

Intolerance of uncertainty, anxiety and worry in children and adolescents: a meta-analysis

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Accepted Version

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Osmanagaoglu, N., Creswell, C. and Dodd, H. F. ORCID: <https://orcid.org/0000-0003-1446-5338> (2018) Intolerance of uncertainty, anxiety and worry in children and adolescents: a meta-analysis. *Journal of Affective Disorders*, 225. pp. 80-90. ISSN 0165-0327 doi: <https://doi.org/10.1016/j.jad.2017.07.035> Available at <https://centaur.reading.ac.uk/71459/>

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To link to this article DOI: <http://dx.doi.org/10.1016/j.jad.2017.07.035>

Publisher: Elsevier

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Abstract

Background

Intolerance of uncertainty (IU) has been implicated in the development and maintenance of worry and anxiety in adults and there is an increasing interest in the role that IU may play in anxiety and worry in children and adolescents.

Method

We conducted a systematic review and meta-analysis to summarize existing research on IU with regard to anxiety and worry in young people, and to provide a context for considering future directions in this area of research. The systematic review yielded 31 studies that investigated the association of IU with either anxiety or worry in children and adolescents.

Results

The meta-analysis showed that IU accounted for 36% of the variance in anxiety and 39.69% in worry. Due to the low number of studies and methodological factors, examination of potential moderators was limited; and of those we were able to examine, none were significant moderators of either association. Most studies relied on questionnaire measures of IU, anxiety, and worry; all studies except one were cross-sectional and the majority of the studies were with community samples.

Limitations

The inclusion of eligible studies was limited to studies published in English that focus on typically developing children.

Conclusions

There is a strong association between IU and both anxiety and worry in young people therefore IU may be a relevant construct to target in treatment. To extend the existing literature, future research should incorporate longitudinal and experimental designs, and include samples of young people who have a range of anxiety disorders.

Highlights

- Strong and positive correlation between anxiety and IU in young people.
- Strong and positive correlation between worry and IU in young people.
- Insufficient evidence for whether age or gender moderate either association.
- Proportion of sample from a clinical population was not a moderator.
- Majority of studies were cross-sectional and used only questionnaires.

Intolerance of Uncertainty, Anxiety, and Worry in Children and Adolescents: A Meta-Analysis

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Keywords: anxiety, worry, intolerance of uncertainty, meta-analysis

Introduction

Anxiety disorders are among the most common mental health problems; the lifetime prevalence of anxiety disorders is estimated as 28.8% with onset usually in childhood and adolescence (Kessler et al., 2005). Anxiety disorders follow a chronic course (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003), affect daily life (Jarrett, Black, Rapport, Grills-Taquechel, & Ollendick, 2015; Paulus, Backes, Sander, Weber, & von Gontard, 2015), and are associated with significant global burden (Whiteford et al., 2013). Cognitive Behaviour Therapy (CBT) for anxiety disorders in young people is effective, with recent data showing 58.9% of the children and adolescents were free from any anxiety diagnosis following CBT (James, James, Cowdrey, Soler, & Choke, 2015). However, this leaves a substantial proportion of young people who continue to have an anxiety diagnosis after completing CBT. As such, there is significant scope to improve treatments. To inform the advancement of treatment, we require a better understanding of the factors that underpin the development and maintenance of anxiety disorders in children and adolescents.

Intolerance of Uncertainty (IU) has been defined in a number of ways. Most recently as “an individual’s dispositional incapacity to endure an aversive response triggered by the perceived absence of salient, key, or sufficient information, and sustained by the associated perception of uncertainty” (Carleton, 2016b). At the core of IU is fear of the unknown (Carleton, 2016a, p.31). IU based models of worry hypothesize that individuals with high IU will be more prone to engage in worry as IU sets off a chain of worrying, negative problem orientation and cognitive avoidance as well as directly affecting problem orientation and cognitive avoidance (Dugas & Koerner, 2005). These models have received empirical support and there is evidence that IU has an important role in the maintenance of anxiety disorders in adults.

