

Why are psychotic experiences associated with self-injurious thoughts and behaviours? A systematic review and critical appraisal of potential confounding and mediating factors

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Psychotic experiences (PEs), including hallucination- and delusion-like experiences, are robustly associated with self-injurious thoughts and behaviours (SITB) in the general population. However, it remains unclear as to why there is an association. The purpose of this systematic review was to elucidate the role of other factors that influence the association between PEs and SITB and, in doing so, highlight potential mechanisms underlying the relationship. A search of electronic international databases was undertaken, including PubMed, PsycINFO and EMBASE, and eligible studies were grouped according to seven confounder categories: sociodemographics, mental disorders, alcohol and substance use, environmental, psychological, intervention and family history/genetic factors. The systematic search strategy identified 41 publications reporting on 1 39 427 participants from 16 different countries. In the majority of studies, where adjustment for other variables occurred, the association between PEs and SITB persisted, suggesting PEs have an independent role. Common mental disorders, psychological distress and negative environmental exposures explained a substantial amount of the variance and therefore need to be considered as potential underlying mechanisms. There was high variability in the variables adjusted for in these studies, and so the question still remains as to whether the association between PEs and self-harm/suicidality can be attributed (fully or in part) to confounding and mediating factors or directly causal mechanisms. Regardless of causality, the now extensive literature reporting an association between these two clinical phenomena supports the broad usefulness of PEs as an indicator of risk for SITB.

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Introduction

The high rates of self-harm, suicide attempts and completed suicides among individuals with psychotic disorders (Palmer *et al.* 2005) also extend to those in the general population with psychotic experiences (PEs), i.e. hallucinatory and delusional experiences (Honings *et al.* 2016a). PEs are more common than psychotic disorders, reported by 5–8% of adolescents and adults (Kelleher *et al.* 2012a; McGrath *et al.* 2015), and are strongly associated with self-injurious thoughts and behaviours (SITB), including non-

suicidal self-injury, suicidal ideation, plans and attempts (Koyanagi *et al.* 2015a; DeVlyder *et al.* 2015b). Understanding the mechanisms underlying the association between PEs and SITB may assist identification of people at high risk of suicide and also inform interventions for those with PEs.

A meta-analysis reported increased likelihood of suicidal ideation and suicidal behaviour in those with any PE [odds ratios (ORs) and 95% confidence interval (CI) 2.47; 1.71–3.59 and 3.03; 2.08–4.41, respectively] (Honings *et al.* 2016a). Studies have also reported dose–response relationships with regard to both number of PEs (Nishida *et al.* 2010; Saha *et al.* 2011a; Cederlöf *et al.* 2016) and severity of suicidality (Kelleher *et al.* 2012b; DeVlyder & Hilimire, 2015). Less is known about the association between PEs and non-suicidal self-injury, typically defined as deliberate

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self-injury without suicidal intent (Peterson *et al.* 2008), although two studies report increased risk of non-suicidal self-injury in adolescents (Martin *et al.* 2015) and adults (Koyanagi *et al.* 2015a) with PEs.

The association between PEs and SITB has been well replicated, although underlying mechanisms remain unclear. It may be directly causal where PEs induce self-injurious thoughts or acts via such symptoms as command hallucinations, i.e. voices directing a person to harm themselves (Kelleher *et al.* 2012b). Alternatively, shared risk factors such as depression may result in indirect pathways (see Fig. 1) (Jang *et al.* 2014). A longitudinal study found the PE-suicidality association was only present in those reporting common mental disorders at baseline (Honings *et al.* 2016b), and adding a measure of depressive symptoms to PEs significantly improved prediction of later suicide attempts (Sullivan *et al.* 2015). Conversely, a study of the Adult Psychiatric Morbidity Survey ($n = 7403$) reported the strong association between hallucinations and suicide attempts was independent of common mental disorders such as depression (Kelleher *et al.* 2017). This was somewhat supported by Honings *et al.*'s (2016a) meta-analysis, which found adjusting for depression attenuated but did not negate the PE-SITB association. These studies, however, did not adjust for other co-occurring diagnoses or other confounding factors.

Other potential confounders and mediators (e.g. traumatic experiences, emotional dysregulation) likely play a role in the PE-SITB association (DeVylder *et al.* 2015a), but to date, have been inconsistently investigated: studies have either not adjusted for the same factors (e.g. self-esteem *v.* emotional dysregulation) or not adjusted beyond the more typical variables of sociodemographics, depression, and substance use. In light of these gaps in the literature, we conducted a systematic review and critically analysed third variables (confounders, mediators) that have been examined to date which influence the PE-SITB relationship.

This review aimed to elucidate the role of confounding and mediating factors in the association between PEs and SITB. Specifically, we aimed to extend previous work (Honings *et al.* 2016a) by: (1) including additional studies that have been subsequently published or initially omitted; (2) improving definitions and categorisation of SITB types; (3) presenting associations between SITB and different types of PEs, as well as different populations (adolescent *v.* adult); and (4) systematically examining different types of confounders and mediators not considered in the previous review. In conducting this review, we also identified gaps in the literature where potential mechanisms for the PE-SITB association have yet to be investigated, so as to guide future research.

Methods

Data sources

This systematic review adhered to the PRISMA Guidelines (Moher *et al.* 2009). An electronic literature search was initially conducted in January 2017, which covered relevant international databases, including PubMed, PsycINFO and EMBASE (final search conducted in May 2017). Additional records were identified through citation databases, such as the Web of Science and Scopus, as well as through Google Scholar. Reference lists of included articles were also hand-searched. Authors of included articles were contacted to obtain further details about their analyses.

Definitions

Self-injurious thoughts and behaviours

SITB were defined as actions where an individual deliberately initiates a non-socially or culturally sanctioned behaviour that, without intervention from others, will harm or injure their own body tissue (St. Germain & Hooley, 2012; Larkin *et al.* 2014), as well as thoughts about harming oneself or ending one's life (Nock *et al.* 2007). This definition is consistent with the WHO/EURO multicentre study on self-harm (Platt *et al.* 1992; Hawton *et al.* 2003), and was incorporated to investigate how PEs relate to a wide spectrum of distinct but overlapping self-injury-related constructs.[†] The separation of self-injurious thoughts from behaviours is recommended as they have distinct prevalence rates, functions, correlates, and outcomes (Klonsky *et al.* 2016). For this reason, SITB was divided into two categories. The first was self-harming and suicidal ideation, which included all cognitions (thoughts, feelings, plans) about self-harm and suicide, without engagement in self-injurious behaviour. No study specifically captured self-harming thoughts² and therefore this category was titled 'suicidal ideation'.

The second category was labelled non-accidental self-injury (NASI) and included non-suicidal self-injury, deliberate self-harm (with/without suicidal intent), and suicide attempt. There is expanding evidence for the Gateway Theory (Kapur *et al.* 2013; Whitlock *et al.* 2013), which proposes that non-suicidal self-injury and fatal suicide sit at two ends of the same spectrum, with non-suicidal self-injury being an antecedent to suicide (Linehan, 1986; Stanley *et al.* 1992). Some of the evidence includes considerable overlap in risk factors of non-suicidal and suicidal behaviour (Grandclerc *et al.* 2016), comparable prevalence rates of non-suicidal self-injury and deliberate self-harm

[†] The notes appear after the main text.

