.

For information on how the sponsor should be working with participating NHS organisations in England, please refer to the, participating NHS organisations, capacity and capability and Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria) sections in this appendix.

The following person is the sponsor contact for the purpose of addressing participating organisation questions relating to the study:

Lynne Macrae (01612751436, fmhsethics@manchester.ac.uk)

Section	HRA Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	Following REC approval the applicant submitted a non-substantial amendment to add the following CCGs as participating sites- Lancashire North CCG, Liverpool CCG, North Manchester CCG, South Manchester CCG, Central Manchester CCG and Salford CCG
2.1	Participant information/consent documents and consent process	Yes	A non-substantial amendment was submitted following REC approval to update consent documentation to bring it in line with HRA standards.
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	The applicant has submitted a Statement of Activities and intends it to act as agreement of NHS organisations to take part.

#### **HRA** assessment criteria

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IRAS project ID 196897

Section	HRA Assessment Criteria	Compliant with Standards	Comments
4.2	Insurance/indemnity arrangements assessed	Yes	Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the activities expected of them for this research study
4.3	Financial arrangements assessed	Yes	It is confirmed in the statement of activities that the sponsor will not provide funding to sites
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

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IRAS project ID 196897

#### Participating NHS Organisations in England

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.

There will be two site types for the study-

- Hospital sites the clinical care team will identify and approach potential participants and refer on to the research team. The researchers may then access the site to consent and carry out participant study visits (administering questionnaires and an audio exercise)
- GP sites will display posters for the study to allow interested patients to contact the
  researcher regarding participation. The researchers may then access the site to consent and
  carry out participant study visits (administering questionnaires and an audio exercise) if it is
  the participants preference

HRA Approval will not cover activities where participants are recruited outside of the NHS.

The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. For NIHR CRN Portfolio studies, the Local LCRN contact should also be copied into this correspondence. For further guidance on working with participating NHS organisations please see the HRA website.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the chief investigator, sponsor or principal investigator should notify the HRA immediately at <u>hra.approval@nhs.net</u>. The HRA will work with these organisations to achieve a consistent approach to information provision.

#### **Confirmation of Capacity and Capability**

This describes whether formal confirmation of capacity and capability is expected from participating NHS organisations in England.

Participating NHS organisations in England will be expected to formally confirm their capacity and capability to host this research.

- Following issue of this letter, participating NHS organisations in England may now confirm to
  the sponsor their capacity and capability to host this research, when ready to do so. How
  capacity and capacity will be confirmed is detailed in the Allocation of responsibilities and
  rights are agreed and documented (4.1 of HRA assessment criteria) section of this appendix.
- The <u>Assessing, Arranging, and Confirming</u> document on the HRA website provides further information for the sponsor and NHS organisations on assessing, arranging and confirming capacity and capability.

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#### **Principal Investigator Suitability**

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and the minimum expectations for education, training and experience that PIs should meet (where applicable).

Local collaborators will be expected to facilitate researchers' access to sites.

GCP training is <u>not</u> a generic training expectation, in line with the <u>HRA statement on training</u> <u>expectations</u>.

#### **HR Good Practice Resource Pack Expectations**

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken

Where external researchers access hospital sites Letters of Access will be expected if contractual arrangements are not already in place with the site.

#### Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England to aid study set-up.

The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

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### Appendix E: Demographics questionnaire



Version 1. Date: 26.03.2016

### Study: Psychological Processes involved in voice-hearing.

Research Team:

Samantha Bull: Doctoral Student and Chief Investigator

Jessica Williams: Doctoral Student

Dr Sandra Bucci: Academic Supervisor

Dr Katherine Berry: Academic Supervisor

### **Demographic Questionnaire**

For researcher to complete	Participant II	):	
GP contact details			
Has GP been informed of participation?	Yes/No		
Which study group will the participant	Current No	voices in	Never
belong to?	heard voice- voices	hearer last	6
		months	
Has the key worker confirmed group	Yes/No		
membership?			

