The relationship between stressful life events and suicidality:

A systematic review and meta-analysis

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The candidate confirms that the work submitted is her own and that appropriate credit has been given where reference has been made to the work of others.

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Acknowledgements

Abstract

Background: Suicidality is multi-determined and reflects a complex interaction of social, psychological and environmental risk and protective factors. Though there is extensive evidence for the causes of suicidality, some uncertainties surrounding risk factors remain. Stressful life events are a known risk factor, but the strength and nature of the association between stressful life events and suicidality is unclear. To investigate this, the current review examined the prospective relationship between stressful life events and suicidality.

Methods: MEDLINE, EMBASE, CINAHL, Cochrane, and PsycINFO databases were searched from inception to October 2018 (updated April 2019). Eligible studies included observational, quantitative longitudinal cohort studies which provided data on the association between stressful life events and a subsequent aspect of suicidality in adults or adolescents ($\geq$14 years and older). The Effective Public Health Practice Project (EPHPP) quality assessment guidance was used to conduct a methodological quality assessment. Random-effects meta-analyses model was used to examine the strength of the prospective relationship between the experience of stressful life events and subsequent suicidality. Sub-group analyses and meta-regression analyses was used to examine factors moderating the relationship.

Results: Eight studies were identified in the systematic review, and nine independent comparisons on 2,639 participants from seven studies were included in the meta-analysis (mean age = 37 years, 54% female). Stressful life events were associated with a significantly increased risk for suicidality (9 comparisons: Odds Ratio (OR) = 1.37, 95% CI = 1.10 to 1.70). Statistical heterogeneity was high (I^2 = 76. 48, 95% CI: 55.0 to 87.7%), publication bias was indicated, and methodological quality of the studies was mixed.

Discussion: The analyses suggested that stressful life events can statistically increase the risk of suicidality, which could have implications for subsequent clinical assessment and intervention. Further high-quality research is needed to confirm this tentative link between stressful life events and suicidality.

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1. Introduction

1.1 Overview

Suicidality is a serious health concern worldwide (WHO, 2018), and in recent years suicide has been a leading cause of death in Great Britain (ONS, 2017a). The theoretical and empirical interest in suicidality has led to an extensive and well-establish evidence-base for the different risk factors and causes of suicidality. However, while the development of suicide interventions, such as Dialectical Behaviour Therapy (Linehan, 1993), Cognitive Behavioural Prevention for Suicidality in Psychosis (Tarrier et al., 2013), and Collaborative Assessment and Management of Suicidality (Jobes, 2012), continue to progress, the prevalence of suicidality remains a concern (WHO, 2014). There are still uncertainties surrounding the impact of potential risk factors and the relationship of these with suicidality. One external risk factor which may be important is the occurrence of stressful life events (Franklin et al., 2017). A better understanding of the association between stressful life events and suicidality could allow for the development of more effective risk assessments and interventions. This thesis aims to address this gap by assessing the strength of the prospective relationship between the experience of stressful life events and aspects of suicidality.

1.2 Background

This section will begin by defining suicidality and considering some of the underlying risk factors, introducing the experience of stressful life events. A theoretical understanding of suicidality will then be briefly outlined before discussing the current evidence-base for stressful life events and suicidality in the public domain. The rationale for the current review will then be presented.

1.2.1 Defining suicidality

Suicidality is a continuum encompassing suicidal ideation, suicidal plans, suicide attempts and suicide. A range of discrepancies are found between the definitions and classifications of the aspects of suicidality within the literature (Silverman, 2011). Therefore, this thesis will use the term suicidality to take into account the entirety of the continuum, while also considering the individual aspects

of suicidality, to allow a thorough and considered review of the evidence base. This thesis will use definitions of suicidality used by Nock et al. (2008b). Suicide is defined as the intentional act of ending one's own life; suicidal ideation refers to thoughts of behaving in a manner which would intentionally end one's life; suicidal plan refers to the formulation of specific methods in which one intends to end one's life; and suicide attempt refers to engaging in behaviour intended to end one's life (Nock et al., 2008b). Nock et al.'s (2008b) definitions were established from a collection of consensus papers and have been operationalised in various studies (Borges et al., 2010; Franklin et al., 2017; Gvion & Apter, 2012; Nock et al., 2010; O'Connor & Nock, 2014).

The World Health Organisation (WHO) reported that almost 800,000 people die by suicide every year, which equates to one suicide death every 40 seconds (WHO, 2018). For every suicide there can be up to twenty-five others that make a suicide attempt (IASP, 2017). Cross-national and national studies have found varying lifetime prevalence estimates; suicide has a relatively low base rate (WHO, 2014), and while the other aspects of suicidality seem to be higher worldwide (Bertolote et al., 2005; McManus et al., 2016; Nock et al., 2008a; Nock et al., 2013), a fairly consistent pattern of reduction from ideation to plans to attempt is reported (see Table 1.). Most researchers and mental health professionals differentiate suicidality from non-suicidal self-injury, which refers to self-injurious behaviours in which a person has no intention to end their life (Nock et al., 2008b). However, there is some debate within the research regarding the concept of self-harm, which can refer to both self-injury and self-poisoning with and without suicidal intent, and whether it is possible to distinguish self-harm from suicidality (Hawton et al., 2016; Kappur, Cooper, O'Connor & Hawton, 2013). The focus of non-suicidal self-injury is not within the remit of this review, however self-harming behaviours that involve suicidal intent were considered within the continuum of suicidality.

1.2.2 Impact of suicidality

The experience of suicidality can have a profound impact on the individual. Suicidality can transition from ideation to plan to attempt during the first year of ideation onset, with prevalence studies finding around 60% of ideation to attempt transitions occurring within this timeframe (Nock et al., 2008a; Nock et al., 2013). Although this immediate progression of suicidality is not the case for all those who

experience suicidality (Bertolote et al., 2005), current suicidality can lead to suicidality later in life (Reinherz, Tanner, Berger, Beardslee & Fitzmaurice, 2006; Suominen, Isometsä, Ostamo & Lönnqvist, 2004), and a lifetime risk of suicidality (Herba, Ferdinand, van der Ende & Verhulst, 2007).

Table 1. Lifetime Prevalence of Suicidality

	Ideation (%)	**Plans** (%)	**Attempts** (%)	**Population**
Bertolote et al. (2005)	2.6-25.5	1.1-15.6	0.4-4.2	International, lifespan
Nock et al. (2008a)	9.2	3.1	2.7	International, adults
Nock et al. (2013)	12.1	4	4.1	USA, adolescents
	Thoughts		**Attempts**	**Population**
McManus et al. (2016)	20.6		6.7	England, adults[a]

[a] Sample included adults aged 16 or older.

Suicidality during early life can also predict unfavourable outcomes in other areas of adult life. Early suicidality can increase the likelihood of mental health problems, such as mood disorders, anxiety disorders and other axis I disorders, increase problem behaviours, impact functioning, lower self-perception (Fergusson, Horwood, Ridder, & Beautrais, 2005; Goldman-Mellor et al., 2014; Herba et al., 2007; Reinerz et al., 2006), and dysfunctional relationships in adulthood (Goldman-Mellor et al., 2014; Kerr & Capaldi, 2011). Early suicidality has been found to impact on physical health, including increasing the risk of ischemic heart disease, cardiovascular disease, metabolic syndrome and elevated inflammation later in life (Goldman-Mellor et al., 2014; Larsen, Agerbo, Christensen, Søndergaard & Vestergaard, 2010; Shah, Veledar, Hong, Bremner, & Vaccarino, 2011). Early or lifetime experience of suicidal thinking and behaviour can impact upon subsequent academic performance (Mortier et al., 2015), labour market marginalization (Niederkrotenthaler et al., 2014), and employment (Ettner, Frank & Kessler, 1997; Goldman-Mellor et al.,2014).

Not only does suicidality impact the individual experiencing it, there is additionally a profound impact on the family, friends and others around the individual, historically referred to as 'suicide survivors' in the literature (Cain, 1972). Suicidality can also impact on those involved in the initial response, including witnesses, emergency response and health care professionals. Research estimates that each suicide affects six to twenty-eight people (Knieper, 1999). In the UK there were almost 6,000 deaths by suicide reported in 2016 (ONS, 2017b), which suggests potential estimates of 36,000 to 168,000 people could have been left experiencing trauma (Mind, 2016), or complex bereavement due to the additional association of individual and societal stigma attached to suicide (Cvinar, 2005). As one survivor said, "*Nobody in the family wants to talk about it. You have to pretend that something terrible didn't happen.*" (Lukas & Seiden, 1997, pp. 101). Suicide survivors report higher levels of shame, stigma, rejection, blame and concealment than those bereaved by other causes of death (Hanschmidt, Lehnig, Riedel-Heller & Kersting, 2016; Sveen & Walby, 2008). Similar impacts of suicidality can be seen within communities (Eskin et al., 2016), and potentially further still with popular outlets such as social media sites (O'Dea et al., 2015) and media coverage increasing the potential effects of suicide contagion (Colombo, Burnap, Hodorog & Scourfield, 2016). The resulting impact on the wellbeing and health of those affected by others' suicidality is as important for professionals to explore as that of the individuals directly experiencing suicidality.

1.2.3   Measures of suicidality

A range of tools and questionnaires have been developed to measure suicidality. The main research tool used to collect information about suicide is psychological autopsy, the retrospective investigation of medical history and interviews with family members and friends. A variety of questionnaire measures have been developed to capture suicidal ideation, plans and attempts, from semi-structured interviews (e.g. Suicidal Behaviors Interview (Ivanoff & Jang, 1991); Modified Scale for Suicidal Ideation (Miller, Norman, Bishop & Dow, 1986)), and self-report measures (e.g. Self-Monitoring Suicidal Ideation Scale (Clum & Curtin, 1993); Suicide Behaviors Questionnaire-Revised (Osman et al., 2001)). An extensive review by Brown (2000) into valid and reliable suicide assessment measures found

12 objectively rated and 11 self-report published measures, and new measures have since been developed (Batterham et al, 2015).

Issues with measuring and reporting

While standardised suicidality measures are widely used in research and clinical practice, the use of single-item measurements (Nock et al, 2008a), and the practice of measuring suicidality through items included in other measures, such as depression scales (Hamilton Depression Rating Scale; Hamilton, 1960), is similarly seen within the literature. This practice has been found to substantially increase the probability of false conclusions (Kimberlin & Winterstein, 2008; Millner, Lee & Nock, 2015) and can be characterised by reduced range and lowered likelihood of adequately and accurately measuring a construct they were not primarily intended to assess (Liu & Miller, 2014). While these measures may not be valid and reliable (Juniper, 2009; Kimberlin & Winterstein, 2008), they are still used. Some research suggests measurement by single-item or through depression scales may be valid, regardless as to whether they are administer-led or self-report (Desseilles et al., 2012), though this method of measuring suicidality is rarely reflected in clinical practice. Guidelines commonly advise a thorough assessment of all aspects of suicidality, with many recommending bodies suggesting the use of clinical interviews (Department of Health, 2014, 2019; Wasserman et al., 2012; WHO, 2010, 2014). It stands to reason that suicidality research should reflect this comprehensive approach utilised in clinical practice through the use of standardised, valid and reliable measures.

Discrepancies between definitions and classifications of suicidality have impacted on how suicidality is conceptualised, operationalised and clinically understood (Malone, Szanto, Corbitt & Mann, 1995; Mann et al., 2005; O'Connor, Platt & Gordon, 2011). This is reflected in the diverse way suicidality measures have been developed (Ghasemi, Shaghaghi & Allahverdipour, 2015; O'Connor et al., 2011). Such diversity of measures for assessing suicidal thoughts and behaviours means there is no consensus or 'gold standard' measure used for suicidality (Batterham et al, 2015; Ghasemi et al., 2015). The development of new or modifying of old measures creates more inconsistency within the measurement of suicidality (Brown, 2000), perpetuating the theoretical and conceptual diversity seen around suicidality (Franklin et al, 2017).

Suicidality is still a sensitive and stigmatised issue; the act of suicide remains illegal in some countries (Frey, Hans & Cerel, 2016; Keller, McNeill, Honea & Miller, 2019; Mishara & Weisstub, 2016) and people are often reluctant or unable to share their intentions (Busch, Fawcett & Jacobs, 2003; Nock et al., 2010). Within the research this sensitivity and stigma can influence participant's decision to disclose experiences of suicidality (Fulginiti, Pahwa, Frey, Rice & Brekke, 2016; Hom, Stanley, Podlogar & Joiner Jr, 2017). The accuracy of reporting may therefore vary depending on the type of measure used. For example, self-report measures, i.e. measures completed independently of the researcher, have been found to facilitate a greater proportion of suicidality reporting when compared to face-to-face measures (McManus et al., 2016; Nicholson, Jenkins & Melzer, 2007).

Unfortunately, it is likely that these issues around measures, reporting procedures and data availability, as well as misclassification of suicide as accidents or another cause of death, impact the prevalence figures. These are already known to be under-reported and do not accurately reflect the impact of suicidality (Bantjes & Kagee, 2013; Jobes & Berman, 1985; Jobes, Berman & Josselson, 1987; WHO, 2014).

1.2.4 Risk factors underlying suicidality

Suicidality is multi-determined and reflects a complex interaction of social, psychological, environmental, cultural and other risk and protective factors. Understanding the context of suicidality is important, and recent research has drawn attention to the socio-economic inequality of suicide (Platt, 2016). Therefore, it is important to examine and understand possible factors which increase the risk of suicidality, especially when some of these factors are attributable to the environment and conditions outside of one's control.

Disparities in health and healthcare access can be seen within suicidality, and certain socio-demographic characteristics disproportionally elevate risk of suicidality. Both gender and age are associated with different patterns of suicidality; being female or aged under 35 years old increases risk of ideation, plans and attempts (Borges, Angst, Nock, Ruscio & Kessler, 2008; Nock et al., 2008a; ONS, 2017b), while being male or over the age of 35 years predicts suicide and reduced likelihood of reporting suicidality (ONS, 2017b; Langhinrichsen-Rohling, Friend & Powell, 2009). Physical and intellectual disability increase risk of suicidality (Giannini et al.,

2010; Lund, Nadorff, Thomas & Galbraith, 2018; Meltzer et al., 2012; Milner, Bollier, Emerson & Kavanagh, 2018), as does identifying as a sexual minority (LGBTQ) (King et al., 2008; Marshal et al, 2011; Miranda- Mendizábal, et al., 2017, Plöderl & Tremblay, 2015). Cultural minority groups can experience additional culturally specific risk factors underlying suicidality: cultural sanctions, idioms of distress, minority stress, and social discord (Chu, Goldlum, Floyd & Bongar, 2010). Education and employment are both associated with suicidality; lower levels of education (Denney, Rogers, Krueger & Wadsworth, 2009; Nock et al., 2008a), being a student (Nock et al., 2008a), and unemployment (Nordt, Warnke, Seifritz & Kawohl, 2015; WHO, 2012) increase risk of suicidality. Mental health difficulties, diagnoses and prior hospitalisation regarding mental health are among the strongest predictors for suicidality (e.g. Franklin et al., 2017; Hawton, Sutton, Haw, Sinclair, & Deeks, 2005; Kessler, Borges & Walters, 1999; McClatchey, Murray, Rowat & Chouliara, 2017; Nock et al., 2008a; Nock et al, 2013; Pompili et al., 2013; Pompili, Giardi, Ruberto & Tatarelli, 2005; Pompili, Mancinelli, Giardi, Ruberto & Tatarelli, 2004).

Internal factors consider the individual characteristics of a person which can influence their behaviour and actions. Specific internal risk factors to suicidality include: cognitive abilities, such as poor problem solving (Pollock & Williams, 2001, 2004), lack of positive future expectancies (O'Connor, Fraser, Whyte, MacHale & Masteron, 2008), over-general autobiographical memory (Pollock & Williams, 2001), and implicit identification with death/suicide (Nock et al., 2010); and personality traits, such as pessimistic attribution style (Hirsch, Wolford, LaLonde, Brunk & Parker-Morris, 2009), neuroticism (Brezo, Paris & Turecki, 2006), extraversion (Brezo et al., 2006), and perfectionism (Blankstein, Lumley & Crawford, 2007).

External factors consider experiences that occur outside the individual which influence their behaviour and actions. Well established external risk factors that influence suicidality include: the experience of childhood trauma (Miller, Esposito-Smythers, Weismoore & Renshaw, 2013; O'Connor, Green, Ferguson, O'Carrol & O'Connor, 2018), sexual abuse (Pérez-González & Pereda, 2015), violence (Maclsaac, Bugeja & Jelinek, 2017), maltreatment (McKenna & Gillen, 2015), physical health conditions (Goodwin, Marusic & Hoven, 2003), family history of suicidality (Gould, Fisher, Parides, Flory & Shaffer, 1996), imprisonment (Duthe,

Hazard, Kensey, & Shon, 2013) and release from prison (Pratt, Appleby, Piper, Webb, & Shaw, 2010).