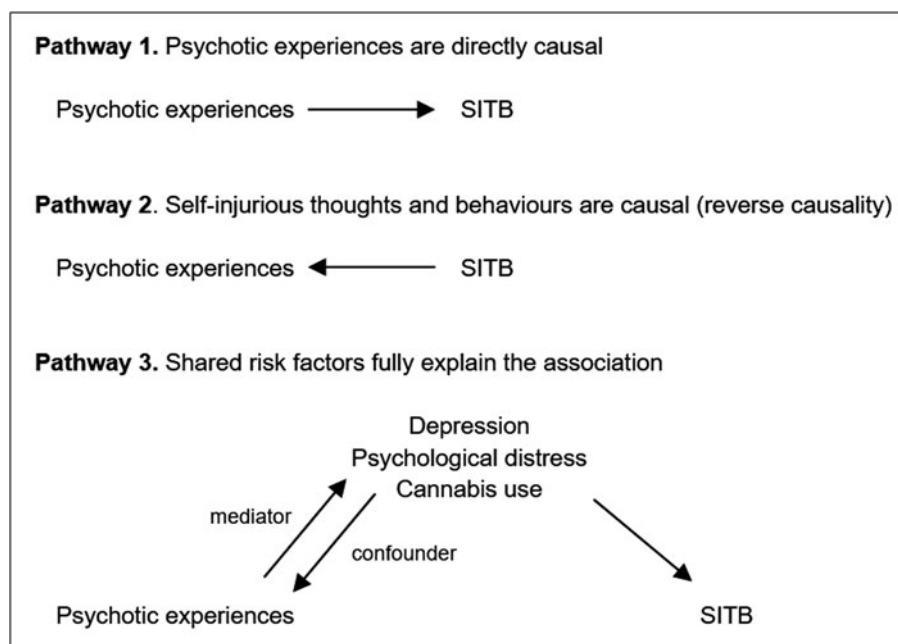


Fig. 1. Three potential pathways to explain the association between psychotic experiences and self-injurious thoughts and behaviours (SITB).

(Muehlenkamp *et al.* 2012), and in prospective studies, non-suicidal self-injury is one of the more robust predictors of suicide attempts (Guan *et al.* 2012; Scott *et al.* 2015). Following the evidence, in this review we presented NASI as a construct that does not assume or preclude suicidal intent. It includes behaviours on a continuum of suicidal intent, ranging from non-suicidal self-injury to suicide attempt, as opposed to discrete intent categories.

Psychotic experiences

PEs were defined as hallucinations and delusions (e.g. persecution, referential and grandiose) endorsed by individuals in the general population that do not occur in the context of sleep or substance use (Johns *et al.* 2004; Linscott & van Os, 2013). They may be appraised as clinically relevant symptoms or as sub-clinical/subthreshold experiences, not prompting help-seeking behaviour (Linscott & van Os, 2010). Although phenotypically PEs lie on a continuum with psychotic disorders, most with PEs do not transition to psychosis (Yung & Lin, 2016). More commonly, PEs are associated with a broader range of adverse health and social outcomes (McGrath *et al.* 2016; Saha *et al.* 2011b).

Eligibility criteria

Inclusion criteria were studies that: (a) were peer-reviewed and published in English language, from inception until May 2017; (b) measured both SITB and PEs; (c) reported on the PE–SITB association;

and (d) were conducted in a general population or non-clinical community sample.

Exclusion criteria were studies limited to: (a) body modification (i.e. cutting, piercing, tattooing) as a cultural practice or expression of creativity; (b) assisted suicide by a physician; (c) indirect forms of self-injurious behaviour (e.g. binge-drinking, excessive exercise); (d) skin picking or hair pulling³; (e) self-injurious behaviour arising in those with development disorder; (f) studies conducted in clinical, mental health or help-seeking populations; or (g) assessment of schizotypy and related personality assessments.⁴

Search strategy

A literature search was conducted in PubMed, PsycINFO and EMBASE⁵ using the following terms: (psychotic exp* OR subclinical psych* OR psychotic-like OR delusion* OR hallucinat*) AND (self-injur* OR self-harm* OR suic*). Search terms were sourced from Honings *et al.*'s (2016a) review, as well as other systematic reviews on PEs (Kaymaz *et al.* 2012; Linscott & van Os, 2010, 2013) and SITB (Larkin *et al.* 2014; Taylor *et al.* 2015; Zetterqvist, 2015). See online Supplementary Material I for full PubMed search.

Data extraction

One author (EH) located eligible studies using the search strategy and downloaded these into EndNote. Titles and abstracts were screened, with at least 10% done independently by two authors (EH and SS)

against the predefined inclusion criteria. A similar process was undertaken for the full-text screen. Data on study design, SITB and PEs measurement, third variables, and key findings were extracted and entered into an excel template by EH.

Data synthesis and confounder analysis

The literature was critically reviewed by narrative synthesis of aggregate-level data. Due to the wide range of third variables measured, and the fact that most studies simultaneously adjusted for multiple variables, meta-analysis was precluded. Potential confounders and mediators were examined using a protocol developed for analysis of epidemiologic studies of parental smoking (Witorsch & Witorsch, 1993). The key aims of our analysis were to determine: (1) which potential confounders/mediators have been considered; (2) frequency at which confounders/mediators have been considered; and (3) whether these variables influenced the PE–SITB relationship.

Considering the variability of third variables, they were grouped into seven higher-level categories: sociodemographics, mental disorders, alcohol and substance use, environmental (e.g. trauma), psychological, intervention, and family history/genetic factors. These categories were derived from extracted data of included studies, as well as known risk factors in the broader self-harm and suicide literature (Klonsky, 2007; Franklin et al. 2017). We examined the influence of these seven categories on: (1) suicidal ideation, and (2) NASI, which was further divided into non-suicidal self-injury, deliberate self-harm and suicide attempt. Despite substantial overlap between risk factors for non-suicidal self-injury and suicide attempts (Grandclerc et al. 2016), it was important to investigate these constructs separately, as some variables may be important for the association between PEs and one self-injurious outcome but not the other.

We labelled all seven categories as confounders, as this was how most studies described these variables. However, some of these variables are mediators, which explain the association between PEs and SITB. Online Supplementary Material II presents a more detailed discussion of each category, and we further address this in the 'Discussion'.

Results

Characteristics of included studies

The systematic search strategy identified 38 individual studies (from 41 publications) reporting on 1 39 427 participants ($M = 3873$, range = 66–16 131) from 16 countries (see Fig. 2). Most studies were cross-sectional (73.7%), with ten reporting longitudinal data (follow-up

range = 3 months–27 years). There was a mixture of data sources: 26.3% of studies reporting national household surveys, 15.8% reporting birth cohorts, and the remainder (57.9%) reporting community samples, e.g. high school and university students. Seven of the 41 publications performed analyses on the same three datasets (see Fig. 2). Because the authors presented different variables of interest (e.g. ideation *v.* attempts) and adjusted for different confounders, the remaining results section presents the literature in terms of number of publications, as opposed to individual studies/datasets.

Most studies ($n = 24$; 58.5%) reported aggregated PEs, as opposed to the association with individual symptoms (e.g. visual hallucinations). All but one study (Kelleher et al. 2012b)⁶ reported on different types of SITB separately. The level of adjustment varied across studies (see Tables 1 and 2), with 11 (26.8%) not controlling for any confounding variables. Only one study (Jang et al. 2014) treated their third variable of interest (depressive symptoms) as a mediating variable.

PEs and suicidal ideation

When broken down by SITB outcomes, 23 studies reported the PE–suicidal ideation association after adjustment for confounders; with just over half (52.2%) confined to an adolescent and/or young adult sample (see Table 3). Three of 23 studies reported the association between suicidal ideation and different types of PEs, yielding mixed findings (Nishida et al. 2010; Capra et al. 2015; Koyanagi et al. 2015b). Most ($n = 14$; 60.9%) controlled for three confounder categories or less, with demographics, mental disorders and/or substance use most common. Only two cross-sectional studies controlled for six out of the seven confounder categories (Nishida et al. 2008; DeVlyder et al. 2015a). Adjusting for these confounders attenuated the strength of the PE–suicidal ideation association (OR range = 1.03–2.10, $p < 0.05$) compared with unadjusted associations and associations found in most other studies.