Although early work on IU focused on the association with generalized anxiety disorder (GAD), there is now evidence that IU might be a transdiagnostic risk factor for the development and maintenance of clinically significant anxiety more broadly as well as for depression (Carleton, Collimore, & Asmundson, 2010; Holaway, Heimberg, & Coles, 2006; McEvoy & Mahoney, 2011; Norr et al., 2013; Tolin, Abramowitz, Brigidi, & Foa, 2003). Indeed, a meta-analysis of the association between IU and GAD, obsessive-compulsive disorder (OCD), and major depressive disorder (MDD) revealed IU as a shared factor in all three syndromes in adults (Gentes & Ruscio, 2011). Further, a recent meta-analysis revealed that six cognitive vulnerability factors associated with anxiety and depression (pessimistic inferential style, dysfunctional attitudes, rumination, anxiety sensitivity, IU, and fear of negative evaluation) loaded onto a single factor. Of these, IU had the strongest factor loading, further indicating that IU may be linked to both anxiety and depression (Hong & Cheung, 2015).

Treatment research in adults has highlighted the potential benefit of focusing on IU; treatments that target tolerating uncertainty have been found to reduce symptoms of GAD (Dugas & Ladouceur, 2000; Dugas et al., 2003; van der Heiden, Muris, & van der Molen, 2012), and social phobia (Mahoney & McEvoy, 2012). Furthermore, a treatment protocol that targets IU led to significant decreases in IU in an adult clinical sample with high comorbidity of anxiety disorders and depression; and importantly, changes in IU significantly predicted changes in anxiety and depressive symptoms in post-treatment (Boswell, Thompson-Holland, Farchione, & Barlow, 2013). Furthermore, examination of the factors underlying IU sets the stage for more specific targeted interventions. For example, prospective IU, which is characterized by the desire for predictability, is associated with worry and anticipatory apprehension, while inhibitory IU, which is a more immediate behaviourally focused facet of IU, is linked with social anxiety and depression (Hong, 2015).

Despite the extensive body of research examining IU in adults and the clinical promise of this work, relatively little research has examined the association of IU with anxiety and worry in children and adolescents. The significant association of IU with anxiety and worry found in adults may not translate directly into a similar association for young people because the ability to detect and reason about uncertainty develops across childhood and adolescence. The basic cognitive skills necessary for detecting and responding to uncertainty are present from a very young age (Lyons & Ghetti, 2011, 2013; Roebbers, von der Linden, & Howie, 2007). For example infants as young as 20 months old show evidence of introspective awareness which is a necessary skill to detect knowledge gaps and to experience uncertainty (Goupil, Romand-Monnier, & Kouider, 2016); children as young as 4 years old implicitly demonstrate that they are able to identify multiple possibilities when uncertainty exists both in their mind and in the physical world (Robinson, Martin, Beck, Dan, & Apperly, 2006), and children as young as 4.5 years old are able to monitor their perceived uncertainty and ask for help under uncertain circumstances (Beran, Decker, Schwartz, & Smith, 2012).

Although children may be aware of uncertainty and able to respond to uncertainty from a young age, many cognitive processes related to uncertainty continue to develop through middle childhood and adolescence. For example introspective awareness continues to improve through to the elementary school years (Roebbers & Howie, 2003; Roebbers et al., 2007). Similarly, meta-cognitive skills such as holding possible predicted outcomes in mind, delaying making an interpretation until further information is received or making a tentative interpretation whilst being open to adjusting this interpretation in light of new information, and asking for help in response to uncertainty develop gradually (Moshman, 2004; Weil et al., 2013). As the cognitive skills necessary for reasoning about uncertainty develop, it seems likely that the nature of IU and the association between IU and anxiety and worry may

change. Despite this, to our knowledge there is no data that indicates whether IU develops linearly with age or waxes and wanes throughout development and there has been little consideration of how age might affect the association between IU and anxiety and worry.