One external risk factor of interest within the research field is the experience of stressful life events. Suicide research has found various specific stressful life events which increase the likelihood of suicidality, such as the death of a family member (Bunch, Barraclough, Nelson & Sainsbury 1971; Rostila, Saarela & Kawachi, 2013), the death of a loved one (Stein et al., 2010), divorce (Stack & Scourfield, 2015), marital separation (Wyder, Ward & De Leo, 2009), demotion (Schoenbaum et al., 2014), unemployment (Milner, Page & LaMontagne, 2013), home eviction (Rojas & Stenberg, 2016), fetal loss i.e. stillbirth, miscarriage, termination (Weng et al, 2018), and major physical health condition (Ahmedani et al., 2017). Reviews of the literature generally find support for specific stressful or adverse life events being a risk factor for suicidality (Ide, Wyder, Kolves & DeLeo, 2010; Kazan, Calear & Batterham, 2016; Kimerling, Makin-Byrd, Louzon, Ignacio & McCarthy, 2016; Peterhansel, Petroff, Klinitzke, Kersting & Wagner, 2013; Ullman, 2004). Suicide researchers have also focused on the experience of multiple stressful life events, considering the accumulation of several stressful events as determining the level of risk of suicidality.

1.2.5 Stressful life events as a risk factor to suicidality

Stressful life events have been defined as objective occurrences likely to require change by an individual to readjust to everyday life (Holmes & Rahe, 1967), and are independent of subjective appraisal (Grant et al., 2003). Stressful life events are everyday regular occurrences experienced on an irregular basis, such as the death of a loved one, the loss of employment, or being a victim of crime[1]. The literature distinguishes stressful life events as dependent and independent, i.e. events which are at least partially influenced by the behaviour or an aspect of the individual, and events which occur regardless of the individual's behaviour or characteristics (Liu & Miller, 2014).

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[1] Within the context of this thesis, the definition of stressful life events does not include trauma events. The experience of traumatic life events and suicidality has been widely studied (Bahraini, Simpson, Brenner, Hoffberg, & Schneider, 2013; Hor & Taylor, 2010; Krysinska & Lester, 2010; Wethington et al., 2008), therefore this thesis aims to separate these constructs to better understand the role of non-traumatic life events.

There are various assessments within this research that measure the experience of multiple stressful life events, commonly using a self-report checklists approach or an interview-based approach. Measurements tend to include both dependent and independent events, and can vary around the assessment of event desirability, weighting of events based on the level of change or readjustment required, and the inclusion of subjective ratings of stress. Most life event measures tend to consider the experience of stressful life events in the last year, as recollection can begin to fade at around a year and sometimes sooner (Brown & Harris, 1982; Johnson, 2005; Paykel, 1997). The use of self-report checklists is common within the life events literature. Checklist measures generally ask respondents to identify whether they have experienced any of the life events on the list usually within a specified timeframe and some may ask the respondent to rate the severity of the event. Common checklist measures include The Social Readjustment Rating Scale (SRRS; Holmes & Rahe, 1967), the Life Experiences Survey (LES; Sarason, Johnson, & Siegel, 1978), and the List of Threatening Experiences (Brugha & Cragg, 1990).

The Social Readjustment Rating Scale (SRRS; Holmes & Rahe, 1967) was one of the earliest measurements of life change events. Using a checklist self-report approach, it aimed to measure the amount of readjustment required by certain life events, both positive and negative events, using life change units assigned to each life event. The SRRS has since been revised and updated (Hobson et al., 1998; Miller & Rahe, 1997; Rahe, 1975), evaluated (Scully, Tosi & Banning, 2000), and normative data has been developed (Hobson & Delunas, 2001); it is still one of the most widely used measure in the literature (Hock, 1995). The Life Experiences Survey (LES; Sarason et al., 1978) was developed to improve upon the limitations of the SRRS and provides a more extensive list of life events with greater item specificity. The measure allows for individual ratings of the impact of the event and the separate assessment of negative and positive life events. The List of Threatening Experiences (LTE; Brugha & Cragg, 1990) provides a briefer assessment of life events. This measure only includes major events, covering several life domains, that are known for their impact on an individual's health and omits common events. Checklist measures can be scored in different ways. The SRRS totals the life change units of each event endorsed, while the LES is scored by the total sum of the

subjective impact ratings for each event in the list, and the LTE focuses on the total number of events endorsed to provide a summary scale.

However, the checklist approach to measuring stressful life events is not without limitations (Kessler, 1997). The provision of adequate instructions and contextual descriptions within the measures can be poor to non-existent, meaning that checklist items can be open to interpretation by participants, leading to low agreement between the investigator and participant on the life event definitions (Harkness & Monroe, 2016) and results which can be inaccurate or misleading (Dohrenwend, 2006). Certain stressful life events have greater impacts on health outcomes than others (Slavich, 2016), yet the scoring of some checklist measures means that each event is considered equal. The assignment of weights to items acknowledges some events will be more stressful than others, however weighting does not account for an individuals' context and self-efficacy (Yu & Chung, 2004). Researchers have developed measures to include subjective severity ratings to weigh the different cognitive appraisals people have towards life events, however this has in turn been criticised for confounding the measure of objective stress with subjective stress (Kessler, 1997).

In a move to address the limitations of the checklist approach, contextual measures were developed using an interview-based approach. Interview-based measures generally use a semi-structured approach to obtain information about the experience and biographical details of each life event. This contextual information is used to assess the meaning of the stressful life event for the respondent and the impact the event had on their life. An 'objective threat' rating is then given by a blind rater for each event. An example of an interview-based measure is the Life Events and Difficulties Schedule (LEDS; Brown & Harris, 1989; Harris, 1991). The LEDS allows for the identification of dependent and independent events, as well as expected and unexpected events. Interview-based measures have also received criticism; some have suggested an individual's life circumstances could impact on their response to the interview, influencing the objective threat rating given, e.g. the experience of depression may impact on how the experience of life events are recalled and described within the interview (Kessler, 1997). Furthermore, the approach is incredibly labour- and time-intensive as well as costly (Slavich & Auerbach, 2018).

While the contextual, interview-based approach has clear advantages over the checklist approach (Coyne, Thompson & Pepper, 2004; Dohrenwend, 2006; Monroe, 2008), the SRRS and other self-report checklists have been found to generate similar results as interview-based assessments (e.g. Lewinsohn, Rohde, & Gau, 2003; Wagner, Abela, & Brozina, 2006), and are favoured by research due to their ease of administration, and time and cost effectiveness (Buri, Post, Cromett, Landis & Alliegro, 2015; Liu & Miller, 2014; Slavich & Auerbach, 2018).

1.3   Theoretical understanding of suicidality

Stressful life events are experienced by most people at some point in their lives, however this does not mean that everyone experiences suicidal thoughts or engages in suicidal behaviour. Therefore, it is important to understand how the experience of stressful life events may interact with other factors to increase a person's vulnerability to suicidality (O'Connor & Nock, 2014). Several prominent models of suicidality include or consider the experience of stressful life events, such as the Cry of Pain model (CoP; Williams, 1997), the Schematic Appraisals Model of Suicide (SAMS; Johnson, Gooding & Tarrier, 2008), the Integrated Motivational-Volitional model (IMV; O'Connor, 2011), and the Interpersonal Theory of Suicide (Joiner, 2005, 2011). These models tend to view stressful life events as contextual factors which become suicidogenic in the context of cognitive biases, interpretations, or vulnerabilities of the individual.

Williams' (1997) Cry of Pain model describes the psychological conditions which explain suicidal behaviour. The model proposes the presence of stressors, such as stressful life events, and their consequences are appraised in terms of defeat. Information-processing biases, negative memory schema, and problem-solving deficits, may influence these appraisals and contribute to perceptions of entrapment such that inflexible negative perceptions of self, negative responses to others, and negative responses to circumstances become more likely. Subsequently perceived alternative escape routes become limited, increasing a sense of hopelessness and furthering intractable feelings of entrapment. This can be accentuated by a real or perceived absence of rescue factors, such as available and important social support resources, and associated feelings of social isolation. A situation in which these conditions occur can cause a 'cry of pain' in the presence of imitation models and

access to methods of suicide. Empirical research has found evidence in support of the Cry of Pain model (e.g., O'Connor, 2003).

The Schematic Appraisals Model of Suicide (SAMS; Johnson, Gooding & Tarrier, 2008) was influenced by the strengths and limitations of the Cry of Pain model. The SAMS replaces the concepts of defeat, entrapment and absence of rescue with three main components: information processing biases, the presence of a suicide schema, and a multi-stage appraisal system. The model proposes that negative information processing biases feed into a suicide schema (i.e., a network of suicide related thoughts and semantic memories). When activated, the schema triggers thoughts of suicide as a strategy of escape from intolerably emotional or situational states. Suicide behaviour occurs when the suicide schema interacts with a four-stage appraisal system (i.e. appraisals of current situation, historical context, future, and self), and stressors are appraised in terms of defeat and entrapment. The suicide schema strengthens and expands its network each time it is activated, as well as by the appraisal system and information biases which activate it, preventing alternative schemas being accessed. Triggers of suicidal behaviour may seem to become less obviously distressing, and suicide attempts may appear to be impulsive or to have occurred for 'no reason'. Research empirically testing the SAMS has found support for the model (Pratt, Gooding, Johnson, Taylor & Tarrier, 2010; Tarrier, Gooding, Gregg, Johnson, & Drake, 2007; Taylor, Wood, Gooding, Johnson, & Tarrier, 2009). The model conceptualises stressful life events as contextual factors which become suicidogenic in the context of cognitive biases.

The Integrated Motivational-Volitional model (IMV; O'Connor, 2011, O'Connor & Kirtley, 2018) was likewise influenced by the Cry of Pain model, as well as three other theoretical perspectives, the diathesis-stress model (Schotte & Clum, 1987), Theory of Planned Behaviour (Ajzen, 1991), and Differential Activation Hypothesis (Teasdale & Dent, 1987, Williams, Barnhofer, Crane & Beck, 2005). The IMV is a three-phase model which distinguishes between suicidal ideation and behaviour. The pre-motivational phase describes the biopsychosocial and environmental context in which vulnerability to suicidal ideation and behaviour may increase, including the experience of stressful life events. These pre-motivational factors can heighten the sensitivity to appraisals of defeat. The motivational phase describes the factors and psychological processes, such as defeat, that lead to suicidal ideation and intent, with entrapment bridging defeat and suicidal

ideation. The volitional phase describes the factors that moderate the transition from suicidal ideation to suicide behaviour. Greater motivational and volitional factors are observed in individuals who have previously attempted suicide, which in turn creates greater distress for those individuals, and over time the transition from suicidal ideation and intent to suicidal behaviour increases in speed (O'Connor & Kirtley, 2018). Research empirically testing the IMV has found support for the model (Dhingra, Boduszek, O'Connor, 2015; Mars et al., 2019; O'Connor, Smyth, Ferguson, Ryan & Williams, 2013; Owen, Dempsey, Jones & Gooding, 2018; Wetherall, Robb & O'Connor, 2019), however there have also been inconsistencies in the findings (Tucker, O'Connor & Wingate, 2016).

The Interpersonal Theory of Suicide (Joiner, 2005, 2011) proposes a framework of three central constructs to understand suicidal ideation and behaviour; thwarted belongingness, perceived burdensomeness and capability for suicide. Suicidal desire (or ideation) occurs with the simultaneous presence of thwarted belongingness (i.e. a lack of social connection or integration) and perceived burdensomeness (i.e. the view that one is a hindrance on others). The transition to suicide attempts and suicide occurs in the context of suicidal desire and capability for suicide (i.e. the ability to enact self-injury). Research empirically has found support for the theory (Cornette et al., 2009; Jahn & Cukrowicz, 2011; Manetta & Cox, 2014; Selby et al., 2010; Van Orden et al., 2010). The theory views stressful life events as implicit in the development of the two key cognitive-affective states which create suicidal desire (Van Orden et al., 2010), such as the loss of a loved one increasing social isolation, or the loss of employment creating the need to rely on others.

1.4   Evidence for stressful life events and suicidality

A considerable amount of research has investigated the experience of stressful life events and suicidality, with studies using retrospective (Cavanagh, Owens & Johnstone, 1999; Cheng, Chen, Chen & Jenkins, 2000; Fortune, Stewart, Yadav & Hawton, 2007; Heikkinen, Aro & Lonnqvist, 1992; Palacio et al., 2007; Zhang, Conwell, Zhou & Jiang, 2004) cross-sectional (Beautrais, Joyce & Mulder, 1997; Casey et al., 2006; Chang, Sanna, Hirsch & Jeglic, 2010; Cole, Protinsky & Cross, 1992; King et al., 2001; Lin et al., 2018; Özer, Uluşahin, Batur, Kabakçi & Saka, 2002; Panadero, Martín & Vázquez, 2018; Paul, 2018; Schillani et al., 2009; Turvey, Stromquist, Kelly, Zwerling, & Merchant, 2002) and prospective designs

(e.g. Christensen, Batterham, Mackinnon, Donker & Soubelet, 2014; Oquendo et al., 2014; Rew, Young, Brown & Rancour, 2016; Stone, Liu & Yen, 2014; Wong et al., 2008). The primary study literature has found mixed results regarding the support of an association between stressful life events and suicidality, which can partially be explained by methodological limitations of the research. Given the considerable interest in this area, reviews of the literature have attempted to provide an overview of the evidence-base (Franklin et al., 2017; Liu & Miller, 2014; Serafini et al., 2015).

Liu and Miller (2014) were the first to systematically review the literature investigating the association between both traumatic and non-traumatic life events and suicidality. Their narrative review identified 95 eligible articles and found a generally consistent association between life events and suicidality. They reported that associations were most consistent when the specific suicidality outcome was suicide, followed by suicide attempts, and then suicide ideation, while additionally highlighting several studies that failed to find any association. The authors suggested that variations in methodologies could explain this finding. They highlighted that studies of suicide used more rigorous methodologies, while studies investigating suicide ideation employed weaker methodologies. Methodological limitations of the eligible studies included: the broad definition of life events used, which included both traumatic and non-traumatic events such as sexual assault, depression, smoking and "nothing to do"; most studies used self-report checklists to measure life events; a lack of operational definitions included for the aspect of suicidality being measured; single-item self-report measures of suicidality derived from larger scales, some of which were not primarily designed to measure a suicidality construct; the temporal overlap between the measurement of life events and suicidality; and small sample sizes leading to underpowered results. There were also some limitations of the review itself. The use of a narrative approach, while able to identify whether a relation between two variables may exist, does not allow for the strength, or moderators, of the association to be identified. Furthermore, the review mainly relied upon cross-sectional studies; the authors reported only 9.5% of the literature had a prospective design, meaning that inferring causality between life events and suicidality was not possible.

Serafini et al. (2015) investigated the experience of adverse or negative life events and suicide behaviour in young people aged 10 to 25 years. From the 28 eligible articles included, an association between the number of adverse or negative

life events and suicidal behaviour was found, although the authors advised the strength of the association seemed to vary depending on the number and type of event experienced. Like the previous review, Serafini et al. (2015) used a broad definition of life events, which included sexual and physical abuse, death of a parent, and homelessness, which meant they too were unable to carry out a meta-analysis and provide information on the strength, or moderators, of the association.

Franklin et al. (2017) completed a comprehensive meta-analysis of 365 longitudinal studies from the last 50 years of suicidality research that have attempted to identify risk factors of suicidality. Their meta-analysis found stressful life events were associated with suicide (23 comparisons; weighted OR = 2.18, CI = 1.63 to 2.93), which made stressful life events one of the top five predictors for suicide. The paper did not report the heterogeneity of the association, nor whether stressful life events were associated with any other aspect of suicidality as it only reported the top five predictive risk factors. Perhaps due to the sheer size of the meta-analysis, the review did not describe the details of how stressful life events were defined or operationalised, the timeframe in which both stressful life events and suicide were individually measured and follow-up time between their measurement, nor did it consider the potential moderators of stressful life events and suicidality outcomes. Therefore, caution should be used when interpreting this analysis due to the high degree of uncertainty regarding the methodological approach utilised.

While the evidence-base appears to indicate a clear association between the experience of stressful life events and suicidality, the various methodological limitations of the research mean that it is difficult to estimate the nature and strength of the association between experiencing stressful life events and subsequent aspects of suicidality.