PEs and NASI

Table 4 outlines the studies ($n = 20$; non-suicidal self-injury = 2, deliberate self-harm = 4, suicide attempt = 15) reporting the PE–NASI association, adjusted for confounders. All deliberate self-harm studies focused on adolescents, non-suicidal self-injury studies equally covered adolescents and adults, whereas most suicide attempt studies ($n = 10$; 66.7%) reported adult populations. Four of 20 studies compared the association of NASI with different PEs, and all found individual PEs were differentially associated with all three NASI

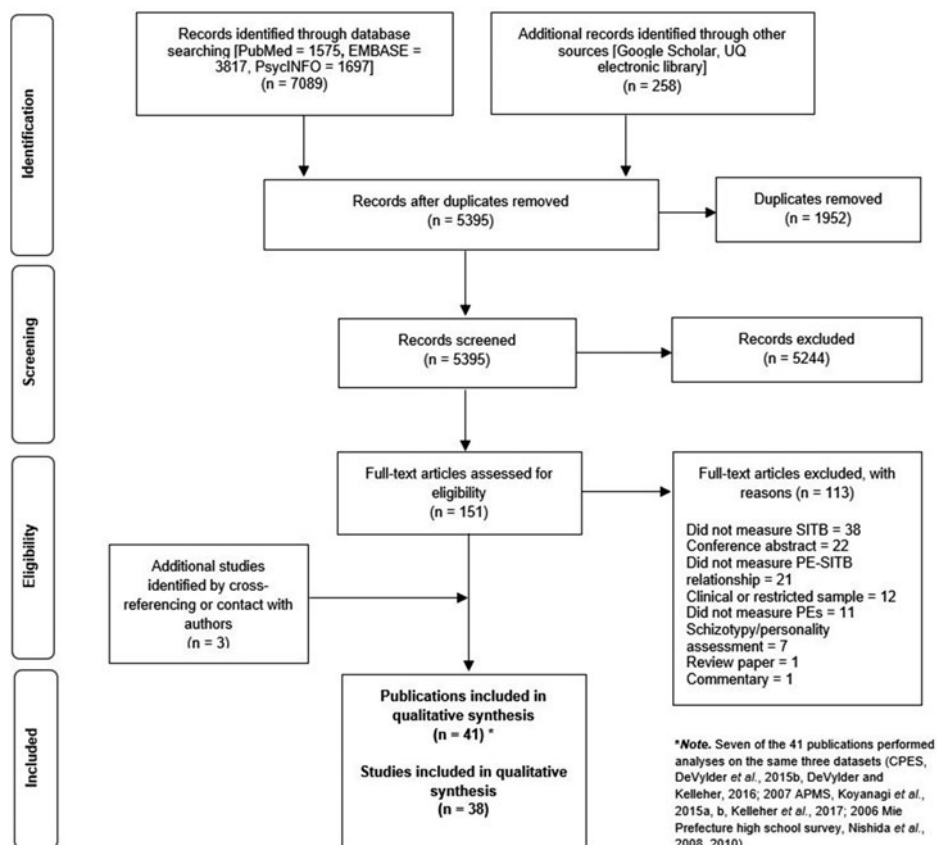


Fig. 2. PRISMA flow chart of literature search.

outcomes (Nishida *et al.* 2010; Capra *et al.* 2015; Koyanagi *et al.* 2015a, b). Similar to suicidal ideation studies, most NASI studies ($n = 15$; 75.0%) controlled for three or less confounder categories, with demographics, mental disorders and substance use again the most common (see Table 4). Only two studies controlled for six of seven confounder categories, reporting barely significant associations between both deliberate self-harm (OR 1.37, 95% CI 1.00–1.86, Nishida *et al.* 2008) and suicide attempts (OR 1.01, 95% CI 0.98–1.04, DeVlyder *et al.* 2015a) with PEs. Each confounder category is further discussed below with reference to all SITB outcomes.

Sociodemographics

Most studies ($n = 28$; 68.3%) adjusted for sociodemographics, incorporating diverse variables ranging from age and sex to sexual orientation and employment status. Four studies (9.8%) presented point estimates of the PE–SITB relationship after adjusting for demographics (see Tables 3 and 4) and associations remained significant (OR range: 2.07–7.79). Further adjustment for such variables as mental disorders and substance use substantially attenuated the strength of the association (OR range: 2.49–3.37; Fisher *et al.*

2013; DeVlyder *et al.* 2015b), with some estimates becoming non-significant (OR range: 1.32–1.60; Nishida *et al.* 2014; Honings *et al.* 2016b), suggesting considerable residual confounding when only sociodemographics were included in the model.

Mental disorders

Less than half of the studies ($n = 20$; 48.8%) adjusted for mental disorders, most commonly depression (12-month or lifetime diagnosis, episode, or symptoms), anxiety disorders and mixed anxiety/depression diagnosis. Five studies controlled for mental disorders individually, or in separate steps in their models (Polanczyk *et al.* 2010; Fisher *et al.* 2013; Koyanagi *et al.* 2015a; Honings *et al.* 2016b; Kelleher *et al.* 2017). Most studies adjusting for comorbid depressive symptoms and common mental disorders (depression, anxiety, personality disorders) reported reduced ORs, but the PE–SITB association remained significant (OR range: 2.00–3.20; Polanczyk *et al.* 2010; Fisher *et al.* 2013; Kelleher *et al.* 2017). This was somewhat supported by Honings *et al.*'s (2016a) meta-analysis, where they included only studies that controlled for depression and found an attenuated (but significant) pooled OR for all SITB outcomes except deliberate self-harm (OR for SITB = 2.02, 95% CI

Table 1. Frequency of consideration of potential confounders in studies examining the association between psychotic experiences and self-injurious thoughts and behaviours

| Confounder no. | Potential confounder ^a | Studies (41 total) |
|----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| 1. | Sociodemographics <ul style="list-style-type: none"> Sex, age, race/ethnicity, years of education (participant and parents), marital status, income (participant and household or family), migrant status (participant and parents), socioeconomic status of family and neighbourhood, urbanicity, sexual orientation, employment status, country of birth (participant and parents), family structure (i.e. living apart from one or both parents), household type, primary language, English language proficiency, school grade, religious/spiritual affiliation | Twenty-eight (68.3% of studies) |
| 2. | Mental disorders <ul style="list-style-type: none"> Depression (symptoms, episode and diagnosed disorder; both 12 months and lifetime), any anxiety disorder and mixed anxiety/depression (symptoms and diagnosed disorder; past month, 12 months, and lifetime), generalised anxiety disorder, phobic disorder or phobia (specific and social), panic disorder, obsessive-compulsive disorder, lifetime mood (depression, mania), borderline personality (symptoms and diagnosed disorder), agoraphobia, behavioural disorders (ADHD, oppositional defiant, conduct), internalising/externalising psychopathology, eating disorders (anorexia and bulimia nervosa), somatisation, separation anxiety, PTSD, schizophrenia spectrum disorders, bipolar disorder, antisocial personality disorder, self-induced vomiting for dieting purposes, ataque de nervios, count of lifetime psychiatric disorders, self-reported mental health | Twenty (48.8% of studies) ^b |
| 3. | Alcohol and substance use <ul style="list-style-type: none"> Alcohol and substance use (cannabis, ecstasy, methamphetamines, amphetamines, cocaine, opiates, hallucinogens, sedatives, tranquilisers, amyl nitrate, anabolic steroids, glues, cigarettes, polysubstance; past month, 12 months, and lifetime), alcohol use disorder (past 6 months, 12 months and lifetime), other substance use disorder (both 12 months and lifetime), any substance (alcohol/drug) use disorder (lifetime), hazardous drinking | Fifteen (36.6% of studies) |
| 4. | Environmental factors <ul style="list-style-type: none"> Stressful and traumatic life events (e.g. death of a family member, raped or assaulted), history of bullying and victimisation (past 12 months and lifetime), violence from adults in the home (past month), total support group (i.e. size of support group), history of childhood trauma (sexual, physical), school mobility (no. of schools attended between kindergarten and high school graduation), school problems, bullying others/physically assaulting others (past 12 months), family relationship/support, time spent watching television or using personal computers | Ten (24.4% of studies) |
| 5. | Psychological factors <ul style="list-style-type: none"> Psychological distress (GHQ-12), self-esteem (Rosenberg Self-Esteem Scale), stress (Psychological Stress Index), emotional regulation (suppression and reappraisal), irritability when exchanging emails (past week), trait anger (Anger Expression Inventory), self-awareness of mental distress, stereotype awareness (i.e. mental illness stigma), difficulty falling asleep due to hypersensitivity to noises (past month), difficulty concentrating due to hypersensitivity to noises (past month), interpersonal sensitivity, hostility, WRAT-4 reading score, preference for being alone or with others | Nine (21.9% of studies) |
| 6. | Intervention factors <ul style="list-style-type: none"> Hospitalisation admissions (lifetime psychiatric and general), current contact with medical services, ever talked with professional (school counsellor, psychologist, social work, psychiatrist or other) for feelings or problems with mood or behaviour, current help-seeking behaviour (both with professionals and non-professionals, e.g. friends), lifetime psychiatric medication | Five (12.2% of studies) |
| 7. | Family history/genetic factors <ul style="list-style-type: none"> Family history of mental illness | Two (4.9% of studies) |