An emerging body of research has begun to examine IU in the context of anxiety and worry in young people, with studies including children (e.g. Kertz & Woodruff-Borden, 2013) and adolescents (e.g. Laugesen, Dugas, & Bukowski, 2003). Age and gender vary widely across studies and most of the studies include children and young people from broad age ranges such as age 4 to 18 years. In general, there appears to be a lack of consideration of the effects of age and gender on the associations between IU and both anxiety and worry. Where they have been examined, results appear to be inconsistent. For example, while the link between IU and worry was not moderated by gender in one study (Boelen, Vrinssen, & van Tulder, 2010); in another study IU was found to be associated with worry in females only (Barahmand, 2008). As such, it is not clear what effect age and gender have on the strength of the association of IU with anxiety and worry in young people.

In making sense of divergent findings, it is important to note that methods vary considerably across studies including the study population (clinical vs community), method of anxiety assessment (questionnaire vs diagnostic interview), the measure used to assess IU, the person who reports on the child's anxiety and IU, and study design (cross-sectional or longitudinal). Variation in each of these factors may also influence the magnitude of the associations between IU and both anxiety and worry.

Considering the promise of IU based psychological therapies with adults, it is timely to examine what we know about IU in young people in the context of anxiety and worry and to consider directions for future work in this field. To date there has been no systematic review of IU in relation to child and adolescent anxiety or worry. The aims of this review are

therefore 1) to examine the existing evidence for an association between IU and both anxiety and worry in children and adolescents by conducting a meta-analysis; 2) to provide a summary of the critical gaps in the existing literature and the priorities for future work in this area. More specifically, the meta-analysis has 3 objectives: 1) to estimate the mean association between IU and anxiety in children and adolescents, 2) to estimate the mean association between IU and worry in children and adolescents, 3) to test whether these associations are moderated by age, gender, sample type, study design, method of anxiety assessment, IU questionnaire used, and informant of anxiety, worry, and IU. The focus in this work is on worry and anxiety; to our knowledge only one study examined IU and depression in young people (Boelen et al., 2010); therefore, a meta-analysis of an association of IU and depression in young people would be premature.

Method

Eligibility Criteria

Studies were included in the meta-analysis if they met each of the following eligibility criteria:

1. The study must be based upon empirical research. Only research that offers extractable quantitative data is included. Reviews, presentations, and posters are not included due to the potential for overlap with published data.
2. The sample consists of child and adolescent participants, defined as all participants in the study must be under the age of 21 years with a mean age <18 years.
3. Participants are children and adolescents without a diagnosed developmental disorder.
4. Studies include at least one standardized measure of child/adolescent anxiety (state or trait) or worry, completed by either the child/adolescent or parents. Questionnaires must show internal consistency of at least 0.7 and evidence of construct validity. If a

standardized semi-structured diagnostic interview is used, there is evidence of inter-rater reliability of at least 0.7 and evidence construct validity. Interviews can be completed either with child, parent, or both.

5. Studies include at least one measure of IU, completed by either the child or parent. The measure is described in the study as a measure of IU by the authors.
6. The association of IU with anxiety or worry is available (reported or provided by the authors).
7. Studies are written in English. Non-English papers are not included due to lack of resources and facilities for translation.

Preliminary Search Strategy

The literature search was conducted in May 2017 using Web of Science, PubMed, ScienceDirect, and Psych Info/ PsychArticles to identify studies published between 1990 and May 2017. The search was limited within the years from 1990 to 2017 as the term IU was first coined in 1994 (Freeston, Rhéaume, Letarte, Dugas, & Ladouceur, 1994). We used 14 anxiety related key terms, *anxi**, *worry*, *anxi* disorder*, *fear*, *GAD*, *OCD*, *SA*, *obsess**, *compul**, *panic*, *generali* anxiety disorder*, *phobi**, *social anxiety*, and *separation anxiety*. These were crossed with key terms to identify intolerance of uncertainty dimensions: “*intolerance of uncertainty*”, “*need for certainty*”, “*need for predictability*”, “*intolerance of ambiguity*”, and “*need for cognitive closure*”. The bibliographic software, EndNote, was utilized to import references from electronic databases. Titles and abstracts were screened based on criteria 1, 2 and 7 to select the studies that were eligible for the full-text assessment. The full text assessment was then conducted to identify eligible studies for the review based on all inclusion criteria listed. Next, the reference lists of the studies meeting all inclusion criteria were hand searched in order to identify further studies of interest. In addition, first and corresponding authors of the eligible studies were contacted to request any unpublished,