1.5   The systematic review and meta-analysis

The limitations of the three significant reviews of the literature (Franklin et al., 2017; Liu & Miller, 2014; Serafini et al., 2015) highlight gaps in the research which need addressing. The first is whether stressful life events prospectively predict increases in subsequent suicidality. This would check that suicidality does not simply increase perceptions of stressful life events, but that experiences of stressful life events precede increased experiences of suicidality. While establishing the presence of a prospective relationship cannot be regarded as evidence of causality, it would

suggest that individuals experiencing stressful life events could subsequently be more vulnerable to suicidality.

A second is regarding the strength of the association. Of the three current reviews in this area, two were narrative reviews (Liu & Miller, 2014; Serafini et al., 2015). While evidence for an association was suggested, these reviews were unable to provide any evidence regarding the magnitude of this association. The only review which has sought to meta-analyse the strength of the association did not describe the details of how stressful life events were defined or operationalised (Franklin et al., 2017). Similarly, the timeframe in which both stressful life events and suicide were individually measured and followed-up were not reported, nor were potential moderators of stressful life events and suicidality outcomes considered (Franklin et al., 2017). Understanding moderators of the association may explain what protects or increases an individuals' vulnerability to suicidality when they experience stressful life events.

The third concerns whether there is a significant association between stressful life events and suicidality when the concept of stressful life events is not confounded by the inclusion of traumatic life events. Traumatic life events are distinctly different from stressful life events, as they consider events which put either the individual or someone close to them at risk of serious harm, death, or threaten one's personal integrity (APA, 2000). Stressful life events, on the other hand, consider everyday regular occurrences experienced on an irregular basis, and they are likely to be more common and widespread than traumatic life events. Evidence suggests stressful life events are independently associated with suicidality (e.g. Campos et al., 2016; Kang et al., 2014; Woodhead et al., 2014), indicating they are important in their own right. However, the previous three reviews did not distinguish between traumatic and non-traumatic stressful life events, and there is currently no systematic synthesis which has investigated non-traumatic, stressful life events.

A forth relates to the definition and measurement of stressful life events. The broad methodological variation regarding the validity of stressful life event measures created ambiguity in the findings of previous reviews (Liu & Miller, 2014; Serafini et al., 2015). The use of a consistent definition of stressful life events, and consideration around the validity of measure used, may increase methodological quality and provide further clarity regarding the association between stressful life events and suicidality.

Understanding the strength and variability of the association between stressful life events and suicidality could inform understanding of how different aspects of the models of suicidality are linked and interact (O'Connor & Nock, 2014). In contrast, no significant association would contradict the models and indicate the need for theoretical revision. Understanding of the role of stressful life events as a risk factor for suicidality, as well as the factors which moderate the relationship, could also be important clinically. Ascertaining the strength and variability of the prospective relationship between stressful life events and suicidality could help inform psychological risk assessments, psychological interventions and the extent to which these should focus on resilience building and proactive approaches.

The purpose of the present review was to explore the prospective association between experiencing stressful life events and subsequent suicidality. In particular, there were two specific research questions:

1. What is the strength of the prospective relationship between the experience of stressful life events and subsequent suicidality?
2. Which factors moderate this relationship?

2. Methods

This section will outline the approach to identifying appropriate studies, data extraction, quality assessment, and data analysis in line with the Cochrane handbook for systematic reviews (Deeks, Higgins & Altman, 2011a), Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement (Moher, Liberati, Tetzlaff, & Altman, 2009), and introducing items from PRISMA-Equity 2012 (Welch et al., 2012).

2.1 Ethical Considerations

The review analysed data that was publicly available in journal articles and directly from article authors, therefore did not require ethical approval or patient consent.

2.2 Search Methods

2.2.1 Protocol and registration

The review protocol was registered with the PROSPERO (prospective register of systematic reviews) database at the University of York's Centre for Reviews and Dissemination (CRD) before the review commenced. The review's registration number is CRD42018100041. Registering the review in a public domain allowed transparency of the aims and methods of the research and helped avoid research replication.

2.2.2 Criteria for considering studies for analysis

To enable screening of the studies found through the database searches, criteria were set to establish which studies would be included in the review. The criteria used in the current review were adapted from the Liu and Miller (2014) review. For studies to be included, they had to be observational, quantitative longitudinal cohort studies which provided data on the association between stressful life events and a subsequent aspect of suicidality in adults or adolescents ($\geq$14 years and older). Stressful life events were defined as the experience of objective occurrences reported by the participant or informant. The measure of stressful life events was deemed to be credible when it was validated and covered multiple forms

of events; modified measures were also included when based on a single validated measure. Measures of single stressful life events, childhood stressful life events in adults, or trauma experiences, abuse or maltreatment were excluded. Aspects of suicidality could include suicidal ideation, suicidal plans, suicide attempts and suicide; and excluded non-suicide self-injury (NSSI) and self-harming behaviours that did not involve suicidal intent. No restrictions were placed around the measurement of suicidality. Studies in languages other than English were excluded. Studies published in peer reviewed journals were included.

2.2.3   Search strategy and data sources

Individual searches were completed in the following five electronic bibliographic databases: MEDLINE, PsycINFO, EMBASE, CINAHL, and Cochrane. The search strategy included combinations of three key blocks of terms ('life events', 'suicide', 'longitudinal') using a combination of medical subject headings (MeSH terms) and text-words. Filters were used to include only studies written in English. The search strategy did not include the term 'adverse' or 'adversities' as used in Serafini et al. (2015) as it was believed these terms would capture trauma experiences, abuse or maltreatment which are excluded from this review. The search strategy was reviewed by thesis supervisors and a University of Leeds library research support advisor, in order to develop a comprehensive search likely to find all articles relevant to the review.

In addition to database searches, reference lists of eligible studies were searched by hand. In the case of an article or study data not being readily available, the corresponding author was contacted. Full details of the search strategy are provided in Appendix A. Searches were conducted from database inception until October 2018, and then updated to April 2019. The searches started from each database inception date to allow the capture of all eligible studies. No additional articles that met the inclusion criteria were found during the second search.

2.2.4   Study selection

The search results were exported to Endnote version X8.2 (Clarivate Analytics, Philadelphia, USA) and duplicates were removed. Study selection was

undertaken in two stages. Initially, titles and abstracts of identified studies were screened for eligibility by the thesis author (EH). Then ten percent of titles and abstracts (n=199) were independently screened by one of the thesis supervisors (JJ) who was blinded to earlier screening by EH. Interrater reliability was assess using Cohen's kappa statistic (Cohen, 1960), and level of agreement was considered moderate (k=0.768) according to McHugh (2012). Disagreements (n=8) were resolved by discussion. This revealed a conservative approach to screening by EH, explaining the majority of the discrepancy. It was agreed to include all disagreements in the full-text screen. EH screened the remaining titles and abstracts. In the second stage, full-texts of retained studies were accessed and further screened against the inclusion and exclusion criteria. Fifty percent of full-texts (n=80) were screened by EH and two independent reviewers (SW & AH), and interrater reliability was strong (k=0.805). Disagreements (n=4) were resolved by discussion in favour of EH. The remaining full-text screening were completed by EH. Any queries around study eligibility were discussed in supervision.

When data needed for eligibility decisions were not readily available, such as the stressful life events measure used, the timeframe of the association reported, or association data, corresponding authors were contacted by email to request study data. Twenty-two authors were sent requests for study data. Eleven authors responded to initial requests and provided relevant eligibility data. If authors did not reply to the initial request a further follow-up request was sent two weeks later. Six authors responded to follow-up requests and provided relevant eligibility data. One author replied stating the data was not available therefore the study was not able to meet the eligibility criteria and was excluded. If no response was provided after the follow-up request, the study was excluded. This was the case for four studies. A table of contacts with corresponding authors is provided in Appendix B.

2.3   Data Extraction

A data extraction form was devised by adapting Cochrane's Public Health Group Data Extraction and Assessment Template in Excel 2013 (Microsoft Corp., Redmond, Washington) and piloted to ensure all necessary data was captured. Quantitative data on the association between stressful life events and subsequent suicidality were extracted in a separate Excel file for the meta-analysis. All data were

extracted independently by EH and checked by JJ. Discrepancies were resolved through discussion.

Three types of data were extracted from the eligible studies: sample characteristics, study design and study data. If descriptive data was not reported in the paper, then it was marked down as 'not reported'. The following information was extracted from eligible studies:

2.3.1 Sample characteristics

The following aspects of participant information were extracted for each study:

- Age – mean and standard deviation.
- Gender – percentage female.
- Socio-demographic information – percentage of socio-demographics
- Mental health diagnosis – percentage of any mental health diagnosis reported.
- Previous history of suicidality – number of participants reporting previous history of suicidality.
- Treatment or intervention outside of the study – percentage on any medication, receiving medical intervention, or currently in a talking therapy.

2.3.2 Study design

Information was extracted about the key characteristics of the study design, including:

- Sample size – number of participants
- Country – the name of the country where the study was completed.
- Design – categorised as primary study or secondary analysis of data
- Participant population – categorised as clinical or non-clinical
- Length of follow-up assessment – number of months

2.3.3 Study data

The following aspects of study data were extracted for each study:

Measurement of stressful life events.

Information was extracted regarding: a) what measure was used and whether it had been modified; b) type of events included in the measure (i.e. negative and positive events, or only negative events); c) how the measure was scored (i.e. nominal, frequency or weighted/adjusted score); d) the time-frame covered by the measure.

Measurement of suicidality.

Information was extracted regarding: a) the type of suicidality outcome (i.e. ideation, plan, attempt, suicide); b) what type of measure was used (i.e. self-report measure, interview, singular 'yes/no' question); c) how the measure was scored (i.e. nominal, frequency or weighted/adjusted score); d) the time-frame covered by the measure.

Association data.

All eligible studies needed to include quantitative data on the association between stressful life events and a subsequent aspect of suicidality. Effect size data were extracted for all included studies, which consisted of odds ratio (OR), a type of regression analysis or correlations. Where studies conducted separate analysis between subgroups, separate subgroups were created in the data extraction form and both effect sizes were recorded.

2.4 Health Equity

Certain health inequalities are known to disproportionally elevate risk of suicidality (Platt, 2016). The PROGRESS-Plus framework (Evans & Brown, 2003; Oliver et al., 2008; Kavanagh, Oliver & Lorenc, 2008) is used to guide the consideration of health equity in systematic reviews. PROGRESS-Plus is recommended by PRISMA Equity Extension, and the Equity Methods Group and the Public Health and International Development Review Groups from the Campbell and Cochrane Collaborations (O'Neill et al., 2014). PROGRESS-Plus refers to Place of Residence, Ethnicity, Occupation, Gender, Religion, Education, Social Capital, Socio-economic Position (SEP), and other important factors that may impact on health equity, such as Age, Disability and Sexual orientation (Kavanagh et al, 2008). Descriptions of each category can be found in Table 2.

The PROGRESS-Plus framework was used to guide extraction of factors which contribute to health inequity in each study's participant description, methodological approach and results.

Table 2. Categories included in the PROGRESS-Plus framework

PROGESS	
Place of residence	Rural/urban, country/state, housing characteristics
Ethnicity	Ethnic background
Occupation	Professional, skilled, unskilled, employed etc.
Gender	Female, male, non-binary, gender characteristics and identities
Religion	Religious background
Education	Years in and/or level of education attained, school type
Social Capital	Neighbourhood / community / family support
Socioeconomic position (SEP)	Income, means tested benefits/welfare, affluence measures, etc.
Plus	
Age	Age range
Disability	Physical or emotional/mental health condition
Sexual orientation	Heterosexual, gay, lesbian, bisexual

2.5   Methodological Quality and Risk of Bias

All studies included in the review were observational therefore methodological quality was looked at, as opposed to individual risk of bias. An aim of this review was to establish the strength of the association between stressful life events and aspects of suicidality. Any biases relating to the methodological quality of the studies included could therefore influence the reliability of the association. The Effective Public Health Practice Project (Thomas, Ciliska, Dobbins & Micucci, 2004) was used to guide the methodological quality assessment of each individual study. Publication bias analysis was used to assess risk of bias across studies.

2.5.1 The EPHPP quality assessment guidance

Relevant components from the Effective Public Health Practice Project (EPHPP) quality assessment guidance (Thomas et al., 2004) for the assessment of observational studies were used in this review and meta-analysis. The majority of these criteria have been used in previous research to assess the methodological quality of observational studies (Blakemore et al., 2014; Panagioti et al., 2015) and were therefore replicated in this review. The quality assessment of each study included assessment of the methodology and was used as a framework for the narrative synthesis of the results. The following criteria were used to conduct the quality review and studies were allotted one point for each criterion met, with a maximum rating of four. The quality appraisal key criteria were:

1) A response rate or data collection from eligible participants of 70% or greater at baseline

2) Control for a minimum of three important confounding factors in the analysis which comprised a combination of demographic characteristics (e.g. age, gender) and clinical characteristics relevant to suicidality (e.g. mental health diagnosis, previous history of suicide).

3) The use of valid and reliable data collection measures (where not described by the study, the literature of the measure will be looked at).

4) A response rate or data collection of from eligible participants 70% or greater at follow-up

Studies which received a score of three or more were considered high quality and more likely to produce reliable results. As studies needed an observational, longitudinal design for inclusion, components assessing study design and blinding of outcome were not relevant to this review and meta-analysis. All eligible studies were independently reviewed by EH and checked by JJ. Disagreements were resolved by discussion.

2.5.2 Publication bias

Publication bias describes the failure to publish studies with negative or non-significant results (Rothstein, Sutton & Borenstein, 2006). Publication bias can lead to meta-analyses overestimating true effect size as it would more likely be larger than if negative or non-significant studies were published and included. Potential risk of

publication bias was assessed by inspecting the symmetry of a funnel plot and the statistical significance of the Egger's test (Egger, Smith, Schneider & Minder, 1997) in accordance to the Cochrane Handbook (Higgins & Green, 2011). The funnel plot displays the relationship between effect size and standard error. The Egger's test measures the degree of funnel plot asymmetry using regression analysis. If there is no funnel plot asymmetry and the Egger test is non-significant, the meta-analysis is unlikely to be influenced by publication bias. The funnel plot and Duval and Tweedie's trim and fill analysis (Duval & Tweedie, 2000) was also used to compare the observed and computed effect sizes, assessing the influence of the imputed effect sizes on the summary effect.

2.6   Data Analysis

Data were analysed in two stages. Firstly, data regarding participant and study characteristics, stressful life events and suicidality measures were analysed using descriptive statistics. In the second stage, meta-analyses and subgroup analyses, and univariate meta-regression analyses were conducted to explore the association with the primary outcome. All analyses were performed in Comprehensive Meta-Analysis (CMA) software (version 3; Borenstein, Hedges, Higgins & Rothstein, 2013).

2.6.1   Summary measure

The primary outcome of this review was the effect of stressful life events on an aspect of suicidality ('suicidal ideation', 'suicide plan', 'suicide attempt' or 'suicide'). To measure this effect, the same effect metric needs to be used across studies to allow the consistency of the effect to be assessed and a summary effect size to be computed. Odds ratios (ORs) were chosen as the effect size to pool results across the studies as this was the most commonly reported effect size in the primary studies, and it is typically used in prospective studies reporting data as the number of events and non-events in two groups (Borenstein, Hedges, Higgins, & Rothstein, 2009). Within the context of this review, the OR would quantify the ratio of the odds between suicidality and no suicidality in those who had previously experienced stressful life events and those who had not (Figure 1). In other words, an OR would quantify the strength of the relationship between stressful life events and subsequent suicidality.

Suicidality

		Yes	No
Stressful Life Events	**Yes**	A	B
	No	C	D

Figure 1. A 2x2 table of outcome by predictor

The association data reported in the primary studies were usually based on dichotomous outcome data (i.e. 'yes/no' response to suicidality question), however studies also reported association data based on continuous outcome data (i.e. score of suicidality measure) so were transformed to ORs. Effect sizes were transformed in CMA as it allows computation of ORs from various metrics as recommended by the Cochrane Handbook (Higgins & Green, 2011).

2.6.2 Converting among effect sizes

Meta-analysis involves the comparison of effect sizes, therefore studies reporting correlational association data, such as regression or correlations coefficients, were convert to ORs in CMA (Borenstein et al, 2013). Comprehensive Meta-Analysis combines formulas for converting effect sizes and the variance so that correlational data can be converted to binary data, via continuous data. This is shown schematically in Figure 2. Appendix C. gives a description of how CMA converts the effect sizes and variance of correlational data to binary data (i.e. ORs).