Note: All confounders in eligible studies were captured in this table, except for Children's Global Assessment Scale (OR 0.96, 95% CI 0.95–0.97, Calkins *et al.* 2014, 2017), self-reported physical health (OR 0.88, 95% CI 0.60–1.29), and count of lifetime chronic medical conditions (OR 1.20, 95% CI 1.06–1.33; Lewis-Fernández *et al.* 2009). None of these variables fitted our confounder categorisation, and most did not significantly contribute to the fully adjusted models.

^a Confounders are ordered according to how frequently they appear in the literature, both within and across categories.

^b Four of the studies included depressive symptoms only.

Table 2. Consideration of potential confounding variables in studies examining the relationship between psychotic experiences and self-injurious thoughts and behaviours

| Study | Confounder no. ^a | | | | | | |
|------------------------------------------------|-----------------------------|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Calkins <i>et al.</i> (2014) | + | + | – | – | + | + | – |
| Calkins <i>et al.</i> (2017) | + | + | – | + | + | + | – |
| Capra <i>et al.</i> (2015) | + | – | + | – | – | – | + |
| Cederlöf <i>et al.</i> (2016) | – | – | – | – | – | – | – |
| Connell <i>et al.</i> (2016) | + | – | + | – | – | – | – |
| DeVylder <i>et al.</i> (2015a) | + | + | + | + | + | – | + |
| DeVylder <i>et al.</i> (2015b) | + | + | + | – | – | – | – |
| DeVylder <i>et al.</i> (2015c) | – | – | – | – | – | – | – |
| DeVylder & Hilimire (2015) | + | – | – | – | + | – | – |
| DeVylder & Kelleher (2016) | + | – | + | – | – | – | – |
| Engin <i>et al.</i> (2009) | + | + | – | + | + | – | – |
| Fisher <i>et al.</i> (2013) | + | + | – | – | – | – | – |
| Freeman <i>et al.</i> (2011) | – | – | – | – | – | – | – |
| Gatta <i>et al.</i> (2016) | – | – | – | – | – | – | – |
| Honings <i>et al.</i> (2016b) | + | + | – | – | – | – | – |
| Jang <i>et al.</i> (2014) | + | + | – | – | – | – | – |
| Jenkins <i>et al.</i> 2015) | + | + | – | + | – | – | – |
| Kelleher <i>et al.</i> (2012b) ^{b, d} | + | – | – | – | – | – | – |
| Kelleher <i>et al.</i> (2012b) ^{c, d} | + | – | – | – | – | – | – |
| Kelleher <i>et al.</i> (2013a) ^d | + | – | + | – | – | – | – |
| Kelleher <i>et al.</i> (2014) | + | + | + | – | – | – | – |
| Kelleher <i>et al.</i> (2017) | – | + | – | – | – | – | – |
| Kerr & Muehlenkamp (2010) | – | – | – | – | – | – | – |
| Koyanagi <i>et al.</i> (2015a) | + | + | + | + | – | – | – |
| Koyanagi <i>et al.</i> (2015b) | + | + | + | + | – | – | – |
| Krabbendam <i>et al.</i> (2004) | – | – | – | – | – | – | – |
| Lewis-Fernández <i>et al.</i> (2009) | + | + | + | + | – | – | – |
| Martin <i>et al.</i> (2015) | + | – | – | – | + | – | – |
| Nishida <i>et al.</i> (2008) | + | + | + | + | + | + | – |
| Nishida <i>et al.</i> (2010) | + | – | + | + | + | – | – |
| Nishida <i>et al.</i> (2014) | + | – | – | – | + | + | – |
| Núñez <i>et al.</i> (2016) | – | – | – | – | – | – | – |
| Olfson <i>et al.</i> (1996) | – | – | – | – | – | – | – |
| Olfson <i>et al.</i> (2002) | + | + | + | – | – | – | – |
| Östling & Skoog (2002) | – | – | – | – | – | – | – |
| Östling <i>et al.</i> (2007) | – | – | – | – | – | – | – |
| Polanczyk <i>et al.</i> (2010) | – | + | – | – | – | – | – |
| Saha <i>et al.</i> (2011a) | + | + | + | + | – | – | – |
| Sharifi <i>et al.</i> (2015) | + | + | + | – | – | + | – |
| Sullivan <i>et al.</i> (2015) | + | + | – | – | – | – | – |
| Temmingh <i>et al.</i> (2011) | + | – | – | – | – | – | – |
| Zhang <i>et al.</i> (2016) | – | – | – | – | – | – | – |

+, Indicates the potential confounding variables were considered in a particular study.

^a Corresponds to numbers in Table 1.

^b Adolescent Brain Development (ABD) study reported in Kelleher *et al.* (2012b).

^c Challenging Times (CT) study reported in Kelleher *et al.* (2012b).

^d Confounders adjusted for using a stratified analysis were only considered if stratification was performed as part of the main analysis (i.e. overall estimate for psychotic experiences), and if the authors presented the odds ratios in each strata i.e. with and without the third variable of interest. These two publications did not present such information in their psychiatric disorder/psychopathology stratified subanalysis, and therefore ‘mental disorders’ were not counted in their confounder categorisation.

Table 3. Strength of evidence in studies ($n = 23$) examining the psychotic experiences (PEs) – suicidal ideation relationship, after adjustment for confounders