About You			
Sex:	Male	Female	
Age			
Nationality:			

Ethnicity:	White - Caucasian Asian Black Middle-Eastern Mixed-race Other:
First Language:	English

	Ot ler:
Are you married? IF NO: Were you ever?	<ol> <li>married or living with someone as if married</li> <li>widowed</li> <li>divorced or annulled</li> <li>separated</li> <li>never married</li> </ol>
How far did you get in school?	<ol> <li>grade 6 or less</li> <li>GCSE (without doing A-levels)</li> <li>A-levels</li> <li>part university</li> <li>graduated from university</li> </ol>
How many years did you spend at school all together?	
Are you working or studying at the moment?	<ol> <li>Unemployed</li> <li>Working</li> <li>Studying</li> </ol>

Did you EVER receive any of the following diagnosis [select as many as apply]? When was the first time you saw someone for emotional or psychological difficulties? What was it for?	<ol> <li>Schizophrenia (or "Paranoid Schizophrenia)</li> <li>Schizoaffective Disorder</li> <li>Depression with psychotic features (depression with unusual experiences like hallucinations and delusions)</li> </ol>
Have you ever received mental health support or treatment for any of the following [select as many as apply]?	<ol> <li>Hallucinations (hearing voices, visions)</li> <li>Delusions (unusual and sometimes bizarre beliefs) Paranoia (excessive or irrational suspiciousness and distrustfulness of others)</li> <li>Unusual beliefs</li> </ol>
Have you ever been a patient in hospital for mental health difficulties?	
IF YES: What was that for? (How many times?)	
Have you received input from a community mental health team or early intervention service?	
IF YES: What was it for?	
Do you have any psychiatric diagnoses?	
IF YES, what is it?	
Do you take any medication?	
(Write down the name of the medication and the dose).	

### Appendix F Launay Slade Hallucination scale- Revised

# The following questions are about unusual perceptual experiences. Please read the statements given below and select the option that most applies to you.

1 = Never 2 = Sometimes 3 = Often 4 = Almost always

1	I hear a voice speaking my thoughts aloud.	1234
2	I hear the telephone ring and find that I am mistaken.	1234
3	I hear people call my name and find that nobody has done so.	1234
4	I can hear music when it is not being played.	1234
5	I have had the experience of hearing a person's voice and then found that there was no one there.	1234
6	When I look at things they look unreal to me.	1234
7	I see shadows and shapes when there is nothing there.	1234
8	When I look at myself in the mirror, I look different.	1234

9

**Appendix G: Relatioship Questionnaire** 

### **RELATIONSHIP QUESTIONNAIRE**

Following are four general relationship styles that people often report. Place a tick next to the letter corresponding to the style that best describes you or is closest to the way you are.

**A**. It is easy for me to become emotionally close to others. I am comfortable depending on them and having them depend on me. I don't worry about being alone or having others not accept me.

**B.** I am uncomfortable getting close to others. I want emotionally close relationships, but I find it difficult to trust others completely, or depend on them. I worry that I will be hurt if I allow myself to become close to others.

**\_\_\_\_\_ C.** I want to be completely emotionally intimate with others, but often find that others are reluctant to get as close as I would like. I am uncomfortable being without close relationships, but sometimes worry that others don't value me as much as I value them.

\_\_\_\_\_ **D.** I am comfortable without close emotional relationships. It is very important to me to feel independent and self-sufficient, and I prefer not to depend on others or have others depend on me.

Now please rate each of these relationship styles above to indicate how well or poorly each description corresponds to your general relationships style

# Style A

1	2	3	4	5	6	7
Not at all			Neutral/			Very much like me
like me			mixed			

## Style B

1	2	3	4	5	6	7
Not at all			Neutral/			Very much
Like me			mixed			like me

# Style C

1	2	3	4	5	6	7
Not at all			Neutral/			Very much like me
like me			mixed			

# Style D

1	2	3	4	5	6	7
Not at all			Neutral/			Very much like me
like me			mixed			

### Appendix H: Dissociative Expereinces Scale II

### Dissociative Experiences Scale - II (DES-II)

This questionnaire consists of 28 questions about experiences you have had in your daily life. We are interested in how often you have had these experiences. It is important, how-ever, that your answers show how often these experiences happen to you when you are not under the influence of alcohol or drugs.