Borenstein et al. (2009) assert that specific assumptions are made regarding the nature of the underlying effects when different measures are converted. While they acknowledge that these assumptions may not always hold, "the decision to use these conversions is often better than the alternative, which is to simply omit the studies that happened to use an alternate metric" (Borenstein et al, 2009, pp. 46). Including converted studies prevents the loss of information, both within individual meta-analyses and potentially systematically, and avoids biasing the sample.
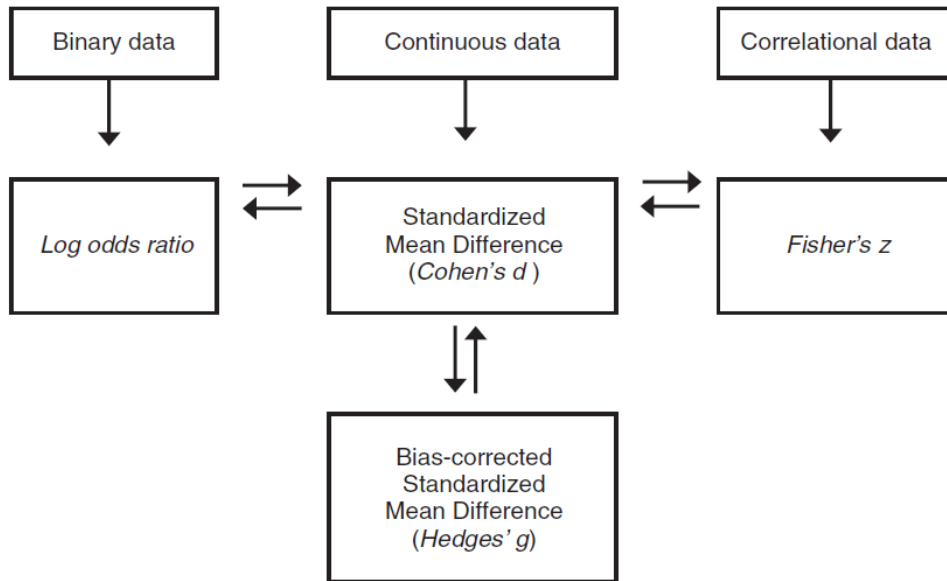
Figure 2. CMA converting effect sizes (image from Borenstein et al, 2009).

Odds ratio calculations are carried out on a log scale for the analysis to maintain symmetry, therefore to perform the meta-analysis the log odds ratio and the standard error of the log odds ratio are computed. The summary log odds ratio is then converted back into odds ratio scale to give the summary OR. This is shown schematically in Figure 3, and the calculations used are described in Appendix D.
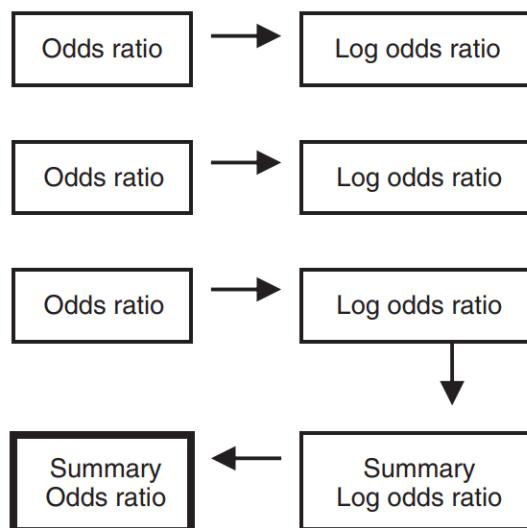
Figure 3. Schematic representation of summary ORs (image adapted from Borenstein et al, 2009).

2.6.3 Meta-analysis to explore the relationship between stressful life events and suicidality

A summary OR together with the 95% confidence intervals were calculated with the available association data from the included studies: OR >1 indicates that stressful life events are associated with increased risk for suicidality, OR <1 indicates that stressful life events are associated with decreased risk for suicidality; OR=1 indicates no association between stressful life events and suicidality. When the 95% confidence intervals did not include 1, the association was statistically significant. Meta-analysis calculations can be found in Appendix E. Where studies reported both adjusted and unadjusted analysis, effect sizes adjusted for potentially confounding variables were selected. It was assumed that the true effect size would vary study-to-study due to a significant degree of heterogeneity, and for this reason the individual ORs across the studies were pooled using random-effects model (Harris et al., 2008). Unlike a fixed-effect model, a random-effects model accounts for within- and between-study variance.

2.6.4 Assessing heterogeneity

Heterogeneity refers to the occurrence of more variation in study outcomes than would be expected by chance alone. When reviews combine the results of various different studies there is the potential for heterogeneity. The emphasis of prospective studies in this review will reduce some possible heterogeneity because of the focus on one research design. Heterogeneity between the included studies was formally examined in the meta-analysis using the I^2 statistic (with 95% test-based confidence intervals), which reports the percentage of overall variation across the studies that is due to heterogeneity as opposed to chance (Higgins, Thompson, Deeks & Altman, 2003). This can sometimes be referred to the 'total true variance', as a meta-analysis can only address variance between the studies included, and not variance within the studies. The formula for calculating I^2 is presented in Appendix F. I^2 values of 25%, 50%, and 75% are regarded as low, moderate, and high heterogeneity, respectively (Higgins et al, 2003). Possible sources of heterogeneity were explored through subgroup analyses and controlling for moderating factors in the univariate meta-regression analysis.

2.6.5 Sensitivity analyses

Two types of sensitivity analyses were undertaken to test the stability and robustness of the results:

One-study removed sensitivity analysis

To evaluate the influence of each study on the overall effect size, a leave-one-out approach (Higgins & Green, 2011) was performed whereby each study was removed from the analysis and the summary OR was recalculated.

Quality assessment rating sensitivity analysis

To evaluate the influence of the methodological quality of the studies on the overall effect size, the analysis was recalculated with only the higher quality studies included (as indicated by quality assessment ratings of 3 or 4 points).

2.6.6 Secondary analyses

Secondary analysis was performed to further understand the relationship between stressful life events and suicidality by exploring whether the strength of the association changes when considering the impact of moderating factors.

Subgroup analysis

Subgroup analyses are used to compare the mean effect for different subgroups of studies. Within this thesis, pre-specified subgroup analyses (Deeks, Higgins & Altman, 2011b) were used to explore potential sources of heterogeneity of the relationship between stressful life events and suicidality, such as age, gender, population sample, and length of follow-up assessment. A random-effect model using separate estimates of between-study variance compared the effect size across subgroups using a Q-test for heterogeneity. The Q-statistic is sensitive to the ratio of observed (i.e. between-study variation) to expected (i.e. within-study error) dispersion, therefore can isolate the true variation explained by subgroup membership between the studies. The calculations of a Q-test and true variance are found in Appendix G.

Meta-regression analysis

Meta-regression analyses are used to assess the relationship between study-level covariates and effect size, and the proportion of variance explained amongst the covariates. While there is currently no definitive requirement around the minimal number of studies needed to complete a meta-regression, Borenstein et al. (2009) suggests a minimum of ten studies per covariate when considering multivariate meta-regressions. Therefore, due to the small number of studies included in this thesis, it was decided that only univariate meta-regression analysis would be used to further explore the association between stressful life events and suicidality. Using a random-effects model, the Z-test was used to test the impact of a single coefficient on the effect size, while other covariates are held constant. This formula is shown in Appendix H.

2.6.7 Data cleaning and preparation

Data cleaning and preparation were conducted. Two papers were found to be using data from the same study at different time-points, therefore the paper with the smaller sample size was removed from the meta-analysis.

Individual reporting of socio-demographic data varied between the included studies; some studies reported socio-demographic data for participants who completed follow-up and were used in analysis, however other studies only considered data from participants who completed baseline and did not account for potential changes in their socio-demographic data due to sample attrition. When considering the use of socio-demographic factors as covariates within the secondary analysis, a decision was made to use baseline socio-demographic data when studies reported no significant differences between the baseline and follow-up samples, noting which studies used baseline data within the footnotes. If studies did report significant differences between baseline and follow-up socio-demographic data, then studies were removed from that specific secondary analysis.

Two studies conducted separate analyses between two independent subgroups. In each case, the data were extracted and entered into the meta-analysis as two separate effect sizes. The study's socio-demographic data was used for both subgroups unless the study explicitly reported the separate sample characteristics for the subgroups (e.g. separate analyses were conducted for females and males).

Developing covariates that adequately captured the characteristic and allowed for the assessment of its impact on the summary effect proved difficult due to the small number of studies and the varying socio-demographic and clinical characteristics reported by the studies. The most consistently reported variables which could be used within the secondary analyses from all included studies were: age, gender, participant population, and length of follow-up assessment. Factors that were not able to be included within the secondary analyses due to inconsistent reporting included further socio-demographic characteristics, common mental health diagnoses, and history of suicidality.

Categorical data covariates were created to limit the spread of the data due to the small number of studies included in the meta-analysis. Each covariate contained two categories. Covariates were categorised in the following ways:

- Age (below the mean vs. above the mean) – the total mean age across the studies was calculated, then each study was categorised as either: below the mean, or above the mean.

- Gender majority (female vs. male) – studies with greater than 50% females were categorised as female, and those with less were categorised as male.

- Participant population (clinical vs. non-clinical) – studies were categorised depending on the population participants were recruited from.

- Length of follow-up assessment ($\leq$ 12 months vs. > 12 months) – studies were categorised depending on whether the length of follow-up assessment was less than or equal to twelve months, or greater than twelve months.

3. Results

The results are presented in three sections. First, an analysis of the studies included, their participants, and the stressful life event and suicidality measures used in the studies. Second, a description of the health equity and methodological quality of the included studies. Finally, the results of the meta-analysis, subgroup and meta-regression analyses will be presented.

3.1   Study selection

The search strategy identified 3,754 records. Two additional records were identified through reference list scanning. After duplicates were removed, the remaining 2,237 titles and abstracts were screened for eligibility; 173 of these were retained for full-text screening. Eight papers meet the inclusion criteria (Campos et al., 2016; Chan, Shamsul & Maniam, 2014; Joiner & Rudd, 2000; Kang et al., 2014; Mazza & Reynolds, 1998; Tyssen, Hem, Vaglum, Grønvold & Ekeberg, 2004; Tyssen, Vaglum & Ekeberg, 2001; Woodhead, Cronkite, Moos & Timko, 2014). Two papers reported on the same study at different timepoints; both papers were included in Table 4., but only one paper was included in the analyses and reporting (Tyssen, Vaglum & Ekeberg, 2001). Figure 4. shows the flow of studies through the search process.

3.2   Characteristics of the studies and participants

Key descriptive data from the studies included are presented in Table 3. Study characteristics and details of data extracted are provided in Table 4. The seven studies included nine independent comparisons on 2,639 participants, published between 1998 and 2016. The majority of studies measured suicidal ideation as the outcome (n = 6); only one study looked at suicide attempts as the outcome. Studies were conducted across five different countries; North America (n = 3), Europe (n = 2), and Asia (n = 2). Overall, the proportion of female to male participants was approximately equal (54% female). Studies included participants with a wide range of ages, with an average age of 37 years. Five studies were conducted with non-clinical populations; three with the general population, one with high school students, and one with medical students. The two studies conducted with clinical populations

included one with psychiatric inpatient participants, and one with participants accepted to take part in a military medical suicide treatment research study.
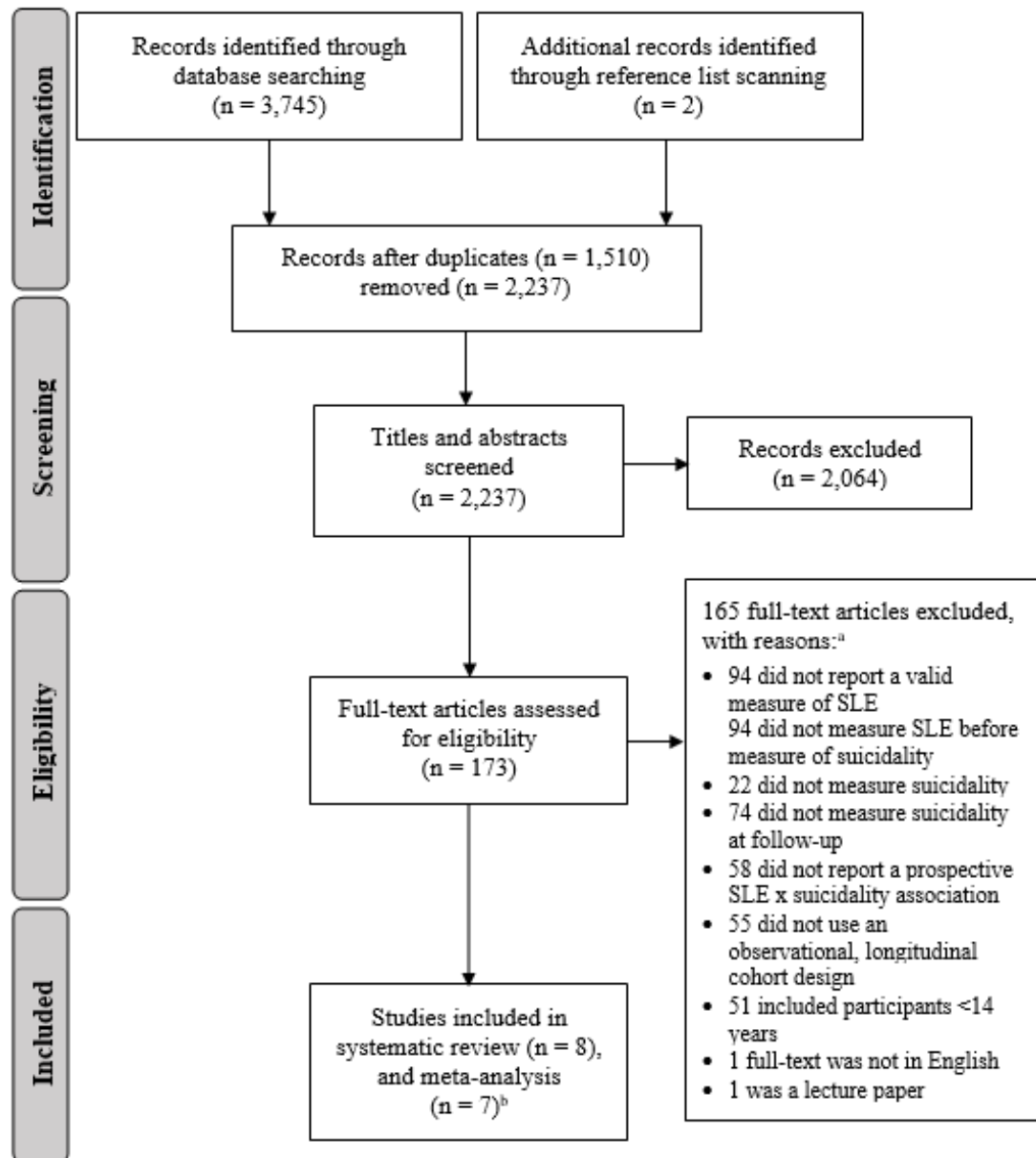
Figure 4. Flowchart of studies included in the review.

[a]Some studies were excluded for more than one reason so the listed studies do not equal 165.
[b]Two papers reported on the same study at different timepoints, only the paper with the larger sample size was included in the analyses and reporting.

Table 3. Descriptive data of studies included in analyses.

Category	Characteristics	N = 7 studies
Study and population	Sample size (range)	2,639 (66 to 909)
	Mean Age	37.23
	% Female[a]	54.3%
	Continent	
	North America	3 (43%)
	Europe	2 (28.5%)
	Asia	2 (28.5%)
Methodological quality (N = 8 studies)	Response rate at baseline >70%	4 (50%)
	Control for confounding variables	5 (63%)
	Valid and reliable measures	1 (12.5%)
	Response rate at follow-up >70%	6 (75%)
Health Equity - PROGRESS-Plus factors	Sample description	8 (100%)
	Confounding factor	4 (50%)
(N = 8 studies)	Differential effects	1 (13%)
Measures	**Stressful life events**	
	Interview-approach	0 (0%)
	Self-report	7 (100%)
	Suicidality	
	Interview-approach	2 (28.5%)
	Self-report	1 (14.25%)
	One-question measure	3 (43%)
	Other	1 (14.25%)
Outcomes	**Suicidality outcome**	
	Suicidal ideation	6 (86%)
	Suicidal plans	0 (0%)
	Suicide attempt	1 (14%)
	Suicide	0 (0%)

[a] Some papers did not report socio-demographic data of participants whose data was included in the analyses. All these papers state participants included in the analyses did not significantly differ in socio-demographics from those not included in the analyses, therefore the authors calculated the gender distribution from the percentage reported in the paper.