| Study | N, Age (years) | Design | Temporality | Confounder(s) ^a | Psychotic experience | Outcome measure | Association between PEs and outcome measure |
|--------------------------------------------------------------|---------------------------|--------|-------------|-------------------------------------------|---------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Studies with adolescents and young adults (≤25 years)</i> | | | | | | | |
| Calkins <i>et al.</i> (2014) USA | 4848 11–21 | CS | N/A | 1, 2, 5, 6 | Psychosis spectrum (LT and past year) | LT suicidal ideation | OR 1.45, 95% CI 1.07–1.96 |
| Calkins <i>et al.</i> (2017) USA | 249 14–18 | L | N | 1, 2, 4, 5, 6 | Persistence of psychosis spectrum over 2 years | LT suicidal ideation | OR 0.85, 95% CI 0.37–1.98 |
| Capra <i>et al.</i> (2015) Australia | 1610 $M = 22.1 \pm 5.1$ | CS | N/A | 1, 3, 7 | LT perceptual abnormalities persecutory ideation LT bizarre experiences | LT suicidal ideation | OR 1.30, 95% CI 1.12–1.50 OR 1.26, 95% CI 1.18–1.35 OR 1.00, 95% CI 0.94–1.06 |
| DeVylder & Hilimire (2015) USA | 622 $M = 18.8$ | CS | N/A | 1, 5 | LT auditory hallucinations | LT suicidal ideation LT suicidal plan | OR 1.90, 95% CI 1.19–3.0 OR 2.18, 95% CI 1.00–4.78 |
| Engin <i>et al.</i> (2009) Turkey | 1992 $M = 20.02 \pm 1.54$ | CS | N/A | 1, 2, 4, 5 | Past week psychotic symptoms/ psychoticism | LT suicidal thoughts | OR 1.27, 95% CI 1.11–1.45 |
| Jang <i>et al.</i> (2014) South Korea | 6977 14–19 | CS | N/A | 1, 2 | Current psychotic-like experiences (last 4 weeks) | Current suicidal ideation | Beta coefficient (β) = 0.13. Depressive symptoms partially mediated association ($\beta = 0.56$) |
| Kelleher <i>et al.</i> (2013a) Ireland | 1112 13–16 | L | Y | 1, 3 | LT auditory hallucinations at baseline | Suicidal ideation (often/always during past 2 weeks) at 3-month follow-up Suicidal ideation (often/always during past 2 weeks) at 12-month follow-up | OR 8.79, 95% CI 2.61–29.60 OR 2.55, 95% CI 0.24–27.36 |
| Kelleher <i>et al.</i> (2014) Sweden | 109 16–17; 179 19–20 | L | Y | 1, 2, 3 | 6-month auditory hallucinations at age 13–14 6-month auditory hallucinations at age 16–17 | 6-month suicidal ideation at age 16–17 6-month suicidal ideation at age 19–20 | OR 0.94, 95% CI 0.19–4.78 OR 5.53, 95% CI 1.33–23.0 |
| Nishida <i>et al.</i> (2008) ^b Japan | 4894 12–15 | CS | N/A | 1, 2, 3, 4, 5, 6 | LT psychotic-like experiences | LT suicidal ideation | OR 2.10, 95% CI 1.83–2.41 |
| Nishida <i>et al.</i> (2010) ^b Japan | 4894 12–15 | CS | N/A | 1, 3, 4, 5 | LT any psychotic experiences LT thoughts read LT special messages LT spied-upon LT hearing voices | LT suicidal feelings | OR 3.1, 95% CI 2.2–4.5 OR 2.47, 95% CI 1.40–4.34 OR 1.93, 95% CI 0.83–4.47 OR 2.44, 95% CI 1.87–3.18 OR 2.26, 95% CI 1.79–2.87 |
| Nishida <i>et al.</i> (2014) Japan | 16 131 12–18 | CS | N/A | 1, 6 ^c 1, 5, 6 ^c | LT psychotic-like experiences LT psychotic-like experiences | Current suicidal ideation Current suicidal ideation | OR 3.1, 95% CI 2.2–4.2 OR 2.1, 95% CI 1.5–2.9 |

| | | | | | | | | | |
|-----------------------------------------------------|-------------------------|--------|------------------------|----|-----|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sullivan <i>et al.</i> (2015) | England | 3171 | 12 and 16 | L | N | 1, 2 | 6-month psychotic experiences at age 12 | LT suicidal ideation at age 16 | OR 1.31, 95% CI 0.99–1.73 |
| <i>Studies with adults (≥ 16 years)^d</i> | | | | | | | | | |
| Connell <i>et al.</i> (2016) | Australia | 654 | 30–33 | L | N | 1, 3 | Auditory or visual hallucinations at age 14 | LT suicidal ideation at age 30 | OR 1.44, 95% CI 0.93–2.23 |
| | | | | | | | Auditory or visual hallucinations at age 14 and 21 | LT suicidal plans at age 30 LT suicidal ideation at age 30 | OR 1.30, 95% CI 0.67–2.52 OR 2.89, 95% CI 1.66–5.02 |
| DeVylder <i>et al.</i> (2015b) ^e | USA | 11 716 | 18+ | CS | N/A | 1 | 12-month psychotic experiences | 12-month suicidal ideation | OR 4.25, 95% CI 2.28–7.89 |
| DeVylder <i>et al.</i> (2015a) | USA | 590 | 17–37 | CS | N/A | 1, 2, 3, 4, 5, 7 | 12-month psychotic experiences Past month psychotic experiences | 12-month suicidal ideation LT suicidal ideation | OR 2.49, 95% CI 1.01–6.13 OR 1.03, 95% CI 1.01–1.05 |
| | | | | | | | | LT ideation with intent/plan Intensity of worst-point ideation | OR 1.01, 95% CI 0.98–1.03 <i>t</i> = 1.84, <i>p</i> > 0.05 |
| DeVylder & Kelleher (2016) ^e | USA | 11 776 | 18+ | CS | N/A | 1, 3 | LT psychotic experiences | LT suicidal ideation | OR 2.53, 95% CI 1.85–3.47 |
| Honings <i>et al.</i> (2016b) | Germany and Netherlands | 15 837 | <i>M</i> = 39.4 ± 13.8 | L | Y | 1 | LT psychotic experiences at baseline | Suicidal ideation at 3-year or 5-year follow-up | OR 2.07, 95% CI 1.50–2.87 |
| | | | | | | 1, 2 | LT psychotic experiences at baseline | Suicidal ideation at 3-year or 5-year follow-up | OR 1.32, 95% CI 0.93–1.87 |
| Jenkins <i>et al.</i> (2015) | Kenya | 1133 | <i>M</i> = 42.0 ± 18.1 | CS | N/A | 1, 2, 4 | Past year psychotic symptoms | LT suicidal thoughts | OR 1.4, 95% CI 0.79–2.43 |
| Koyanagi <i>et al.</i> (2015b) ^f | England | 7363 | 16+ | CS | N/A | 1, 4 | 12-month any psychotic symptom 12-month mania/hypomania 12-month thought control 12-month paranoia 12-month strange experience 12-month auditory hallucination | 12-month suicidal ideation | OR 5.47, 95% CI 3.78–7.91 OR 5.21, 95% CI 2.21–12.32 OR 5.74, 95% CI 2.29–14.37 OR 6.72, 95% CI 3.81–11.84 OR 6.09, 95% CI 3.92–9.46 OR 6.54, 95% CI 2.65–16.13 |
| | | | | | | 1, 2, 3, 4 | 12-month any psychotic symptom 12-month mania/hypomania 12-month thought control 12-month paranoia 12-month strange experience 12-month auditory hallucination | 12-month suicidal ideation | OR 3.13, 95% CI 2.09–4.68 OR 4.00, 95% CI 1.41–11.37 OR 4.20, 95% CI 1.65–10.72 OR 4.03, 95% CI 2.31–7.03 OR 3.22, 95% CI 1.95–5.32 OR 4.05, 95% CI 1.76–9.32 |
| Lewis-Fernández <i>et al.</i> (2009) | USA | 2554 | 18+ | CS | N/A | 1, 2, 3, 4 | LT psychotic symptoms 12-month psychotic symptoms | LT suicidal ideation 12-month suicidal ideation | OR 2.30, 95% CI 1.47–3.60 OR 2.04, 95% CI 1.12–3.74 |
| Olfson <i>et al.</i> (2002) | USA | 1005 | 18–70 | CS | N/A | 1, 2, 3 | LT psychotic symptoms | Current suicidal ideation | OR 3.4, 95% CI 1.9–6.1 |
| Saha <i>et al.</i> (2011a) | Australia | 8773 | 18+ | CS | N/A | 1, 2, 3, 4 | LT delusional-like experiences | LT suicidal ideation | OR 2.73, 95% CI 1.89–3.94 |

Table 3 (cont.)

| Study | N, Age (years) | Design | Temporality | Confounder(s) ^a | Psychotic experience | Outcome measure | Association between PEs and outcome measure |
|--------------------------------------------|----------------|--------|-------------|----------------------------|--------------------------------------|-----------------------------------------|--------------------------------------------------------------------|
| Temmingh <i>et al.</i> (2011) South Africa | 4250 18+ | CS | N/A | 1 | LT auditory or visual hallucinations | LT suicide plan LT suicidal ideation | OR 1.96, 95% CI 1.15–3.35 OR 2.44, 95% CI 1.7–3.5 |

CS, cross-sectional; L, longitudinal; Y, yes, temporality considered; N, no, temporality not considered; N/A, not applicable; LT, lifetime; OR, odds ratio; 95% CI, 95% confidence interval.

Bold represents a significant finding.

^a Corresponds to numbers in Table 1.

^b Reports on data from the 2006 Mie Prefecture high school survey.

^c Variable used as stratification variable in the main analysis, e.g. if mental disorder was the stratification variable, we reported on the influence of psychotic experiences on SITB within the 'no mental disorders' strata.