further published, under review or in-press studies that had not yet been indexed by electronic databases. Response rate from these authors was 75%. Whilst conducting the review we were made aware of four additional unpublished datasets (Dodd & Taylor, 2015; Freeston et al., 2015; Morriss, Christakou, & Reekum, 2014; Osmanagaoglu, Dodd, & Creswell, 2017) that were relevant and these were also included to ensure the review was as complete as possible.

Study Selection

The screening process for inclusion was conducted by a single first coder (NO) and shared between two second coders (MT & CLP), all three were postgraduate students. Initially assessors independently screened the titles and abstracts of the publications. All studies regarded as eligible by either first or second coder were included for further assessment. Inter-assessor reliability between the first and second coders for whether studies met the eligibility criteria at this stage was high ($Kappa = .97$). Subsequently, coders independently screened full-text versions of these studies and inter-coder reliability for inclusion/exclusion at this stage was $Kappa = .96$. Any disagreements at this stage were discussed and resolved by consensus with the second author (CC) after referring to the protocol. Figure 1 provides a flow chart showing the studies remaining at each stage. Where studies met all criteria to be included, corresponding and first authors were contacted to request missing data. The electronic database search resulted in 23 studies that were eligible for the analysis. Additional data for 8 studies (4 unpublished data and 4 under review) were also available, resulting in 31 eligible studies in total.

Insert Figure 1 about here

Quality Assessment

Quality assessment is an integral part of a systematic review and there are several instruments developed to assess the quality of studies included in a systematic review. However there is no agreed gold standard tool for evaluating the quality of studies. In this review, we have used a 13-item checklist adapted from Moncrieff, Churchill, Drummond, and McGuire (2001). The 13-items that were applicable for this review were: (1) description of objectives and questions of the study, (2) magnitude of the sample size, (3) evidence of power calculation, (4) source of subjects, (5) description of sample demographics, (6) use of diagnostic criteria, (7) explicit statement of inclusion/exclusion criteria and number of exclusions reported, (8) clear description of outcome measures, (9) inclusion of all subjects in the analysis, (10) description of analytic method, (11) presentation of results, (12) conclusion of the results, (13) and declaration of interest. All 13 items were rated on a scale from 0 to 2 ($0 = \text{'no'}$, $1 = \text{'partial'}$, and $2 = \text{'yes'}$). One item on the checklist was only applicable to some studies (use of diagnostic criteria); therefore, the mean score was calculated for each study (see Table 1). Enough information to conduct the full quality assessment was available for the 23 published studies and two of the additional studies identified through contact with corresponding authors. The quality of eligible studies was evaluated by a single first assessor (NO) and one of two second assessors (MT&CLP), a high reliability was found based on the 25 studies included in the quality assessment. The average measure ICC was .82 with a 95% confidence interval .594 to .921 ($F(24, 24) = 5.59, p < .001$).

Data Extraction

One reviewer (NO) extracted the data, and two postgraduate students (MT&CLP) checked the data that had been extracted correctly for all items. Study authors were contacted where there was missing data or additional data needed. For each study, the following information was extracted: (a) background and demographic information including study

location and design, (b) number of participants, (c) participants' age range and mean age, (d) child/adolescent gender, (e) sample type (clinical/community), (f) for longitudinal studies, assessment time points, (g) how anxiety was measured (questionnaire, interview), (g) anxiety measure used, (h) anxiety informant, (i) how worry is measured, (j) worry measure used, (k) worry informant, (l) how IU was measured, (m) IU measure used, (n) IU informant, (o) findings, (p) effect sizes, (r), any ethical issues or source of bias.