Table 4. Characteristics of studies, populations and outcomes included in the review.

First author, year	Population (country)	N	Female, no. (%)	Mean age (SD)	Measure of SLE	Aspect of suicidality (measure)	Length of follow-up assessment	Quality assessment score
Campos, 2016	General population (Portugal)	195	104 (53%)	34.88 (12.49)	Modified Life Experiences Survey	Suicidal ideation (single item from Suicide Behaviors Questionnaire-Revised)	Three months	3
Chan, 2014[a]	Psychiatric inpatient (Malaysia)	66	28 (56%)	43.8 (12.1)	Malay version of Social Readjustment Rating Scale	Suicide attempt (questions from the Structured Clinical Interview for DSM-IV, and clinical records)	One year	1
Joiner, 2000[a]	Military medical settings (USA)	249	45 (18%)	22 (2.5)	Modified Life Experience Survey	Suicidal ideation (Modified Scale for Suicidal Ideation)	One month	2
Kang, 2014[a]	General population data (South Korea)	909	527 (58%)	72.2 (5.9)	Modified List of Threatening Experiences	Suicidal ideation (questions from the Geriatric Mental State diagnostic schedule)	Two years	3
Mazza, 1998	High school population (USA)	374	202 (54%)	15.5 (1.02)	Life Events List-Revised	Suicidal ideation (Suicidal Ideation Questionnaire)	One year	1

First author, year	Population (country)	N	Female, no. (%)	Mean age (SD)	Measure of SLE	Aspect of suicidality (measure)	Length of follow-up assessment	Quality assessment score
Tyssen, 2001	Medical students (Norway)	371	208 (56%)	28 (2.8)	Modified Social Readjustment Rating Scale	Suicidal ideation (single question)	One year	3
Tyssen, 2004[b]	Medical students (Norway)	327	176 (54%)	28 (2.8)	Modified Social Readjustment Rating Scale	Suicidal plans (single question)	Two-three years	2
Woodhead, 2014[c]	General population (USA)	475	318 (61%)	44.4 (10.7)	Modified Health and Daily Living Form	Suicidal ideation (single question)	Thirteen years	1

[a] These papers report socio-demographic data at baseline, not follow-up. As the papers state participants lost to follow-up did not significantly differ in socio-demographics from participants who completed follow-up, the authors calculated the gender distribution at follow-up from the percentage reported in the paper.

[b] This paper was not included in the meta-analysis.

[c] This paper reports socio-demographic data at follow-up, not participants included in analyses. As the paper states participants included in the analyses did not significantly differ in socio-demographics from participants at follow-up, the authors calculated the gender distribution for those included in the analyses from the percentage reported in the paper.

3.3 Characteristics of stressful life event and suicidality measures

Studies measured stressful life events using a variety of tools. The most commonly used were the Life Experiences Survey (n =2; Sarason et al., 1978) and the Social Readjustment Rating Scale (n = 2; Holmes & Rahe, 1967). The other measures used were the List of Threatening Experiences (Brugha & Cragg, 1990), the Life Events List-Revised (Gersten, Langer, Eisenberg & Orzeck, 1974; Reynold, 1982), and The Health and Daily Living Form (Moos, Cronkite & Finney, 1992). All measures were modified versions of the original measure and used a self-report approach. Two studies used measures which included both negative and positive events, while the rest only measured the experience of negative events (n = 5). Measures were scored either by the number of events experienced (n = 5), or by totalling the scaled severity scores (n = 2). The time-frame covered by the measures was the last 12 months (n = 6); one study did not state the time-frame used.

A range of approaches were used to measure an aspect of suicidality. Studies mainly looked at suicidal ideation (n = 6), one study had suicide attempts as an outcome. None of the studies measured suicidal plans or suicide as an outcome. The type of measure used by studies varied. The main approach used was a single-item measurement (n = 3), for example "Have you ever during the last year thought of taking your own life, even if you would not really do it?" (Tyssen et al, 2001). Other approaches used included an interview-approach (n = 2), such as the Modified Scale for Suicidal Ideation (Miller et al., 1986), and a self-report approach (n = 1), such as the Suicidal Ideation Questionnaire (Reynolds, 1988). One study appeared to use a combination of questions from a structured clinical interview and professional observations (i.e. clinical notes). Measures were scored by dichotomous 'yes/no' responses (n = 3), summing of multiple scaled responses (n = 2), or using a single scaled score (n = 2). The time-frame covered by measures varied; two studies considered the previous 12 months, three studies asked about the last month, and one study appears to focus on current experiences. The time-frame used was not stated by one study.

3.4 Health equity using PROGESS-Plus

PROGRESS-Plus factors within the eight studies included in the review are presented in Table 5. The use of PROGRESS-Plus factors within the method and

results of the eight studies identified in the systematic review are presented in Table 6. In terms of the PROGRESS-Plus framework, all studies included at least three health equity factors within the description of their participant sample (see Table 5.). The highest number of factors included by a study was eight (n = 1). Six or seven factors were included in three studies, however the majority of studies included three or four factors (n = 4). Age and gender were reported by all studies. None of the studies reported sexual orientation, and only one study reported either place of residence or religion within their description.

Table 5. PROGRESS-Plus factors within 8 studies included in the systematic review.

PROGRESS-Plus factor	Sample description	Confounding factors	Differential effects
Place of residence	1	0	0
Ethnicity	4	1	0
Occupation	3	2	0
Gender	8	5	1
Religion	1	1	0
Education	6	2	0
Social Capital	5	4	0
Socio-economic position (SEP)	2	1	0
Age	8	4	0
Disability	3	4	0
Sexual orientation	0	0	0
Total studies	8	5	1

Five studies reported the use of PROGRESS-Plus factors within their data analysis plan (see Table 6.). Most commonly this involved controlling or adjusting the statistical approached used for a PROGRESS-Plus factor, although one study also described conducting separate analysis according to gender. One study included several factors but used separate analyses for each factor, so no confounding effect was measured. Four studies reported the inclusion of gender within their analysis, and age, social capital (e.g. marital status) and disability were reported to be included by three studies. One study reported the use of occupation and education with their

analysis. Place of residence, ethnicity, religion, social-economic position and sexual orientation were not reported to be included in any study's analysis.

Three studies out of the eight included in the review reported the differential effects (see Table 6.). One study reported separate analyses by gender, finding that the association between stressful life events and suicidal ideation is significant in males but not females. One study reporting differential effects found non-significant association for stressful life events and suicidal ideation in both the adjusted and unadjusted analyses. However, as the adjusted analysis included multiple PROGRESS-Plus factors, it would have been impossible to state which factor/s had influenced the association should the results have been significant. This was the case for the third study, which could not be included within the meta-analysis; while the authors found a significant, adjusted association between stressful life events and suicidal plans, the factor/s influencing the difference in the association were not reported.

Table 6. Methods and results of differential effects analysis of studies (n = 8)

First Author	PROGRESS-Plus	Methodological approach	Reported differential affects
Campos	Occupation, Gender, Education, Age, Disability	Multiple regression analysis controlled for age, gender, marital status, education, unemployment, chronic disease, depressive symptoms, and a previous psychiatric diagnosis when predicting SI at follow-up.	NR
Chan	Ethnicity, Occupation, Gender, Religion, Education, Social Capital, SEP, Age, Disability	Univariate logistic regression analyses were conducted on the separate factors and SLE.	NA
Joiner	NA	NA	NA

First Author	PROGRESS-Plus	Methodological approach	Reported differential affects
Kang	Gender, Social Capital, Age, Disability	Logistic regression models adjusted for age and gender, controlling for 'potentially associated factors' when predicting SI at follow-up.	NR
Mazza	Gender, Social Capital, Disability	Multiple regression analysis was conducted separately by gender, both analyses controlling depression and social support when predicting SI at follow-up.	Baseline SLE were significantly related to suicidal ideation at 12 months for males (p=0.01), but not for females.
Tyssen	Gender, Social Capital, Age	Multivariate logistic regression analysis controlled for age, gender and marital/cohabitant status when predicting SI at follow-up.	Adjusted and unadjusted odds ratios reported for SLE and SI, both were non-significant.
Tyssen[a]	Gender, Social Capital, Age, Disability	NR	Reported adjusted and unadjusted odds ratios for SLE and SP (p<0.01), when controlling for age, gender, marital/ cohabitant status, depression symptoms.
Woodhead	NA	NA	NA

SLE = stressful life events; SI = suicidal ideation; SP = suicidal plan; NA = not applicable; NR = not reported.

[a]Study not included in the meta-analysis

3.5   Methodological Quality

In terms of the individual quality criteria, four studies reported a response rate of 70% or greater, five studies adjusted for confounders in the analyses, one study used valid and reliable measures, and six studies reported response rates of 70% or greater at follow-up. Three studies met at least three of the four quality criteria, indicating high overall quality; the other four studies met one or two quality criteria.

None of the studies met all four criteria or zero of the criteria. See Table 7. for individual study quality criteria scores.

Table 7. EPHPP quality assessment for each included study.

First Author	Response >70% at baseline	Controls for confounding factors	Valid and reliable measures	Response >70% at follow-up	Total score
Campos	1	1	0	1	3
Chan	0	0	0	1	1
Joiner	0	0	1	1	2
Kang	1	1	0	1	3
Mazza	0	1	0	0	1
Tyssen	1	1	0	1	3
Tyssen[a]	1	1	0	0	2
Woodhead	0	0	0	1	1

[a] Study not included in the analysis.

3.6   Meta-Analyses

3.6.1   Stressful life events and suicidality

The summary effect indicated that stressful life events are associated with a statistically significantly increased risk for suicidality, but the heterogeneity measure was high (9 comparisons: OR = 1.37, 95% CI = 1.10 to 1.70, I^2 = 76. 48 (test-based 95% CI: 55.0 to 87.7)%, p = 0.005). See forest plot in Figure 5. No studies reported that stressful life events were related to significantly lower levels of suicidality.

Study ID	Outcome	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Campos 2016	Ideation	1.795	1.067	3.018	2.206	0.027
Chan 2014	Attempt	1.000	0.997	1.003	0.000	1.000
Joiner 2000	Ideation	2.180	1.371	3.465	3.294	0.001
Kang 2014a	Ideation	1.220	0.930	1.600	1.437	0.151
Kang 2014b	Ideation	1.650	0.999	2.726	1.955	0.051
Mazza 1998a	Ideation	1.039	0.628	1.720	0.150	0.881
Mazza 1998b	Ideation	1.902	1.091	3.314	2.268	0.023
Tyssen 2001	Ideation	1.000	0.667	1.500	0.000	1.000
Woodhead 2014	Ideation	1.574	1.131	2.188	2.694	0.007
		1.369	1.101	1.702	2.828	0.005

Figure 5. Main analysis of the association between stressful life events and suicidality.

When analyses were run for the types of suicidality outcome, the effects of stressful life events were slightly higher for suicidal ideation and heterogeneity decreased (8 comparisons: OR = 1.45, 95% CI = 1.20 to 1.75, I^2 = 38.53 (0 to 72.9)%, p=0.0001). See forest plot in Figure 6. As only one study investigated suicide attempts, a meta-analysis of this outcome was not possible.

Study ID	Outcome	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Campos 2016	Ideation	1.795	1.067	3.018	2.206	0.027
Joiner 2000	Ideation	2.180	1.371	3.465	3.294	0.001
Kang 2014a	Ideation	1.220	0.930	1.600	1.437	0.151
Kang 2014b	Ideation	1.650	0.999	2.726	1.955	0.051
Mazza 1998a	Ideation	1.039	0.628	1.720	0.150	0.881
Mazza 1998b	Ideation	1.902	1.091	3.314	2.268	0.023
Tyssen 2001	Ideation	1.000	0.667	1.500	0.000	1.000
Woodhead 2014	Ideation	1.574	1.131	2.188	2.694	0.007
		1.449	1.197	1.754	3.806	0.000

Figure 6. Main analysis of the association between stressful life events and suicidal ideation.

3.6.2 Sensitivity analyses

One-study removed

While the summary ORs fluctuated in strength, from OR = 1.29 (95% CI = 1.05 to 1.58) to OR = 1.45 (95% CI = 1.20 to 1.75), they all remained statistically significant. This indicates that the presence of an association was not driven by any single study, however some studies had a greater impact on the strength of the association more than others. A forest plot is provided in Appendix I.

Analyses of studies of high methodological quality

A similar result was obtained when only the three studies (four comparisons) with sufficient methodological quality scores (appointed 3+ out of 4 quality assessment criteria) were retained in the analyses (OR = 1.31, 95% CI = 1.03 to 1.66, I^2 = 27.71 (0 to 73.0)%, p = 0.03). A forest plot is provided in Appendix J.

3.6.3 Publication bias

Random-effects funnel plot asymmetry of observed comparisons (Figure 7.) and a significant fixed-effects Egger test indicates that the results might be influenced by publication bias (regression intercept = 1.76, SE = 0.42, p = 0.004). The funnel plot and Duval and Tweedie's trim and fill analysis (Duval & Tweedie, 2000) indicated that while there were no missing studies from the right of the mean, there may be three missing studies to the left of the mean. Inclusion of the three missing studies would have resulted in a non-significant association between stressful life events and suicidality (OR = 1.19, 95% CI = 0.99 to 1.43).

3.7 Subgroup analyses and meta-regressions

In this section the findings of the exploratory analyses, i.e. subgroup and meta-regression, will be described. Data will be presented in tables, and statistically significant results will be presented in graphical displays.
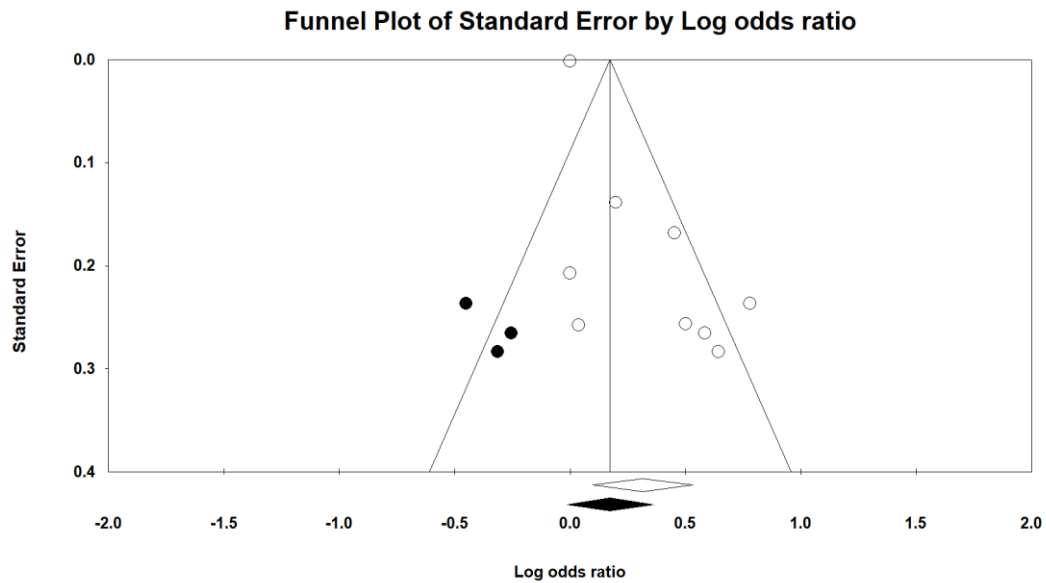
Figure 7. Random-effects funnel plot of observed (white circles) and imputed (black circles) comparisons examining the association between stressful life events and suicidality.

3.7.1 Subgroup Analyses

Subgroup analyses were conducted to compare the mean effect for the different subgroups of studies and explore potential sources of heterogeneity.