^d The adult category (16+) overlaps with the adolescent and young adult category (≤ 25) because most general population samples range from 16 (or 18) to 95 years.

^e Reports on data from the Collaborative Psychiatric Epidemiology Surveys (CPES).

^f Reports on data from the 2007 Adult Psychiatric Morbidity Survey (APMS).

Table 4. Strength of evidence in studies (n=20) examining the psychotic experiences (PEs) – non-accidental self-injury (NASI) relationship, after adjustment for confounders

| Study | N, Age (years) | Design | Temporality | Confounder(s) ^a | Psychotic experience | Outcome measure | Association between PEs and outcome measure |
|----------------------------------------------------------------------------------------------------------------------------|-----------------------------|--------|-------------|----------------------------|----------------------------------------|---------------------------------------------------|---------------------------------------------------------------|
| <i>Non-suicidal self-injury [NSSI; studies with adolescents and young adults (<=25 years)]</i> | | | | | | | |
| Martin <i>et al.</i> (2015) | Australia 1896 12–17 | L | Y | 1, 5 ^b | LT psychotic experiences at baseline | LT NSSI at baseline NSSI at 12-month follow-up | OR 2.88, 95% CI 1.51–5.49 OR 1.63, 95% CI 0.73–3.64 |
| <i>Non-suicidal self-injury [NSSI; studies with adults (>=16 years)]^c</i> | | | | | | | |
| Koyanagi <i>et al.</i> (2015a) ^d | England 7363 16+ | CS | N/A | 1, 4 | 12-month any psychotic-like experience | LT NSSI | OR 2.78, 95% CI 1.88–4.11 |
| | | | | | 12-month mania/hypomania | | OR 2.85, 95% CI 0.98–8.23 |
| | | | | | 12-month thought control | | OR 2.45, 95% CI 1.05–5.74 |
| | | | | | 12-month paranoia | | OR 3.57, 95% CI 1.96–6.52 |
| | | | | | 12-month strange experience | | OR 3.13, 95% CI 1.99–4.93 |
| | | | | 1, 2, 3, 4 | 12-month auditory hallucination | | OR 4.03, 95% CI 1.56–10.42 |
| | | | | | 12-month any psychotic-like experience | LT NSSI | OR 1.30, 95% CI 0.83–2.04 |
| | | | | | 12-month mania/hypomania | | OR 1.13, 95% CI 0.34–3.74 |
| | | | | | 12-month thought control | | OR 1.19, 95% CI 0.39–3.63 |
| | | | | | 12-month paranoia | | OR 2.02, 95% CI 1.03–3.96 |
| | | | | | 12-month strange experience | | OR 1.27, 95% CI 0.73–2.20 |
| | | | | | 12-month auditory hallucination | | OR 2.23, 95% CI 0.75–6.65 |
| <i>Deliberate self-harm [DSH; with/without suicidal intent; studies with adolescents and young adults (<=25 years)]</i> | | | | | | | |
| Nishida <i>et al.</i> (2008) ^e | Japan 4894 12–15 | CS | N/A | 1, 2, 3, 4, 5, 6 | LT psychotic-like experiences | Past year self-harming behaviours | OR 1.37, 95% CI 1.00–1.86 |
| Nishida <i>et al.</i> (2010) ^e | Japan 4894 12–15 | CS | N/A | 1, 3, 4, 5 | LT any psychotic experience | Past year DSH | OR 3.1, 95% CI 2.0–4.8 |
| | | | | | LT thoughts read | | OR 1.56, 95% CI 0.71–3.43 |
| | | | | | LT special messages | | OR 1.62, 95% CI 0.48–5.50 |
| | | | | | LT spied-upon | | OR 1.93, 95% CI 1.34–2.77 |
| | | | | | LT hearing voices | | OR 2.32, 95% CI 1.67–3.22 |
| Nishida <i>et al.</i> (2014) | Japan 16 131 12–18 | CS | N/A | 1, 6 ^b | LT psychotic-like experiences | 12-month DSH | OR 2.1, 95% CI 1.1–3.9 |
| | | | | 1, 5, 6 ^b | LT psychotic-like experiences | 12-month DSH | OR 1.6, 95% CI 0.8–3.1 |
| Polanczyk <i>et al.</i> (2010) | England and Wales 2232 12 | CS | N/A | 2 | LT psychotic symptoms at age 12 | LT DSH at age 12 (parent response) | OR 2.0, 95% CI 1.0–3.9 |
| <i>Suicide attempt [studies with adolescents and young adults (<=25 years)]</i> | | | | | | | |
| Capra <i>et al.</i> (2015) | Australia 1610 M=22.1 ± 5.1 | CS | N/A | 1, 3, 7 | LT perceptual abnormalities | LT suicidal attempt | OR 1.61, 95% CI 1.32–1.97 |
| | | | | | LT persecutory Ideation | | OR 1.34, 95% CI 1.26–1.54 |
| | | | | | LT bizarre Experiences | | OR 0.92, 95% CI 0.84–1.02 |

Table 4 (cont.)

| Study | N, Age (years) | Design | Temporality | Confounder(s) ^a | Psychotic experience | Outcome measure | Association between PEs and outcome measure |
|------------------------------------------------|------------------------|--------|-------------|----------------------------|------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| DeVylder & Hilimire (2015) USA | 622 M = 18.8 | CS | N/A | 1, 5 | LT auditory hallucinations | LT suicide attempt | OR 3.99, 95% CI 1.37–11.61 |
| Kelleher et al. (2013a) Ireland | 1112 13–16 | L | N | 1, 3 | LT auditory hallucinations at baseline | LT suicide attempt at 3-month follow-up LT suicide attempt at 12-month follow-up | OR 10.01, 95% CI 2.24–45.49 OR 11.27, 95% CI 4.44–28.62 |
| Martin et al. (2015) Australia | 1896 12–17 | L | Y | 1, 5 ^b | LT psychotic experiences at baseline | LT attempted suicide at baseline Attempted suicide at 12-month follow-up | OR 3.31, 95% CI 0.55–19.94 OR 1.65, 95% CI 0.33–8.26 |
| Sullivan et al. (2015) England | 3171 12 and 16 | L | N | 1, 2 | 6-month psychotic experiences at age 12 | LT suicide attempt at age 16 | OR 1.75, 95% CI 1.20–2.54 |
| Connell et al. (2016) Australia | 654 30–33 | L | N | 1, 3 | Auditory or visual hallucinations at age 14 | LT suicide attempt at age 30 | OR 2.63, 95% CI 1.04–6.63 |
| DeVylder et al. (2015b) ^f USA | 11 716 18+ | CS | N/A | 1, 2, 3 | 12-month psychotic experiences | 12-month suicide attempt | OR 7.79, 95% CI 2.97–20.41 |
| DeVylder et al. (2015a) USA | 590 17–37 | CS | N/A | 1, 2, 3, 4, 5, 7 | 12-month psychotic experiences Past month psychotic experiences | 12-month suicide attempt LT suicidal behaviours (attempts, aborted or interrupted) | OR 3.37, 95% CI 1.17–9.70 OR 1.01, 95% CI 0.98–1.04 |
| DeVylder & Kelleher (2016) ^f USA | 11 776 18+ | CS | N/A | 1, 3 | LT psychotic experiences | LT suicide attempt | OR 3.47, 95% CI 1.56–7.75 |
| Fisher et al. (2013) New Zealand | 1037 11 and 38 | L | Y | 1, 2 | LT psychotic symptoms at age 11 LT psychotic symptoms at age 11 | Past year suicide attempts/completes at age 38 Past year suicide attempts/completes at age 38 | RR 3.82, 95% CI 1.67–8.75 RR 2.58, 95% CI 1.10–6.08 |
| Honings et al. (2016b) Germany and Netherlands | 15 837 M = 39.4 ± 13.8 | L | Y | 1, 2 | LT psychotic experiences at baseline LT psychotic experiences at baseline | Suicide attempt at 3-year or 5-year follow-up Suicide attempt at 3-year or 5-year follow-up | OR 3.95, 95% CI 1.85–8.43 OR 3.44, 95% CI 1.54–7.69 |
| Jenkins et al. (2015) Kenya | 1133 M = 42.0 ± 18.1 | CS | N/A | 1, 4 | Past year psychotic symptoms | LT suicide attempt | OR 5.1, 95% CI 2.00–13.03 |