To answer the questions, please determine to what degree the experience described in the question applies to you and circle the appropriate number to show what percentage of the time you have had the experience.

Example: 0% 10 20 (30) 40 50 60 70 80 90 100%

1. Some people have the experience of driving a car and suddenly realizing that they don't remember what has happened during all or part of the trip. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

2. Some people find that sometimes they are listening to someone talk and they suddenly realize that they did not hear part or all of what was just said. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

3. Some people have the experience of finding themselves in a place and having no idea how they got there. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

4. Some people have the experience of finding themselves dressed in clothes that they don't remember putting on. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

5. Some people have the experience of finding new things among their belongings that they do not remember buying. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

6. Some people sometimes find that they are approached by people that they do not know who call them by another name or insist that they have met them before. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

7. Some people sometimes have the experience of feeling as though they are standing next to themselves or watching themselves do something, and they actually see themselves as though they were looking at another person. Circle a number what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

8. Some people are told that they sometimes do not recognize friends or family members. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

9. Some people find that they have no memory for some important events in their lives (for example, a wedding or graduation). Circle a number to show what percentage of the important events in your life you have no memory for.

0% 10 20 30 40 50 60 70 80 90 100%

10. Some people have the experience of being accused of lying when they do not think that they have lied. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

11. Some people have the experience of looking in a mirror and not recognizing themselves. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

12. Some people sometimes have the experience of feeling that other people, objects, and the world around them are not real. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

13. Some people sometimes have the experience of feeling that their body does not seem to belong to them. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

14. Some people have the experience of sometimes remembering a past event so vividly that they feel as if they were reliving that event. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

15. Some people have the experience of not being sure whether things that they remember happening really did happen or whether they just dreamed them. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

16. Some people have the experience of being in a familiar place but finding it strange and unfamiliar. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

17. Some people find that when they are watching television or a movie they become so absorbed in the story that they are unaware of other events happening around them. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

18. Some people sometimes find that they become so involved in a fantasy or daydream that it feels as though it were really happening to them. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

19. Some people find that they sometimes are able to ignore pain. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

20. Some people find that they sometimes sit staring off into space, thinking of nothing, and are not aware of the passage of time. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

21. Some people sometimes find that when they are alone they talk out loud to themselves. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

22. Some people find that in one situation they may act so differently compared to another situation that they feel almost as if they were two different people. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

23. Some people sometimes find that in certain situations they are able to do things with amazing ease and spontaneity that would usually be difficult for them (for example, sports, work, social interactions, etc.). Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

24. Some people sometimes find that they cannot remember whether they have done something or have just thought about doing that thing (for example, not knowing whether they have just mailed a letter or have just thought about mailing it). Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

25. Some people sometimes find evidence that they have done things that they do not remember doing. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

26. Some people sometimes find writings, drawings, or notes among their belongings that they must have done but cannot remember doing. Mark the line to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

27. Some people sometimes find that they hear voices inside their head which tell them to do things or comment on things that they are doing. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

28. Some people sometimes feel as if they are looking at the world through a fog so that people and objects appear far away or unclear. Circle a number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

#### Appendix I: Calgary Depression Scale for Schizophrenia

### Interviewer: Ask the first question as written. Use follow up probes or qualifiers at your discretion. Time frame refers to last two weeks unless stipulated. **N.B.** The last item, #9, is based on observations of the entire interview.

1. DEPRESSION: How would you describe your mood over the last two weeks? Do you keep reasonably cheerful or have you been very depressed or low spirited recently? In the last two weeks how often have you (own words) every day? All day?

- 0. Absent
- 1. Mild Expresses some sadness or discouragement on questioning.
- Moderate Distinct depressed mood persisting up to half the time over last 2 weeks: present daily.
- 3. Severe Markedly depressed mood persisting daily over half the time interfering with normal motor and social functioning.

2. HOPELESSNESS: How do you see the future for yourself? Can you see any future? - or has life seemed quite hopeless? Have you given up or does there still seem some reason for trying?