Study Sample

Table 1 provides the details of the data extracted for each of the 31 eligible studies. Here we provide an overview of these studies. All 31 studies that were eligible for the meta-analysis were conducted within the last decade. Nine studies were conducted in the U.S.A (Comer et al., 2009; Cornacchio et al., under-review; Cowie, Clementi, & Alfano, 2016; Kertz & Woodruff-Borden, 2013; Krain et al., 2008; Krain et al., 2006; Read, Comer, & Kendall, 2013; Sanchez et al., 2017; Sanchez, Kendall, & Comer, 2016), eight in the U.K. (Boulter, Freeston, South, & Rodgers, 2014; Dodd & Taylor, 2015; Fialko, Bolton, & Perrin, 2012; Freeston et al., 2015; Morriss et al., 2014; Neil, Olsson, & Pellicano, 2016; Osmanagaoglu et al., 2017; Perrin, Bevan, Payne, & Bolton, under review), three in Canada (Dugas, Laugesen, & Bukowski, 2012; Laugesen et al., 2003; Wright, Lebell, & Carleton, 2016), three in Australia (Donovan, Holmes, & Farrell, 2016; Donovan, Holmes, Farrell, & Hearn, 2017; Hearn, Donovan, Spence, & March, 2017), two in Sweden (Cervin, Olsson, Lindvall, & Perrin, under review ; Lunderg, Gustafsson, & Perrin, under-review), two in the Netherlands (Boelen et al., 2010; Dekkers, Jansen, Salemink, & Huizenga, 2017), one in Iran (Barahmand, 2008), one in Germany (Thielsch, Andor, & Ehring, 2015), one in China (Lin, Xie, Yan, & Yan, 2017), and one in Italy (Aloi & Segura-Garcia, 2016). One study also included data on participants outside the age range of our criteria (Krain et al., 2006) and two included children with a developmental disorder (Boulter et al., 2014; Neil et al., 2016). In

these cases effect sizes were extracted for data that only referred to typically developing participants and participants within our specified age range. Of the eligible studies, 29 out of 31 were cross-sectional. The remaining two studies were a randomised control trial of CBT for GAD (Perrin et al., under review) and a longitudinal study with 10 distinct time points (Dugas et al., 2012) respectively. Multiple relevant effect sizes (ES) were available at several but not all time points in the later study; therefore, the ES from the first time point provided was included in the analysis (see Table 1).

Most of the participants in the eligible studies were recruited through schools and by local advertisement. Ten studies included clinical participants drawn from child study centres/clinics (Cervin et al., under review ; Comer et al., 2009; Cornacchio et al., under-review; Cowie et al., 2016; Donovan et al., 2016; Hearn et al., 2017; Krain et al., 2008; Perrin et al., under review ; Read et al., 2013; Sanchez et al., 2017). The sample size of individual studies ranged from 12 to 2286 and the overall age range was 3-20 years. Ethnic composition of the samples were available in 15 studies (Comer et al., 2009; Cornacchio et al., under-review; Cowie et al., 2016; Dodd & Taylor, 2015; Donovan et al., 2016; Donovan et al., 2017; Dugas et al., 2012; Fialko et al., 2012; Hearn et al., 2017; Kertz & Woodruff-Borden, 2013; Laugesen et al., 2003; Read et al., 2013; Sanchez et al., 2017; Sanchez et al., 2016; Wright et al., 2016). For most of these studies the majority of participants were Caucasian; two studies had a majority of Hispanic participants (Cornacchio et al., under-review; Sanchez et al., 2017) and in one study half of the sample were African American (Sanchez et al., 2016). Socio-economic level of the participants was available in nine studies; in six of these studies the majority of the participants came from middle and high SES (Comer et al., 2009; Dodd & Taylor, 2015; Donovan et al., 2016; Hearn et al., 2017; Laugesen et al., 2003; Sanchez et al., 2017), and participants were mostly of low SES in three studies (Fialko et al., 2012; Sanchez et al., 2016; Wright et al., 2016). Two studies reported family intactness; with

72.3% (Dugas et al., 2012) of the participants reported to have intact families and 79.82% (Donovan et al., 2017) of the participants living with both parents.