| | | | | | | | |
|--------------------------------------------------------|------------|----|-----|----------------|---------------------------------------------|--------------------------|------------------------------------|
| Kelleher <i>et al.</i> (2017) ^d England | 7403 16–95 | CS | N/A | 2 ^b | Past year auditory or visual hallucinations | LT suicide attempt | OR 3.20, 95% CI 1.71–5.98 |
| Koyanagi <i>et al.</i> (2015b) ^d England | 7363 16+ | CS | N/A | 1, 4 | 12-month any psychotic symptom | 12-month suicide attempt | OR 6.52, 95% CI 2.84–14.95 |
| | | | | | 12-month mania/hypomania | | OR 15.67, 95% CI 3.40–72.14 |
| | | | | | 12-month thought control | | OR 2.88, 95% CI 0.71–11.69 |
| | | | | | 12-month paranoia | | OR 19.06, 95% CI 7.48–48.58 |
| | | | | | 12-month strange experience | | OR 6.58, 95% CI 2.57–16.85 |
| | | | | 1, 2, 3, 4 | 12-month auditory hallucination | | OR 6.14, 95% CI 1.36–27.76 |
| | | | | | 12-month any psychotic symptom | 12-month suicide attempt | OR 3.84, 95% CI 1.67–8.83 |
| | | | | | 12-month mania/hypomania | | OR 10.23, 95% CI 2.23–46.93 |
| | | | | | 12-month thought control | | OR 1.71, 95% CI 0.45–6.49 |
| | | | | | 12-month paranoia | | OR 9.89, 95% CI 3.48–28.11 |
| | | | | | 12-month strange experience | | OR 3.95, 95% CI 1.44–10.85 |
| | | | | | 12-month auditory hallucination | | OR 5.84, 95% CI 1.25–27.21 |
| Saha <i>et al.</i> (2011a) Australia | 8773 18+ | CS | N/A | 1, 2, 3, 4 | LT delusional-like experiences | LT suicide attempt | OR 2.77, 95% CI 1.58–4.85 |

CS, cross-sectional; L, longitudinal; Y, yes, temporality considered; N, no, temporality not considered; N/A, not applicable; LT, lifetime; OR, odds ratio; RR, relative risk; 95% CI, 95% confidence interval.

Bold represents a significant finding.

^a Corresponds to numbers in [Table 1](#).

^b Variable used as stratification variable in the main analysis, e.g. if mental disorder was the stratification variable, we reported on the influence of psychotic experiences on SITB within the ‘no mental disorders’ strata.

^c The adult category (16+) overlaps with the adolescent and young adult category (≤ 25) because most general population samples range from 16 (or 18) to 95 years.

^d Reports on data from the 2007 Adult Psychiatric Morbidity Survey (APMS).

^e Reports on data from the 2006 Mie Prefecture high school survey.

^f Reports on data from the Collaborative Psychiatric Epidemiology Surveys (CPES).

2.33–4.40). However, most studies controlled for a number of confounders simultaneously, making it difficult to interpret the proportion of the PE–SITB relationship attributable to depression.

Analyses stratified by presence of mental disorder provided further insight. A longitudinal study reported the association was only present in the subsample of participants with PEs who reported mental disorders at baseline (Honings *et al.* 2016b). By contrast, other cross-sectional and longitudinal studies found the PE–SITB relationship persisted even when the sample was restricted to those without mental disorders (Saha *et al.* 2011a; Sullivan *et al.* 2015; Kelleher *et al.* 2017). Mental disorders consistently explain, in part, the PE–SITB association, although the association is frequently evident even in those without mental illness endorsing PEs.

Alcohol and substance use

Almost 40% of studies adjusted for substance use, most controlling for past 12 month or lifetime substance use as opposed to abuse or dependence. Substance use was typically adjusted for in the same step as mental disorders preventing any conclusions about their role in the PE–SITB relationship. Alcohol and cannabis use were not significant contributors in DeVlyder *et al.*'s (2015a) fully adjusted model, whereas Capra *et al.* (2015) found lifetime cannabis use was a significant predictor in both suicidal ideation and attempts models (β -coefficient range: 0.10–0.18). The strong association between substance use and both suicidality (Vijayakumar *et al.* 2011) and PEs (Rognli *et al.* 2017) suggests it may be important in the PE–SITB relationship.

Environmental factors

Although traumatic life events are associated with both suicidality and PEs (Scott *et al.* 2007; Kelleher *et al.* 2013b), fewer than 25% of studies adjusted for these and no study independently controlled for such factors. In DeVlyder *et al.*'s (2015a) fully adjusted models, bullying, school mobility and childhood sexual trauma were key variables, resulting in large attenuation of all suicidal outcomes with only broadly defined suicidal ideation remaining significant (OR 1.03, 95% CI 1.01–1.05). Although PEs and suicidal behaviour appear to co-occur in the context of severe social stressors, these environmental exposures did not entirely account for the PE-suicidality association (β -coefficient range: 0.19–2.23).

Psychological factors

Psychological factors (e.g. psychological distress) were adjusted for in 21.9% of studies. Martin *et al.* (2015)

found PEs, in the absence of psychological distress, were not associated with increased risk of future non-suicidal self-injury and suicide attempts (OR range: 1.63–1.65). The only other study independently controlling for psychological distress (Nishida *et al.* 2014) reported attenuated ORs of deliberate self-harm and suicidal ideation in those with PEs, with only suicidal ideation remaining significant (OR 2.1, 95% CI 1.5–2.9). Some suggest that PEs are manifestations of distress (Saha *et al.* 2011a; Koyanagi *et al.* 2015b). DeVlyder *et al.* (2015a) investigated other psychological factors such as self-esteem and stereotype awareness (i.e. mental illness stigma), which explained a significant amount of variance between PEs and intensity of suicidal ideation (β -coefficient range: 0.10–0.29), but did not entirely account for the relationship.

Intervention factors

Only five studies adjusted for intervention factors, including hospitalisation history and help-seeking behaviour. Only Nishida *et al.* (2014) individually adjusted for such factors, by stratifying their sample by help-seeking. Risk of both suicidal ideation and deliberate self-harm were highest among non-help-seeking adolescents (who had a need for care) with PEs; however, the PE–SITB relationship persisted regardless of help-seeking status.

Family history/genetic factors

Only two studies adjusted for family history of mental illness (Capra *et al.* 2015; DeVlyder *et al.* 2015a), with both simultaneously adjusting for multiple confounders; however, family history explained little of the variance.

Discussion

There is consistent evidence that PEs are an important clinical indicator of suicide risk. However, no study has explained if the relationship is causal or if their co-occurrence arises from shared risk factors. This distinction is critical to inform the clinical assessment and interventions for those with PEs. In this review, almost 30% of all general population and community sample studies did not adjust for any confounding variables, possibly resulting in an assumption that SITB is directly attributable to PEs, without taking into consideration factors which confound or mediate this association (see confounder *v.* mediator discussion below). In the majority of studies, where adjustment for confounders occurred, the association persisted albeit with attenuated effect sizes, suggesting PEs are independently associated with self-harm and suicidality, in both adolescent and adult populations. There

was high variability in the confounders adjusted for in these studies, with less than half controlling for mental disorders, and less than one-quarter controlling for environmental and psychological factors. Because most studies simultaneously adjusted for multiple variables, no conclusions could be reached as to the influence of an individual factor. However, mental disorders, environmental and psychological factors explained a substantial amount of the variance, whereas most sociodemographic (except for age of PEs in adolescence and sexual orientation) and family history variables were of less importance.