Age (mean). The summary effect size of stressful life events was associated with a higher risk for suicidality for those below the mean age of 37.23 years old (5 comparisons; OR = 1.48, 95% CI = 1.06 to 2.07, I^2 = 57.60 (0 to 84.3)%, p = 0.02), whereas the effect of those above the mean age was non-significant (4 comparisons; OR = 1.26, 95% CI = 0.97 to 1.64, I^2 = 77.17 (37.8 to 91.6)%, p = 0.08) See Figure 8. for forest plot.
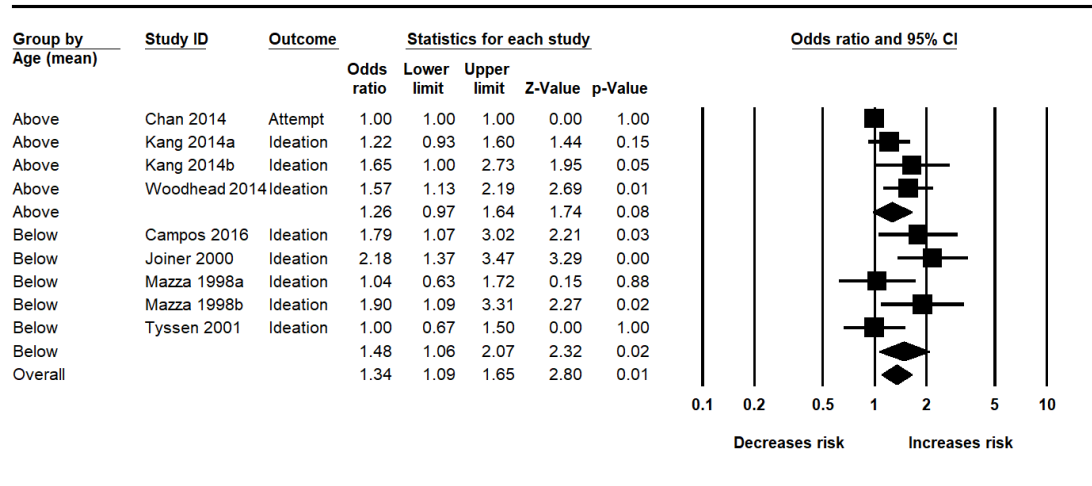
Figure 8. Subgroup analysis of the association between stressful life events and suicidality analysed by age.

Gender majority. The summary effect size of stressful life events was associated with a higher risk for suicidality for males (2 comparisons; OR = 2.06, 95% CI = 1.44 to 2.94, I^2 = 0 (0 to 82.1)%, p = 0.0001), when compared to females (7 comparisons; OR = 1.23, 95% CI = 1.01 to 1.50, I^2 = 66.71 (25.7 to 85.1)%, p = 0.04). See Figure 9. for forest plot.
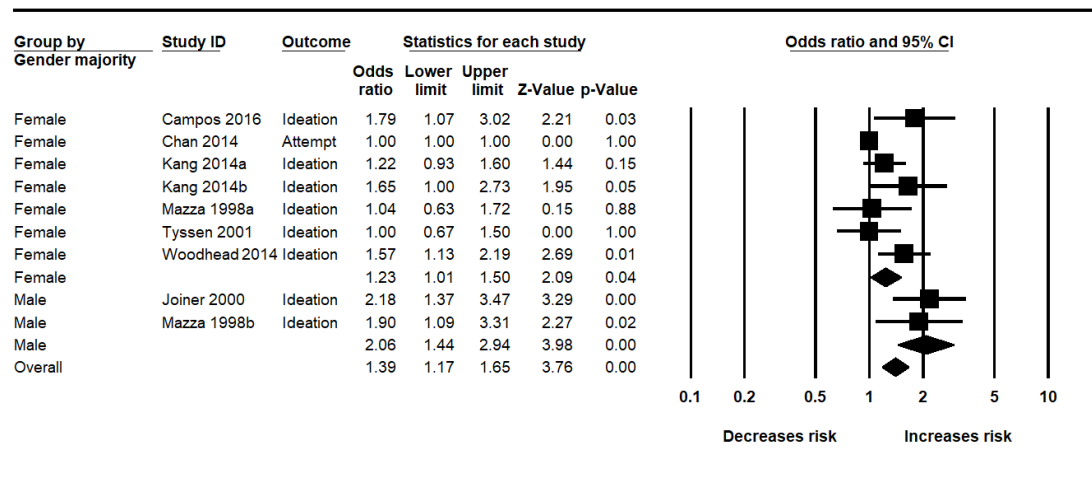
Figure 9. Subgroup analysis of the association between stressful life events and suicidality analysed by gender majority.

Length of follow-up. The summary effect size of stressful life events was associated with increased risk for suicidality greater than a year later (3 comparisons; OR = 1.39, 95% CI = 1.15 to 1.69, I^2 = 0 (0 to 89.6)%, p = 0.0008), whereas less

than or equal to a year later the effect was non-significant (6 comparisons; OR = 1.35, 95% CI = 1.00 to 1.82, I^2 = 76.05 (46.2 to 89.3)%, p = 0.05 – see Figure 10.)

Group by FU period	Study ID	Outcome	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	Odds ratio and 95% CI
=<1yr	Campos 2016	Ideation	1.79	1.07	3.02	2.21	0.03	
=<1yr	Chan 2014	Attempt	1.00	1.00	1.00	0.00	1.00	
=<1yr	Joiner 2000	Ideation	2.18	1.37	3.47	3.29	0.00	
=<1yr	Mazza 1998a	Ideation	1.04	0.63	1.72	0.15	0.88	
=<1yr	Mazza 1998b	Ideation	1.90	1.09	3.31	2.27	0.02	
=<1yr	Tyssen 2001	Ideation	1.00	0.67	1.50	0.00	1.00	
=<1yr			1.35	1.00	1.82	1.93	0.05	
>1yr	Kang 2014a	Ideation	1.22	0.93	1.60	1.44	0.15	
>1yr	Kang 2014b	Ideation	1.65	1.00	2.73	1.95	0.05	
>1yr	Woodhead 2014	Ideation	1.57	1.13	2.19	2.69	0.01	
>1yr			1.39	1.15	1.69	3.36	0.00	
Overall			1.38	1.17	1.62	3.87	0.00	

0.1 0.2 0.5 1 2 5 10

Decreases risk   Increases risk

Figure 10. Subgroup analysis of the association between stressful life events and suicidality analysed by length of follow-up.

Population. The summary effect size of stressful life events was associated with an increased risk for suicidality in non-clinical populations, whereas the effect in clinical populations was non-significant (7 comparisons; OR = 1.37, 95% CI = 1.14 to 1.63, I^2 = 22.38 (0 to 65.4)%, p = 0.0006, and 2 comparisons; OR = 1.42, 95% CI = 0.67 to 3.05, I^2 = 90.78 (66.9 to 97.4)%, p = 0.36, respectively – see Figure 11.).

| Group by Population	Study ID	Outcome	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	Odds ratio and 95% CI
Clinical	Chan 2014	Attempt	1.00	1.00	1.00	0.00	1.00	
Clinical	Joiner 2000	Ideation	2.18	1.37	3.47	3.29	0.00	
Clinical			1.42	0.67	3.05	0.91	0.36	
Non-clinical	Campos 2016	Ideation	1.79	1.07	3.02	2.21	0.03	
Non-clinical	Kang 2014a	Ideation	1.22	0.93	1.60	1.44	0.15	
Non-clinical	Kang 2014b	Ideation	1.65	1.00	2.73	1.95	0.05	
Non-clinical	Mazza 1998a	Ideation	1.04	0.63	1.72	0.15	0.88	
Non-clinical	Mazza 1998b	Ideation	1.90	1.09	3.31	2.27	0.02	
Non-clinical	Tyssen 2001	Ideation	1.00	0.67	1.50	0.00	1.00	
Non-clinical	Woodhead 2014	Ideation	1.57	1.13	2.19	2.69	0.01	
Non-clinical			1.37	1.14	1.63	3.45	0.00	
Overall			1.37	1.15	1.63	3.57	0.00	

0.1 0.2 0.5 1 2 5 10

Decreases risk   Increases risk

Figure 11. Subgroup analysis of the association between stressful life events and suicidality analysed by population.

Methodological quality. The summary effect size of stressful life events was associated with an increased risk for suicidality in high methodological quality studies, whereas the effect in low methodological quality studies was non-significant (4 comparisons; OR = 1.31, 95% CI = 1.03 to 1.66, I^2 = 27.71 (0 to 73)%, p = 0.03, and 5 comparisons; OR = 1.42, 95% CI = 1.00 to 2.01, I^2 = 82.81 (60.7 to 92.5)%, p = 0.05, respectively – see Figure 12.).

Group by Methodological quality	Study ID	Outcome	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
High	Campos 2016	Ideation	1.79	1.07	3.02	2.21	0.03
High	Kang 2014a	Ideation	1.22	0.93	1.60	1.44	0.15
High	Kang 2014b	Ideation	1.65	1.00	2.73	1.95	0.05
High	Tyssen 2001	Ideation	1.00	0.67	1.50	0.00	1.00
High			1.31	1.03	1.66	2.22	0.03
Low	Chan 2014	Attempt	1.00	1.00	1.00	0.00	1.00
Low	Joiner 2000	Ideation	2.18	1.37	3.47	3.29	0.00
Low	Mazza 1998a	Ideation	1.04	0.63	1.72	0.15	0.88
Low	Mazza 1998b	Ideation	1.90	1.09	3.31	2.27	0.02
Low	Woodhead 2014	Ideation	1.57	1.13	2.19	2.69	0.01
Low			1.42	1.00	2.01	1.96	0.05
Overall			1.34	1.10	1.63	2.94	0.00

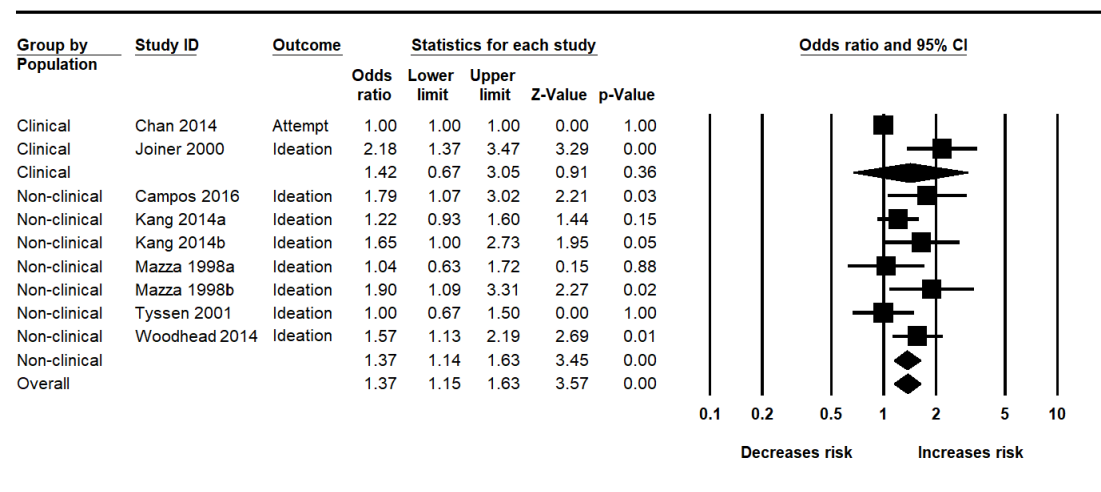**Figure 12.** Subgroup analysis of the association between stressful life events and suicidality analysed by methodological quality.

3.7.2 Meta-regression Analyses

Univariate meta-regression analyses were conducted to further investigate covariates which might moderate the association between stressful life events and suicidality. Specifically, age (below 37.23 years, n=5 vs. above 37.23 years, n=4), gender majority (female, n=7 vs. male, n=2), length of follow-up (≤ a year, n=6 vs. > a year, n=3), population (clinical, n=2 vs. non-clinical, n=7), and methodological quality (high, n=4 vs. low, n=5) were explored as potential moderators. Gender majority (β = 0.51, SE = 0.24, 95% CI = 0.03-0.99, p<0.05) was a significant moderator in the relationship between stressful life events and suicidality (see Table 8.). Moreover, no covariate explained more than 1% of the between-study variance (R^2), with heterogeneity remaining moderate to high.

Table 8. Univariate meta-regressions for suicidality outcomes.

Covariate of interest	Coefficient	Standard Error	95% CI	P-value	I^2	R^2
Age (mean): Below vs. Above	-0.15	0.21	-0.56, 0.26	-0.463	68.99%	0.18%
Gender majority: Female vs. Male	**0.51**	**0.24**	**0.03, 0.99**	**0.036**	61.46%	0.51%
Length of follow-up: Less than or equal to a year vs. Greater than a year	0.08	0.23	-0.37, 0.53	0.726	69.24%	0.01%
Population: Clinical vs. Non-clinical	0.05	0.25	-0.43, 0.53	0.832	62.32%	0.04%
Methodological quality: High vs. low quality	0.04	0.24	-0.43, 0.52	0.855	74.47%	0.00%

4. Discussion

In this section, the findings of the review will be summarised in relation to the research questions. The strengths and limitations of the review and analysis will then be addressed, followed by consideration of the findings in relation to previous research and models of suicidality. The implications of the findings for clinicians and researchers will then be discussed.

4.1 Summary of Results

The purpose of this systematic review and meta-analysis was to explore the prospective relationship between experiencing stressful life events and subsequent suicidality, and in particular to (1) assess the strength of the prospective relationship between the experience of stressful life events and subsequent suicidality, and (2) assess which factors moderate this relationship.

This systematic review found eight studies which investigated the prospective relationship between the experience of stressful life events and subsequent suicidality, seven of which were included in the meta-analysis compromising nine comparisons and 2,639 participants. The meta-analysis found that the experience of stressful life events was associated with a significantly increased risk for suicidality, indicating a 37% increased risk for people experiencing high levels of stressful life events. The risk dropped slightly, however, when only high methodological quality studies were included in the analysis, whereby risk for suicidality was increased 31% when experiencing stressful life events. With regards to the different aspects of suicidality, stressful life events were significantly associated with a 45% increased risk for suicidal ideation. The evidence base was too limited to test the relationship between stressful life events and suicide attempts. None of the studies included in the analysis used suicidal plans or suicide as an outcome.

Gender was found to significantly moderate the relationship between stressful life events and suicidality. Subgroup analysis found the relative risk of suicidality for males was twice as high when experiencing stressful life events, compared with females where risk was 23% higher. Two majority male sample comparisons appeared to drive this result. The relationship between stressful life events and suicidality was also moderated by mean age of the sample was below 37 years, when follow-up assessment was more than a year later, and in non-clinical populations.

4.2   Strengths and Limitations

In this section the strengths and limitations of the review methodology and results will be discussed.

4.2.1   Strengths

This systematic review and meta-analysis had several strengths. The focus on prospective studies within the review enabled the examination of the temporal effects of stressful life events on suicidality, giving a clearer indication of the direction of the relationship and strengthening our ability to establish predictive links between stressful life events and suicidality and the mechanisms that underpin them.

The review was designed, performed and reported following the guidance of the Cochrane handbook for systematic reviews (Deeks et al., 2011a), Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement (Moher et al., 2009). Following these guides meant the review was based on unambiguous, pre-specified and replicable methods, clarifying the effects of bias introduced by the methodological quality of the studies, heterogeneity and publication bias. A pre-specified protocol was registered on the PROSPERO database, providing transparency regarding the original aim of the review and the method chosen to investigate the research questions. When checked against a validated checklist for the methodological assessment of systematic reviews and meta-analyses, a measurement tool for the Assessment of Multiple Systematic Reviews (AMSTAR; Shea et al., 2007), the review met nine out of the 11 items indicating the review was of sound methodological quality (see Appendix K.).

The eligibility criteria for the review were adapted from Liu and Miller's (2014) systematic review of life events and suicidal ideation and behaviour to replicate and extend upon their findings. This allowed for a more consistent approach to the development of the evidence-base; by extending the criterion to account for the methodological concerns reported by the authors, this review addressed some of the ambiguity described in the previous findings. The decision to include a criterion regarding the validity of stressful life events measures increased the methodological quality of the studies included in the review and, therefore, the validity and reliability of the results. The assessment of stressful life events (and suicidality) can vary significantly in the quality of the measure used within the literature; the inclusion of

all measures of stressful life events would have likely increased the number of studies included in the review, but it could also have led to potentially misleading results. Various measures were taken when designing and developing the search strategy to ensure it would comprehensively identify all relevant literature, such as seeking expert advice from outside the thesis team, as well as checking search terms against those used by pervious reviews. This high sensitivity produced over 2,000 hits (i.e. low precision) as anticipated (Higgins & Green, 2011).

Heterogeneity and publication bias were both assessed using formal statistical tests as they present two of the main challenges to meta-analysis. Heterogeneity was addressed by using random-effects models in all analyses to allow and adjust for between-study variation as they assume underlying effects follow a normal distribution. Sensitivity analyses, subgroups analyses and meta-regressions were also undertaken to identify other factors which may have explained the variation identified. The inclusion of only prospective studies in this review reduced methodological heterogeneity because of the focus on one research design.

A strength of the findings is the large number of participants (n = 2,639) included in the meta-analysis. Suicidality has a relatively low international base rate (Bertolote et al., 2005; Nock et al., 2008a; WHO, 2014) therefore larger samples are needed within suicidality research to increase statistical power.