Anxiety was measured in 26 studies; however, the correlation between anxiety and IU was only available in 24. Of these 24 studies, 20 relied on questionnaire measures only for anxiety assessment, two of them only used a diagnostic interview with clinical severity ratings (Donovan et al., 2016; Read et al., 2013), and two used both questionnaires and clinical severity ratings (Cowie et al., 2016; Hearn et al., 2017). In the latter case, the association between IU and the questionnaire measure of anxiety was included in the analysis as it provides a more general measure of anxiety. Worry was measured in 22 studies and all of these reported the correlation between the worry measure and IU. All studies used a child self-report questionnaire measure for worry. IU was measured using questionnaire measures in all 31 studies; seven studies used the Intolerance of Uncertainty Scale for Children (IUS-C) child report (Cowie et al., 2016; Dodd & Taylor, 2015; Donovan et al., 2016; Donovan et al., 2017; Kertz & Woodruff-Borden, 2013; Osmanagaoglu et al., 2017; Read et al., 2013), three studies used the IUS-C parent report (Neil et al., 2016; Sanchez et al., 2017; Sanchez et al., 2016), three studies used both the parent and child report of IUS-C (Boulter et al., 2014; Comer et al., 2009; Cornacchio et al., under-review), eight studies used the Intolerance of Uncertainty Scale (IUS) which is a standardized adult measure to assess IU (Aloi & Segura-Garcia, 2016; Barahmand, 2008; Dugas et al., 2012; Krain et al., 2008; Krain et al., 2006; Laugesen et al., 2003; Morriss et al., 2014; Thielsch et al., 2015), six studies used the IUS-12 which is a shortened version of the IUS (Boelen et al., 2010; Dekkers et al., 2017; Freeston et al., 2015; Hearn et al., 2017; Lin et al., 2017; Wright et al., 2016), and four studies assessed IU by using only 5 items from the IUS (Cervin et al., under review ; Fialko et al., 2012; Lunderg et al., under-review; Perrin et al., under review). Where both child and parent reported IU was available, the child report was used in the analysis, as there is poor

agreement between parent and child report of IU; and it has been suggested that children are better reporters of their own IU (Comer et al., 2009). Where multiple effect sizes for the association between IU and both anxiety and worry were reported for independent subgroups such as male and female (Barahmand, 2008), summary effects were calculated across subgroups in order for each study to contribute one ES to the analysis (Borenstein, Hedges, Higgins, & Rothstein, 2009).

Insert Table 1 about here

Meta-Analytic Method

Pearson's product-moment correlation coefficient (r) was chosen as the effect size for this meta-analysis as r is readily interpretable in terms of practical importance and in comparison to other effect sizes (Field, 2001; Rosenthal & DiMatteo, 2001). Meta-analyses were conducted using RStudio (version 3.2.3) and the Metafor package (Viechtbauer, 2010). The Hedges-Olkin approach (Hedges & Olkin, 1985) was applied. A random-effects model was chosen as this approach allows meta-analytic results to be generalized to a more extensive population of studies (Field, 2001). To interpret the effect sizes Cohen (1988) guidelines were used (small effect $r = .10$, moderate effect $r = .30$, large effect $r = .50$).