Understanding the role of confounders is important because such variables may mask an actual association or, more commonly, falsely demonstrate an apparent association between the exposure and outcome measure (Skelly *et al.* 2012). When studies appropriately control for such variables, they present a more accurate estimate of the true association due to the exposure (Skelly *et al.* 2012). Results of the current review supported pathway one (see Fig. 1) where PEs are directly causal of SITB. However, the inconsistent and incomplete adjustment for confounders prevents rejection of pathway three (fully explained by shared risk factors) as an explanatory model. Also of note, the associations between PEs and SITB were essentially eliminated in two adolescent/young adult studies with exhaustive adjustments (Nishida *et al.* 2008; DeVlyder *et al.* 2015a), suggesting the relationship may indeed be spurious, although these findings would benefit from replication in more broadly representative samples. Alternatively, reverse causality may also be possible, in which the mind's way of adapting to severe distress of SITB results in PEs (Forman *et al.* 2004) (pathway two in Fig. 1). No study to date has tested the reverse causality pathway in the general population, although this explanation is less consistent with broad clinical assumptions.

It is also important to recognise that even if the PE–SITB association becomes non-significant after adjustment, this does not necessarily mean that PEs are not causally important to SITB. Rather it could be the case that the confounders of interest are in fact mediators which explain the association between PEs and SITB on the causal pathway (Christenfeld *et al.* 2004). Jang *et al.* (2014), for example, found support for depressive symptoms as a partial mediator of the PE–suicidal ideation relationship; however, the authors incorporated a cross-sectional mediation analysis, which has faced considerable criticism (Cole & Maxwell, 2003). Confounders and mediators cannot be differentiated statistically, but rather this differentiation is derived from theory and an understanding of the temporal precedence among variables (MacKinnon *et al.* 2000; Babyak, 2009). As explained

in online Supplementary Material II, sociodemographics and family history/genetic factors should be treated as confounders, as PEs cannot precede these variables. All other categories should likely be treated as mediating variables, except for substance use and certain environmental factors (e.g. childhood abuse), which have both been consistently shown to precede PEs (Kelleher *et al.* 2013b; McGrath *et al.* 2016). It is also important to consider that some variables may in fact be moderators (e.g. intervention factors), which influence the strength or direction of the association. All these factors need to be considered in order to advance our understanding of the relationships at play.

Studies with consistent and comprehensive adjustment of third variables are required to explain the PE–SITB relationship. Furthermore, future studies should examine associations of SITB with different PE characteristics, as these have been differentially associated with each NASI outcome. Such PE characteristics include the frequency and emotional valence of content (DeVlyder *et al.* 2015a). Theoretical models of self-harm and suicidality may also provide frameworks to better understand the PE–SITB relationship. This includes theories which focus on the transition from suicidal thoughts to actions (Three-Step Theory, Klonsky & May, 2015; Interpersonal Theory, Van Orden *et al.* 2010), as well those which integrate both non-suicidal and suicidal behaviours (Hamza *et al.* 2012), which ideally should be tested using longitudinal data. Schimanski *et al.* (2017) focused on the schizotypy–suicidal ideation relationship and found stronger support for the Interpersonal Theory than for the Three-Step Theory of suicide, suggesting constructs such as thwarted belongingness and perceived burdensomeness should be considered in future investigations. In addition to these theoretical components, there are other potentially confounding variables (e.g. genetic factors), which have yet to be investigated (see the section 'Future research').

Strengths and weaknesses of the review

This systematic review considered and classified all confounding factors, enabling interpretation of individual variables in the PE–SITB relationship. However, meta-analysis was precluded, preventing quantitative measurement of the impact of individual variables on the association. Statistical approaches (e.g. structural equation modelling) are required in existing datasets, as well as in future studies to further test the specific effect of individual confounders and mediators.

Studies should also give consideration to the temporal association between the variables in order to inform possible causality using a discrete-time survival

modelling approach. Approximately 30% of all longitudinal studies did not account for SITB at baseline measurement of PEs, and then administered lifetime SITB measures at follow-up, which prevented conclusions as to which occurred first. Also, many studies did not adjust for borderline personality disorder (BPD) or psychotic disorders (only seven studies excluded participants with psychotic disorders). Both BPD and psychosis have high rates of suicide (Hor & Taylor, 2010) and for low prevalence outcomes such as suicide attempts, inclusion of participants with these diagnoses may inflate the PE–SITB association. Koyanagi *et al.* (2015a) found BPD symptoms had a substantial influence on the PE–non-suicidal self-injury association, whereas Kelleher *et al.* (2017) found the PE–suicide attempt association persisted in those without BPD diagnosis or traits. Future studies should consistently account for these diagnoses, where BPD is of particular interest in the PE–non-suicidal self-injury association.

Future research

The PE–SITB association is in part attributable to common mental disorders such as depression; however, more research is required to determine their specific role as either a confounder or mediator (Jang *et al.* 2014), particularly given evidence that PEs are indicative of greater severity of underlying depressive and anxiety disorders. To date, environmental factors have not been controlled for in longitudinal studies which consider temporality. In addition, the role of social isolation in the PE–SITB association has not been examined. Isolation and loneliness are associated with both PEs (Lim & Gleeson, 2014) and SITB (Trout, 1980), and are relevant to the Interpersonal Theory construct of thwarted belongingness. Only two studies controlled for emotional dysregulation (Nishida *et al.* 2008; DeVlyder *et al.* 2015a), which is surprising considering its key role in the development of non-suicidal and suicidal self-injury (Klonsky, 2007).

There are no studies examining shared genetic risk factors underlying the PE–SITB relationship. Mental disorders, environmental and psychological factors explained much of the variance; however, it is possible that these risk factors are themselves partly explained by genetic factors (DeVlyder *et al.* 2015a). In addition, cognition, including IQ and other neurocognitive function (e.g. working memory), has not been properly investigated. Calkins *et al.* (2014, 2017) included an academic achievement variable (WRAT-4 reading subtest) into their PE–suicidal ideation model, and found it had negligible effects (OR range: 0.99–1.00, $p \geq 0.05$). Considering that this variable is modestly related to IQ (Reilly *et al.* 2014; Olsen *et al.* 2015), cognitive

intelligence may be of less importance. However, other aspects of cognitive function such as working memory and executive function may be of more interest for future research. Finally, poor sleep is a strong risk factor for both PEs (Reeve *et al.* 2015) and SITB (Hysing *et al.* 2015) and may be important in the PE–SITB relationship.

Conclusion

This systematic review critically examined confounders and mediators adjusted for in the PE–SITB association. In most studies, the association between PEs and both suicidal ideation and NASI remained significant after adjustments, suggesting an independent association. A substantial amount of the variance was explained by mental disorders, psychological distress and environmental exposures. Interventions to target these symptoms of mental ill health in those with PEs may assist in reducing risk of self-harm and suicide. In order to fully understand the mechanisms underpinning the PE–SITB association, hypothesis driven studies with more consistent and comprehensive adjustment for third variables are required, as well as studies which clarify the phenomenological aspects of different types of PEs. Such efforts will inform intervention, which in turn may reduce the risk of morbidity and mortality by suicide in those with PEs.

Notes

- ¹ This broader term takes into account the fact that motivation for self-injurious behaviour is often complex (Hjelmeland *et al.* 2002).
- ² For example, have you thought about hurting yourself?
- ³ Skin picking (or dermatillomania/excoriation disorder) and hair pulling (or trichotillomania) have been established as separate disorders in the clinical literature (Zucker *et al.* 2011; Grant & Chamberlain 2015).
- ⁴ Schizotypy is typically defined as traits stable over time with anomalies across multiple dimensions (perceptual, interpersonal), whereas PEs are more transitional anomalies (Pedrero & Debbane 2017).
- ⁵ Separate search strategies were devised for each database. Relevant index terms were incorporated, including MeSH Terms for PubMed, Emtree terms for EMBASE, and the Thesaurus of Psychological Index Terms for PsycINFO.
- ⁶ Because this study (Kelleher *et al.* 2012b) collapsed across SITB outcomes (suicidal ideation, suicide attempt, non-suicidal self-injury), it was excluded from results in Tables 3 and 4.

Supplementary material

The supplementary material for this article can be found at <https://doi.org/10.1017/S0033291717002677>

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Declaration of Interest

None.

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