4.2.2 Limitations

A limitation of the review methodology was the language restrictions included within the eligibility criteria; studies in languages other than English were excluded. While the review still includes studies from countries where English is not the native language, this criterion may have limited the generalisability of the findings. The review is further limited in its exclusion of grey literature. It was agreed by the review team that high quality prospective quantitative studies were not likely to be found in unpublished literature, although this may have introduced publication bias to the review.

An important limitation of the meta-analysis was the high levels of heterogeneity between studies. This was likely due to homogeneity present across the included studies with considerably different populations, length of follow-up assessment, country, as well as the diverse measures used to assess stressful life events and suicidality. Even though the review attempted to account for this large

amount of variance within the analyses, the small number of studies included in the review meant that the secondary analyses were limited. It was also not possible to explore any further sources of variance known to be a risk factor for suicidality due to inconsistent data reporting by the included studies, such as mental health difficulties, history of suicidality, and other socio-demographic characteristics. These risk factors may have better explained the variance observed within the relationship between stressful life events and suicidality, and this may be important for future studies to consider. There is a case for not conducting meta-analysis when differences between studies are thought to be too large clinically, methodologically or statistically. However, others still argue for the use of a meta-analysis as long as the assumptions and limitations are acknowledged, as it allows for a statistical comparison of results across studies, quantifies and examines the consistency of effects, and further analysis exploring variables that may explain the variance (Ioannidis, Patsopoulos & Rothstein, 2008).

Visual inspection of the random-effects funnel plot indicated asymmetry, with three missing studies to the left of the mean suggested; the fixed-effect Egger test also identified evidence of publication bias in the review. However, five out of the nine comparisons included in the review did not find an association between stressful life events and suicidality. There is also an argument for assuming it would be highly unlikely to find the experience of stressful life events reducing the risk of suicidality in a research or clinical setting. Therefore, while the analysis suggests the association identified by the review between stressful life events and suicidality may be a spurious one, the assumptions made about publication bias within the context of this research area should be held in mind.

The statistical testing of the association between stressful life events and suicidality, and particularly the analyses of the moderating effects of socio-demographic and clinical characteristics, were restricted due to the limited number of studies included in the review and the smaller numbers in each subgroup. Although the main analysis compromised of nine comparison points from the seven included studies, which equated to over 2,600 participants, the statistical power of the meta-analyses may still have been too low resulting in a possible increase of a type I error (Higgins & Green, 2011). Statistical under-powering may also be present in the secondary analyses as the process divided the studies into smaller numbers still to enable subgroup effect size comparisons.

Another limitation of the literature identified in the review was the variation in the quality of methodology of the primary studies. Three out of the eight studies included in the review were considered high quality and more likely to produce reliable results due to meeting at least three of the four methodological quality criteria. However, no study met all four methodological quality criteria. And this was mainly due to the valid and reliable measure criterion. The studies utilised various tools to measure the experience of stressful life events, however all used a modified, self-report approach. Measures were most commonly modified by omitting a number of items from the list of events, only one study used a measure which allowed a split of subscales (Joiner & Rudd, 2000). The reduced or lack of validity of these modified measures, alongside the lack of context information surrounding the stressful life events and potential idiosyncratic reporting biases that can occur with self-report checklist (refer to section 1.2.5 Stressful life events as a risk factor to suicidality), could result in misleading or inaccurate information being captured by the measure. This could impact on the findings of the primary studies and the review alike.

Measures collected information on either the frequency or severity rating of participants experiences of stressful life events. This difference in scoring made it harder to ascertain the nature of the relationship between stressful life events and suicidality; whether this was affected by the number of stressful life events or by the magnitude of the impact of individual stressful life events. The inclusion of both positive and negative events in some of the measures used by studies also increased the ambiguity of the relationship. In their systematic review, Liu and Miller (2014) reported that no associations were found between positive life events and an aspect of suicidality in the four studies they identified, which suggested the inclusion of positive events in measures of stressful life events may mask or change the association found with suicidality. Secondary analyses were not planned within the review with regards to measurement idiosyncrasies, but this may be an area for future research to explore.

An interesting observation regarding the measures of stressful life events was the age of the assessment tools. The original measures were designed between 1967 and 1992, indicating around a 20+ year gap between the creation of the measures and the studies they were used in, in the review. The relevance of such dated measures to the stressful life events experienced today may be tenuous or reduced which may

limit the reliability and generalisability of the findings of the primary studies, and therefore the review.

The majority of studies focused on suicidal ideation, and only one investigated suicide attempts. The approach to suicidality measurement varied within the studies, from single-item questions to a semi-structured interview approach. Similar to the issues seen with stressful life event measures, the different approaches used to measure suicidality varied in: the clarity given around the definition of suicidality being used (i.e. single-item questions may not explicitly ask about intent); the information collected regarding the presence (or absence) or frequency of suicidality experiences; and the timeframe considered. Again, these differences may have impacted on validity and reliability of the information captured.

Unfortunately, the evidence base was too limited to comment further on the effects of health inequities on the relationship between stressful life events and suicidality. While all eight studies included PROGRESS-Plus factors in their sample descriptions, indicating the data had been collected, only one study included in the review reported differential effects of a specific PROGRESS-Plus factor (Mazza & Reynolds, 1998). This highlights the need for future suicide research to better attend to the health equity in the design of studies within the suicide field.

4.3   Comparisons to previous research and reviews

This is the first systematic review and meta-analysis to look exclusively at the prospective relationship between stressful life events and subsequent suicidality. However, the findings are in line with two previous narrative systematic reviews on the broader association between stressful life events and an aspect of suicidality (Liu & Miller, 2014; Serafini et al., 2015), and one meta-analytic review of risk factors for suicidal thoughts and behaviours (Franklin et al., 2017).

Unlike the current review, the two narrative systematic reviews (Liu & Miller, 2014; Serafini et al., 2015) considered both traumatic and non-traumatic life events within their definition of negative life events. Conflating these two constructs is likely to have masked the true association between non-traumatic stressful life events and suicidality, particularly considering the considerable evidence-base there is around the relationship between trauma and suicidality (Bahraini et al., 2013; Hor & Taylor, 2010; Krysinska & Lester, 2010; O'Connor et al., 2018; Wethington et al., 2008). The current review did not include traumatic events within its definition of

stressful life events, which meant the association found considered the experience of everyday stressful life events, such as the death of a loved one, or the loss of employment, to significantly increased risk of suicidality. The findings of the current review highlight the potential impact of (non-traumatic) stressful life events on suicidality and identify an important area of further research. Unfortunately, Franklin et al. (2017) did not report how stressful life events were defined within their meta-analysis, so a direct comparison of findings within this regard is not possible.

This review extends previous reviews by focusing exclusively on prospective studies. This allowed the temporal relationship between stressful life events and suicidality to be investigated. Liu and Miller (2014) reported substantial temporal overlap between the measurement of stressful life events and suicidality in several of the studies they reviewed. This methodological limitation was controlled for in the current review, which required the measurement of suicidality to be taken in a follow-up period subsequent to stressful life events measures. This distinction allowed greater confidence in considering the experience of stressful life events as a risk factor (i.e. longitudinal predictor) to suicidality.

The current review also extends on a previous meta-analysis by exploring potential moderating factors to the prospective relationship between the experience of stressful life events and subsequent suicidality. Moderating factors can affect the strength of an association; investigating moderating factors of the association between stressful life events and suicidality can provide further understanding regarding when the association will or will not hold. While Franklin et al. (2017) reported stressful life events as a risk factor to suicide, they did not explore this association further, nor did they report on whether an association was found with any other aspect of suicidality. The current review conducted subgroup and meta-regression analyses to explore potential sources of heterogeneity and investigate factors which might moderate the association.

Gender was observed to significantly moderate the relationship between stressful life events and suicidality, with the strength of the association being higher in males than females. While it is important to keep in mind the small number of comparisons in each group (females: n = 7; males: n = 2) used within the analyses, this finding could further aid the understanding of gender within suicidality. Previous research suggests females are at higher risk of suicidal ideation, plans and attempts, and males are at greater risk of suicide (Nock et al., 2008b; ONS, 2017b). However,

the finding of the review indicates when experiencing stressful life events, the opposite effect is observed with regards to suicidal ideation; males are at higher risk of suicidal ideation.

The review found stressful life events were associated with a higher risk for suicidality for those below the mean age of 37.23 years old. This finding supports a previous meta-analysis on cortisol levels (which is released when experiencing stress) and suicidal behaviour. O'Connor, Ferguson, Green, O'Carroll and O'Connor (2016) found a similar positive association regarding the younger sample subgroups, whereby suicidal behaviours were associated with greater cortisol levels in studies where the mean sample age was below 40 years, but not for those where mean age was 40 or above.

Additionally, the review found the experience of stressful life events potentially increase risk of experiencing suicidality over time (i.e. when length of follow-up assessment was greater than one year). While further research is needed to corroborate this finding, it seemingly contradicts previous suicide research (Liu & Miller, 2014) and models of suicide (O'Connor, 2011) which suggest stressful life events are more proximal, as opposed to distal, risk factors of suicidality. However, this is broadly consistent with Miller, Chen and Zhou (2007), who have argued that the temporal features of stressors are important and that stressors that are prolonged (possibly reflected in length of follow-up here) are most damaging for health and wellbeing.

The present review found no negative associations reported between stressful life events and suicidality. This finding is similar to two previous reviews (Liu and Miller, 2014; Serafini et al., 2015). While both reviews identified positive associations, and Liu and Miller (2014) also found some studies reporting no association between stressful life events and suicidality, neither review reported any negative or inverse associations between stressful life events and suicidality. This finding may further support the argument for the assumptions made within publication bias analysis not being suitable within the context of this research area.

Liu and Miller (2014) reported that the associations between life events and suicidality were least consistent for the outcome of suicidal ideation. This may have contributed to the varying levels of heterogeneity they found among those studies, with methodological quality also potentially having been an influencing factor. Similar limitations around high heterogeneity and methodological quality were found

within the current review, particularly similarities around the limitations of the type of measures used to capture both life events and suicidal ideation. Liu and Miller (2014) observed the consistency of support increasing as the research moved along the suicidality continuum, with support for an association between life events and suicide being the most consistent. Unfortunately, the findings of the current review were unable to extend on this finding due to the majority of the studies looking at suicidal ideation.

4.4   Considerations for models of suicidality

The findings of the review indicated that while the experience of stressful life events was associated with increased risk of suicidality, there were other factors which influenced or interacted with this relationship. This suggests that not everyone who experiences stressful life events will also experience suicidal thoughts or engage in suicidal behaviour. The findings of the review will be considered in relation to the models of suicidality previously discussed in the introduction.

The Cry of Pain model (Williams, 1997) considers the presence of stressors as initiating a series of psychological conditions which can lead to suicidality. Stressful life events could be the initial stressor in the model, as the events can include the loss of important relationships and social support, the loss of finances, and the loss of health. It would be reasonable to formulate that individuals may evaluate these experiences in terms of defeat, entrapment, and hopelessness. The Cry of Pain model may explain the variation in the associations found in the primary studies as the difference between how individuals appraised the experience of stressful life events and their consequences, i.e. whether an individual's information-processing, memory schema, and problem-solving abilities protect from, or increase vulnerability to, suicidality.

The Schematic Appraisals Model of Suicide (SAMS; Johnson, Gooding & Tarrier, 2008) could view the findings of this review as a result of stressful life events becoming suicidogenic in the context of cognitive biases, activating the suicide schema. The nature of stressful life events, i.e. the death of a loved one, or the experience of multiple stressful life events could contribute to intolerable emotional or situational states, in which thoughts of suicide could become seen as a strategy of escape. The findings of the review seem congruent with the predictions of suicidal ideation within the SAMS. However, no association between stressful life

events and suicide attempts was found by the one study in the review which investigated suicidal behaviour. While this individual finding does not appear to support the model, a tentative hypothesis may consider that the experience of stressful life events may trigger the suicide schema (i.e. suicidal ideation occur) but that this activation is not strong enough to initiate the schema to interact with the appraisal system therefore stressful life events are not appraised in terms of defeat and entrapment (i.e. suicide attempts do not occur).

The Integrated Motivational-Volitional model (IMV; O'Connor, 2011, O'Connor & Kirtley, 2018) predicts that the experience of life events may increase vulnerability to suicidal ideation. The findings of this review fit with this prediction; stressful life events were found to increase the risk of suicidality. While life events are included in the pre-motivational phase of the model, the experience of stressful life events may also have the potential to impact on the motivational phase; the varied nature of stressful life events may alter or heighten appraisals around social or financial support, coping, dependency, belongingness, and thoughts of the future, all of which the IMV model contribute to suicidal ideation.

While the Interpersonal Theory of Suicide (Joiner, 2005, 2011) also considers the appraisals of belongingness and burdensomeness as central to understand suicidality, it differs slightly from the other models of suicidality in the way it positions stressful life events. The theory views the experience of stressful life events with the potential to implicitly develop the two key cognitive-affective states simultaneously needed for suicidal thoughts, due to the different impacts stressful life events can have on people's lives. The general findings of the review fit with the theory, and the varying nature of the association may be explained by the inclusion of stressful life events which do not impact on belongingness and burdensomeness.

4.5   Implications for clinicians and researchers

Within the theoretical context of the models of suicidality, the findings have implications for suicide risk assessment and suicidality interventions provided by clinical psychologists and other mental health professionals.

Clinicians should explore both recent and past experiences of stressful life events as part of suicide risk assessments, particularly for younger adults and males, as the findings of this review suggests these will increase risk of suicidality. While the use of stressful life event measures may not always be appropriate within the

therapeutic setting, the evidence around these measures could be used to guide a clinician's approach. Combining a checklist style approach to aid information gathering, with the ability to seek further contextual and appraisal information as necessary, may allow the clinician to better assess the individuals' risk of suicidality.

Recommendations for suicidality interventions from the findings of the review are limited due to the restricted selection of fixed moderators available from the data reported by the small number of primary studies. A suggestion for interventions could include adding a component which focuses on developing resilience and coping ability for future stressful life events. Increasing the range of responses and appraisals available to an individual when stressful life events are experienced may reduce vulnerability to suicidality in the future. These suggestions are consistent with the majority of models of suicidality, which place the experience of stressful life events as the initiating stressor or precipitating event, as well as current evidence-based suicidality risk assessments and interventions (Pratt, Gooding, Kelly, Johnson & Tarrier, 2015). However, future research would first need to explore the impact of resilience and coping ability on suicidality after the experience of stressful life events before this suggestion could be supported.

The review highlights several limitations in the current evidence base, which could be addressed in future research. First, only one study measured suicide attempts as a suicidality outcome (Chan et al., 2014), and there is a need for primary studies to investigate whether stressful life events are a risk factor for other aspects of suicidality further along the continuum than suicidal ideation, particularly given that evidence of a potential association between stressful life events and suicide has been suggested by a previous meta-analysis (Franklin, et al., 2017).

Second, there is a need to improve the methodological quality of primary studies. None of the studies included in the meta-analysis met all the methodological quality criteria used, with the majority of studies not meeting the valid and reliable measure criterion due to the use of modified or potential bias measures to assess both the experience of stressful life events and an aspect of suicidality. A previous narrative systematic review which also focused on the association between life events and suicidality encountered similar problems in terms of variability in methodological quality (Liu & Miller, 2014). The development of up-to-date, valid and reliable measures would ensure that future syntheses are not hampered by inconsistent presentation of data. With regards to stressful life events measures,

further research should consider updating the measures to account for societal and contextual changes, establishing a consistent method of scoring, and use validated measures, specifically interview-based approach when the experience of stressful life events is the primary focus of the research. This would place future research in a more advantageous position to investigate the nature of the association between stressful life events and suicidality, which may allow for a better understanding of the variable findings of this and previous reviews in the context of suicidality theories. With regards to suicidality measures, future research should focus on the use of validated and reliable measures, as opposed to the use of single-item measures, alongside the development of common terminology and operationalised definitions, to improve the consistency and application of the evidence-base. Another consideration may include the explicit or prioritised use of interview-based approaches when the experience of suicidality is the primary focus of the research.

4.6   Conclusion

This systematic review and meta-analysis suggested that stressful life events are associated with a significantly increased risk for suicidality, specifically suicidal ideation. The association was higher in males, and possibly higher in younger, non-clinical samples when followed up more than year after stressful life events were measured. Further research is needed to confirm this association and determine whether stressful life events are associated with other aspects of suicidality.