Two separate meta-analyses were carried out, one for the association between IU and anxiety, and one for the association between IU and worry. To assess heterogeneity χ^2 test and I^2 statistic were used. 95% confidence intervals were calculated for the associations between IU and anxiety and for IU and worry. Fisher's Z was used for the meta-analysis, and the final reported effect size was converted back to Pearson r . Funnel and forest plots were

created to provide a visual representation of the data and to facilitate examination of publication bias. Rank correlation (Begg & Mazumdar, 1994) and regression tests (Egger, Smith, Schneider, & Minder, 1997) were then conducted to assess the evidence of publication bias. In addition, Rosenthal's fail-safe N (Rosenthal, 1979) was conducted to assess whether the effects of the analyses were artefacts of publication bias.

The following variables were extracted as potential moderators: mean age, gender (coded as proportion male), study population (coded as the proportion of the sample that were from a clinical population), method of anxiety assessment (questionnaire vs diagnostic interview), measure used to assess IU, and study design (cross-sectional vs longitudinal). Moderator analysis is suitable to conduct when there are at least four studies in each subcategory (Bakermans-Kranenburg, 2003). Due to the limited number of studies and variability/non variability of the measures used in the studies, only age, gender, sample type (proportion of the clinical participants), and IU measure were taken into account as moderator variables. Meta-regression analysis was conducted when the moderator variable was a continuous variable to quantify the relationship between the magnitude of the moderator and the IU- anxiety/IU-worry effects (Borenstein et al., 2009).

Results

Meta-Analysis of IU-Anxiety

The meta-analysis examining the association between IU and anxiety (see Figure 2) identified a significant mean ES of $r = .60$ ($p < .001$, 95% CI .55, .64) which meets the criteria for a large effect and suggests that IU explains 36% of the variance in anxiety. Heterogeneity was significant, $Q(23) = 121.71$, $p < .001$, $I^2 = 84.29\%$, indicating the presence of moderator variables; however, there was no significant moderator effect of age ($QM(1) = 0.03$, $p = .86$), gender ($QM(1) = 0.81$, $p = .37$), sample type ($QM(1) = 1.26$, $p = .26$), or IU measure ($QM(4) = 2.94$, $p = .57$) on the association of IU and anxiety.

Insert Figure 2 about here

Meta-Analysis of IU-Worry

The mean effect size for the association between IU and worry (see Figure 3) was $r = 0.63$ ($p < .001$, 95%CI .58, .67) which meets the criteria for a large effect and suggests that IU was associated with approximately 39.69% of the variance in worry. There was significant heterogeneity, $Q(21) = 108.28$, $p < .001$, $I^2 = 84.98\%$ suggesting the presence of moderator variables; however, no significant moderator effects of age ($QM(1) = 3.05$, $p = .08$), gender ($QM(1) = 0.50$, $p = .48$) sample type ($QM(1) = 0.56$, $p = .45$), or IU measure ($QM(3) = 6.09$, $p = .11$) on the association between IU and worry were found.

Insert Figure 3 about here

Publication Bias

Funnel plots were inspected for all analyses and no evidence for publication bias was found. The results of the rank correlation tests (Begg & Mazumdar, 1994) and regression tests (Egger et al., 1997) were all non-significant (smallest $p = 0.50$). For the association between IU and anxiety, the fail-safe N (Rosenthal, 1979) was 17943, suggesting 17943 studies with an effect size of zero would be required to increase the p -value of this analysis to above 0.05 (Orwin, 1983). For the association between IU and worry, a fail-safe N of 20939 was found.

Discussion

Consistent with the adult literature, this systematic review and meta-analysis revealed a strong positive correlation between IU and both anxiety and worry in children and adolescents. There was significant heterogeneity between studies; however, the source of heterogeneity remains unclear. Few potentially moderating variables could be examined and, where they could, no significant moderator effects were found. The review revealed clear methodological limitations with the existing body of work. These limitations and the consequences of them will now be discussed in turn, along with associated recommendations for future research.