- 0. Absent
- 1. Mild Has at times felt hopeless over the last two weeks but still has some degree of hope for the future.
- 2. Moderate Persistent, moderate sense of hopelessness over last week. Can be persuaded to acknowledge possibility of things being better.
- 3. Severe Persisting and distressing sense of hopelessness.
- 3. SELF DEPRECIATION: What is your opinion of your self compared

to other people? Do you feel better, not as good, or about the same as others? Do you feel inferior or even worthless?

0. Absent

- 1. Mild Some inferiority; not amounting to feeling of worthlessness.
- 2. Moderate Subject feels worthless, but less than 50% of the time.
- 3. Severe Subject feels worthless more than 50% of the time. May be challenged to acknowledge otherwise.
- 4. GUILTY IDEAS OF REFERENCE: Do you have the feeling that you are being blamed for something or even wrongly accused? What about? (Do not include justifiable blame or accusation. Exclude delusions of guilt.)
- 0. Absent
- 1. Mild Subject feels blamed but not accused less than 50% of the time.
- 2. Moderate Persisting sense of being blamed, and/or occasional sense of being accused.
- 3. Severe Persistent sense of being accused. When challenged, acknowledges that it is not so.
- 5. PATHOLOGICAL GUILT: Do you tend to blame yourself for little

things you may have done in the past? Do you think that you deserve to be so concerned about this?

- 0. Absent
- 1. Mild Subject sometimes feels over guilty about some minor peccadillo, but less than 50% of time.
- 2. Moderate Subject usually (over 50% of time) feels guilty about past actions the significance of which he exaggerates.
- 3. Severe Subject usually feels s/he is to blame for everything that has gone wrong, even when not his/her fault.
- 6. MORNING DEPRESSION: When you have felt depressed over the last 2 weeks have you noticed the depression being worse at any
- particular time of day?
- 0. Absent No depression.
- 1. Mild Depression present but no diurnal variation.
- 2. Moderate Depression spontaneously mentioned to be worse in a.m. 3. Severe Depression markedly worse in a.m., with impaired functioning
- which improves in p.m.

**7.** EARLY WAKENING: Do you wake earlier in the morning than is normal for you? How many times a week does this happen?

0. Absent No early wakening.

- 1. Mild Occasionally wakes (up to twice weekly) 1 hour or more before normal time to wake or alarm time.
- 2. Moderate Often wakes early (up to 5 times weekly) 1 hour or more before normal time to wake or alarm.
- 3. Severe Daily wakes 1 hour or more before normal time.

8. SUICIDE: Have you felt that life wasn't worth living? Did you ever feel like ending it all? What did you think you might do? Did you actually try?

- 0. Absent
- 1. Mild Frequent thoughts of being better off dead, or occasional thoughts of suicide.
- 2. Moderate Deliberately considered suicide with a plan, but made no attempt.
- 3. Severe Suicidal attempt apparently designed to end in death (i.e.: accidental discovery or inefficient means).

9. OBSERVED DEPRESSION: Based on interviewer's observations during the entire interview. The question "Do you feel like crying?" used at appropriate points in the interview, may elicit information useful to this observation.

- 0. Absent
- 1. Mild Subject appears sad and mournful even during parts of the interview, involving affectively neutral discussion.
- 2. Moderate Subject appears sad and mournful throughout the interview, with gloomy monotonous voice and is tearful or close to tears at times.
- 3. Severe Subject chokes on distressing topics, frequently sighs deeply and cries openly, or is persistently in a state of frozen misery if examiner is sure that this is present.
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Appendix J: Table 6. Correlations between dissociation and secure, preoccupied and dismissing attachment scores for aggregate sample

	Secure attachment	Preoccupied attachment)	Dismissing attachment
DES-II total	-0.353, (p=.012)	0.158, (p=.274)	0.156 (p= .279)
DES-II amnesia	-0.360, (p=.010)	0.194, (p=.176)	0.227 (p=.113)
DES-II absorption	-0.236, (p=.098)	0.087, (p=.550)	0.216 (p=.113)
DES-II depers.	-0.113, (p=.434)	0.189, (p=.188)	0.063 (p=.663)

**Table 6**. Correlations between dissociation and secure, preoccupied and dismissing measures for aggregate sample.