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Appendices

Appendix A. Search Strategy

MEDLINE search strategy (via OVID), database inception (01/01/1946) to 04/10/18

1.	life change events/	21877
2.	life stress*.tw	3952
3.	stressor*.tw	33478
4.	(life or stress*) adj2 event*.tw	18016
5.	or/1-4	66235
6.	suicide/ or suicidal ideation/ or suicide, attempted/ or self-injurious behavior/	56951
7.	suicid*.tw	60644
8.	parasuicid*.tw	594
9.	self-harm*.tw	3731
10.	or/6-9	79174
11.	(prospective* or longitudinal* or cohort or follow-up or predict*).mp	2921887
12.	5 and 10 and 11	728
13.	limit 12 to English language	684

UPDATE TO 02/04/19 = 20

Appendix B. Author Email Correspondence

Author	Date	Paper Title	Data Request	Response	Outcome
D. Gunnell	11/01/19 & 22/02/19	F actors influencing the development Factors influencing the development and amelioration of suicidal thoughts in the general population in the general population - Cohort study	SLE measure	Provided reference for primary data but it did not state SLE measure	Emailed primary data study author, but no response so paper excluded
L. Stone	22/02/19	Adolescent inpatient girls' report of dependent life events predicts prospective suicide risk	Participant age range	Ages 13-17	Paper excluded
M. Oquendo	22/02/19 & 19/03/19	Life events: A complex role in the timing of suicidal behavior among depressed patients	Participant age range & association timeframe	Ages 18-75, SLE measured at timepoints proximal to time of follow-up evaluation.	Paper excluded
L. Rew	22/02/19	Suicide Ideation and Life Events in a Sample of Rural Adolescents	Participant age range	Ages 13-19	Paper excluded
J. Boden	22/02/19	Anxiety disorders and suicidal behaviours in adolescence and young adulthood: Findings from a longitudinal study	SLE measure timeframe	Confirmed concurrent SLE score used	Paper excluded

H. Christensen	08/01/19 & 22/02/19	Predictors of the risk factors for suicide identified by the interpersonal-psychological theory of suicidal behaviour	SLE measure	Confirmed measure included trauma	Paper excluded
E. Woodhead	22/02/19	Coping strategies predictive of adverse outcomes among community adults	SLE measure	Confirmed valid measure	Paper included
M. Kennedy	22/02/19	Life stress, 5-HTTLPR and mental disorder: Findings from a 30-year longitudinal study	SLE measure	Confirmed invalid measure	Paper excluded
N. Karaoglu	22/02/19	Is medical education really stressful? a prospective study in Selcuk University, Turkey	SLE measure	Confirmed invalid measure	Paper excluded
R. Tyssen	23/02/19	Suicidal ideation among medical students and young physicians: A nationwide and prospective study of prevalence and predictors	SLE measure	Confirmed valid measure	Paper included
J. Mazza	22/02/19 & 08/03/19	A longitudinal investigation of depression, hopelessness, social support, and major and minor life events and their relation to suicidal ideation in adolescents	Participant age range	Ages 14+	Paper included
S. Yen	19/03/19	Recent life events preceding suicide attempts in a personality disorder sample: findings from the collaborative longitudinal personality disorders study	Association timeframe & data	Did not analyse for study, provided raw data but unable to use as data points did not match the participant number stated in the paper	Paper excluded

J. Kim	22/02/19, 08/03/19 & 19/03/19	Suicidal ideation in elderly Korean population: A two-year longitudinal study	SLE measure & data source	Confirmed valid measure & secondary data source	Paper included
A. Van der Watt	19/03/19	Prospective interepisodal mood monitoring in patients with affective disorders: A feasibility study	Association timeframe	Did not analyses for study, and currently looking at association in own research	SLE included trauma, so paper excluded
T. Joiner	19/03/19	Intensity and duration of suicidal crises vary as a function of previous suicide attempts and negative life events	Association data request	Did not analyses for study, unable to provide	Paper excluded
L. Fong Chan	19//03//19	Are predictors of future suicide attempts and the transition from suicidal ideation to suicide attempts shared or distinct: A 12-month prospective study among patients with depressive disorders	Association data request	Provided regression analysis	Paper included
A. Fanous	22/02/19 & 08/03/19	The prediction of thoughts of death or self-harm in a population-based sample of female twins	SLE measure	No response	Paper excluded

JS Yoon	22/02/19 & 08/03/19	Interactions between a serotonin transporter gene, life events and social support on suicidal ideation in Korean elders	SLE measure	No response	Paper analysed the same secondary data as another study so SLE valid. However, analysis was cross-sectional, so paper excluded
J. Bolton	15/03/19 & 22/03/19 & 08/04/19	A population-based longitudinal study of recent stressful life events as risk factors for suicidal behavior in major depressive disorder	SLE measure	Responded advising measure was not based on a pre-existing measure.	Paper excluded
A. Wu	19/03/19 & 25/03/19	Clinical determinants and short-term prognosis of suicidal behaviours in Chinese older persons in Hong Kong	Association timeframe	Responded advising of non-sig association, requested data but no response.	Paper excluded
F. Law	22/02/19 & 08/03/19	Association Between Changes in Risk Factor Status and Suicidal Ideation Incidence and Recovery	SLE measure	No response	Paper excluded
E. Isometsä	12/04/19 & 25/04/19	Prospective study of risk factors for attempted suicide among patients with DSM-IV major depressive disorder	Association data	No response	Paper excluded

Appendix C. Converting effect size and variance

Comprehensive Meta-Analysis used the following equations to convert effect size and variance of correlational data to binary data (Borenstein et al, 2009). Correlational effect size and variance were first converted to continuous data using the formulations shown in Equation 1 and Equation 2, where r is the correlation, d is the standardised mean difference, and V is the variance.

Equation 1

$$d = \frac{2r}{\sqrt{1 - r^2}}$$

Equation 2

$$V_d = \frac{4V_r}{(1 - r^2)^3}$$

The continuous effect size and variance were then converted to binary effect size (i.e. log odds ratio) using the formulations shown in Equation 3 and Equation 4, where $LogOddsRatio$ is the log odds ratio, and π is the mathematical constant.

Equation 3

$$LogOddRatio = d\frac{\pi}{\sqrt{3}}$$

Equation 4

$$V_{LogOddsRatio} = V_d\frac{\pi^2}{3}$$

Two sets of assumptions were made during this two-step conversion: 1) the correlation data had a bivariate normal distribution and one of the two variables was dichotomised to create two groups; 2) the continuous data had a logistic distribution. While this first assumption is about the predictor variable only, the second assumption is only about the outcome therefore has no implications for the validity of the other (Hasselblad & Hedges, 1995).

Appendix D. Odds Ratio calculation

Odds ratio were calculated using Equation 5, where *A*, *B*, *C*, and *D* were the number of events and non-event in the two groups (Borenstein et al, 2009).

Equation 5

$$OddsRatio = \frac{AD}{BC}$$

Log odds ratio, approximate variance, and approximate standard error were then calculated using Equation 6, Equation 7, and Equation 8, respectively; where $LogOddsRatio$ is log odds ratio, V is the variance, and SE is standard error.

Equation 6

$$LogOddsRatio = \text{In}(OddsRatio)$$

Equation 7

$$V_{LogOddsRatio} = \frac{1}{A} + \frac{1}{B} + \frac{1}{C} + \frac{1}{D}$$

Equation 8

$$SE_{LogOddsRatio} = \sqrt{V_{LogOddsRatio}}$$

The log odds ratio and its variance were then used to calculate the summary effect and confidence interval limits, where LL is the lower limit, and UL is the upper limit.

Equation 9

$$OddsRatio = \exp(LogOddsRatio)$$

Equation 10

$$LL_{OddsRatio} = \exp(LL_{LogOddsRatio})$$

Equation 11

$$UL_{OddsRatio} = \exp(UL_{LogOddsRatio})$$

Appendix E. Meta-analysis calculations

The combined effect sizes were used to calculate the OR summary effect and 95% confidence interval using weighted scores. Calculating the weighted mean allows the most precise estimate of the overall mean as it minimises the variance. The weights used were based on the within- and between-study variance for each study (V_{Yi}^*). The calculations are represented in the following five steps (Borenstein et al, 2009):

1. Weight (W_i^*) assigned to each study (i) was calculated in Equation 12,
2. Weighted mean (M^*) was then calculated in Equation 13, where Y_i is the study effect size,
3. Variance of the summary effect (V_{M^*}) was calculated in Equation 14,
4. Estimated standard error of the summary effect (SE_{M^*}) was calculated in Equation 15,
5. The 95% lower limits (LL_{M^*}) and upper limits (UL_{M^*}) of the summary effect were then calculated as shown in Equation 16 and Equation 17.

Equation 12

$$W_i^* = \frac{1}{V_{Yi}^*}$$

Equation 13

$$M^* = \frac{\sum_{i=1}^{k} W_i^* Y_i}{\sum_{i=1}^{k} W_i^*}$$

Equation 14

$$V_{M^*} = \frac{1}{\sum_{i=1}^{k} W_i^*}$$

Equation 15

$$SE_{M^*} = \sqrt{V_{M^*}}$$

Equation 16

$$LL_{M^*} = M^* - 1.96 \times SE_{M^*}$$

Equation 17

$$UL_{M^*} = M^* + 1.96 \times SE_{M^*}$$

The log scales were then converted back to the odds ratio scale (previously described in Equations 9 to 11) to provide the summary odds ratio and 95% confidence interval.

Appendix F. Calculating heterogeneity

The formula for I^2 was calculated using Equation 18 (Borenstein et al, 2009).

Equation 18

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

Where Q is the chi-squared statistic and df is its degrees of freedom (Higgins & Green, 2011). This describes the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (i.e. chance).

Appendix G. Subgroup analysis equations

A random-effect model using separate estimates of between-study variance compared the effect size across subgroups using a Q-test for heterogeneity, illustrated in Equation 19. The Q statistic is sensitive to the ratio of observed (i.e. between-study variation) to expected (i.e. within-study error) dispersion, therefore can isolate the true variation explained by subgroup membership between the studies (Borenstein et al, 2009).

Equation 19

$$Q = \sum_{i=1}^{k} W_i Y_i^2 - \frac{\left(\sum_{i=1}^{k} W_i Y_i^2\right)^2}{\sum_{i=1}^{k} W_i}$$

The proportion of true variance explained by subgroup membership between the included studies was then calculated in Equation 20, where T_{within}^2 is the between-studies variance within subgroups, and T_{total}^2 is the total between-studies variance.

Equation 20

$$R^2 = 1 - \left(\frac{T_{within}^2}{T_{total}^2}\right)$$

Appendix H. Meta-regression analyses equations

Using a random-effects model, the Z-test was used to test the impact of a single coefficient on the effect size, while other covariates are held constant. Equation 21 shows this formula, where B^* is the covariate and SE_{B^*} is the standard error of the covariate (Borenstein et al, 2009).
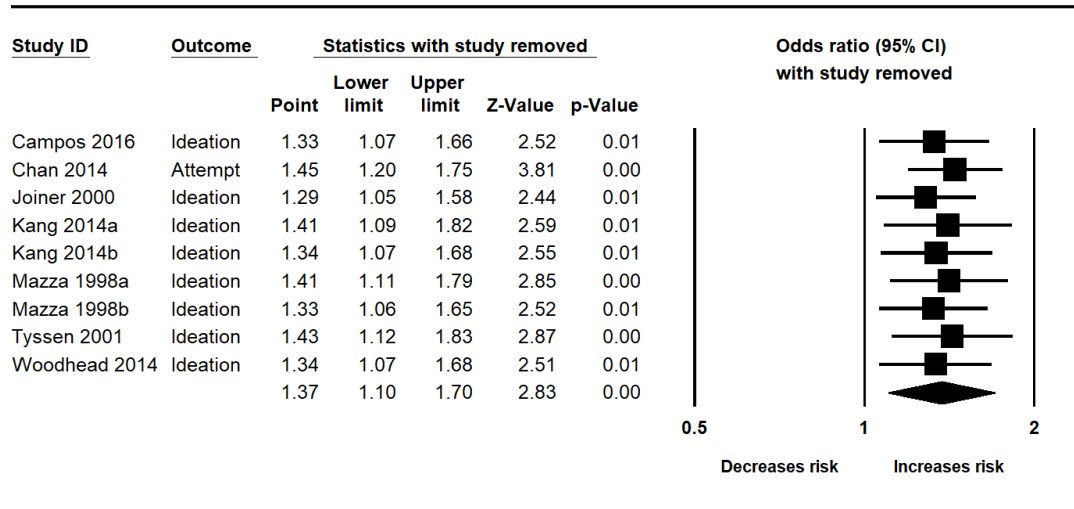
Equation 21

$$Z^* = \frac{B^*}{SE_{B^*}}$$

The proportion of true variance explained by the covariates was then calculated using Equation 22, where $T^2_{explained}$ is the between-studies variance explained by the covariate, and T^2_{total} is the total between-studies variance.

Equation 22

$$R^2 = \left(\frac{T^2_{explained}}{T^2_{total}}\right)$$

Appendix I. Forest plot of the effects of stressful life events on suicidality with one study removed.

Study ID	Outcome	Statistics with study removed					Odds ratio (95% CI) with study removed
		Point	Lower limit	Upper limit	Z-Value	p-Value	
Campos 2016	Ideation	1.33	1.07	1.66	2.52	0.01	
Chan 2014	Attempt	1.45	1.20	1.75	3.81	0.00	
Joiner 2000	Ideation	1.29	1.05	1.58	2.44	0.01	
Kang 2014a	Ideation	1.41	1.09	1.82	2.59	0.01	
Kang 2014b	Ideation	1.34	1.07	1.68	2.55	0.01	
Mazza 1998a	Ideation	1.41	1.11	1.79	2.85	0.00	
Mazza 1998b	Ideation	1.33	1.06	1.65	2.52	0.01	
Tyssen 2001	Ideation	1.43	1.12	1.83	2.87	0.00	
Woodhead 2014	Ideation	1.34	1.07	1.68	2.51	0.01	
		1.37	1.10	1.70	2.83	0.00	

0.5   1   2

Decreases risk   Increases risk

Appendix J. Forest plot of the effects of stressful life events on suicidality across studies with high methodological quality scores

Study ID	Outcome	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	Odds ratio and 95% CI
Campos 2016	Ideation	1.79	1.07	3.02	2.21	0.03	
Kang 2014a	Ideation	1.22	0.93	1.60	1.44	0.15	
Kang 2014b	Ideation	1.65	1.00	2.73	1.95	0.05	
Tyssen 2001	Ideation	1.00	0.67	1.50	0.00	1.00	
		1.31	1.03	1.66	2.22	0.03	

0.1 0.2 0.5 1 2 5 10

Decreases risk   Increases risk
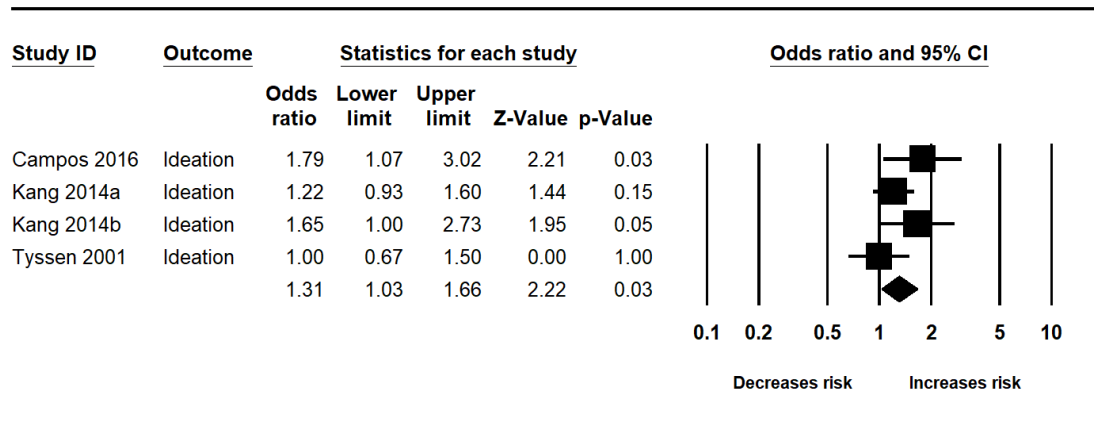
Appendix K. AMSTAR measurement tool (Shea et al., 2007)

1. Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review.	**Yes** No Can't answer Not applicable
2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.	**Yes** No Can't answer Not applicable
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.	**Yes** No Can't answer Not applicable
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	Yes **No** Can't answer Not applicable
5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.	Yes **No** Can't answer Not applicable
6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.	**Yes** No Can't answer Not applicable

7. Was the scientific quality of the included studies assessed and documented? 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.	**Yes** No Can't answer Not applicable
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.	**Yes** No Can't answer Not applicable
9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi squared test for homogeneity, I2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).	**Yes** No Can't answer Not applicable
10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).	**Yes** No Can't answer Not applicable
11. Was the conflict of interest stated? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.	**Yes** No Can't answer Not applicable