First, all but one of the studies eligible for this review was cross-sectional, thus little can be concluded about the direction of the association of IU with anxiety and worry. The only longitudinal study identified indicated that the relationship between IU and both anxiety and worry over time is likely reciprocal (Dugas et al., 2012). Further longitudinal research and experimental work that includes a manipulation of IU or anxiety is required to delineate the exact nature of the association between IU and anxiety, and IU and worry in young people. Given potential implications for intervention, it will be particularly valuable to test whether IU might play a causal role in the development and maintenance of anxiety disorders in young people. This fact has recently been highlighted by Shihata, McEvoy, Mullan, and Carleton (2016) who specifically called for focused research on IU in children and adolescents with longitudinal designs that are also able to examine the factors that may moderate IU throughout development.

Second, all but two studies (Krain et al., 2008; Krain et al., 2006) relied entirely on questionnaires to measure IU. Whilst questionnaires provide an efficient way of collecting data on a large sample, they are relatively limited in what they can tell us about the exact

nature of IU and they are subject to limitations such as reporter bias and shared method variance with questionnaire measures of anxiety and worry. Now that a robust association of IU with anxiety and worry has been observed, it is time for the field to begin to move beyond documenting these associations using questionnaires and to begin to consider more objective and developmentally appropriate measures of IU. One notable example of how a behavioural task might be used can be seen in the work of Krain and colleagues (Krain et al., 2008; Krain et al., 2006) in which difference between reactions to certainty and uncertainty was examined. There is significant scope for more behavioural and experimental work of this nature. Behavioural tasks designed to measure reactions to uncertainty have a number of benefits over questionnaire measures. First, behavioural tasks are objective, which minimizes response bias and overcomes issues around shared method variance. Further by observing reactions to certain vs uncertain situations, behavioural tasks have the potential to provide more nuanced insights into the nature of anxiety-linked IU. For example, through behavioural tasks it may be possible to capture distinct responses to uncertainty such as avoidance or information seeking under uncertain conditions, both of which could result from IU. In addition, it may be possible to gain insight into physiological responses to uncertainty, which individuals may not be consciously aware of and able to report.

A third limitation of the existing work relates to the questionnaire measures used. Less than half of the eligible studies (K=13) used the IUS-C, which was specifically developed for use with children. The remaining studies utilized questionnaire measures of IU which have been developed and validated for use with adults rather than children. Given age related differences in the understanding of and response to uncertainty (Beck & Robinson, 2001; Lyons & Ghatti, 2011, 2013; Robinson et al., 2006; Roebbers & Howie, 2003; Roebbers et al., 2007), wherever possible, the measures used to capture IU should be designed to be appropriate for the developmental level of study participants. In addition, while the IUS-C

demonstrates favourable psychometrics (Comer et al., 2009), this measure also has some limitations. In terms of psychometrics, the test-retest reliability of the questionnaire, both the child and parent form, has yet to be examined and the factor structure of the questionnaire needs to be explored. Although there is a support for a two-factor structure of the IUS-C (Cornacchio et al., under-review), consistent with that found for the adult measure (Birrell, Meares, Wilkinson, & Freeston, 2011; Carleton et al., 2010; Sexton & Dugas, 2009), there is some evidence that parents may not be able to reliably report on IUS-C items which indicate future oriented cognition of their children (Cornacchio et al., under-review). Finally, the IUS-C is designed to measure IU in young people aged between 7 and 17 which is a broad age range considering the developmental changes that occur throughout childhood and adolescence. Younger children are more likely to have a difficult time understanding items (Cowie et al., 2016) and potentially as a result; the scale shows poorer utility to distinguish children with and without anxiety disorders in younger (7-8) than older (9-15) participants (Comer et al., 2009). Taken together, there is clear scope to improve questionnaire measures of IU in young people.

Fourth, more than half the studies (K=22) relied exclusively on community participants and where participants with an anxiety diagnosis were included, most of these participants has a diagnosis of GAD. Note that this was true even of a study that focused on young people with social anxiety disorder, where almost 79% of the sample had comorbid GAD (Hearn et al., 2017). Although the association between IU and anxiety appears to be strong and robust, more work with clinical samples, including children with and without GAD is needed if we are to begin to consider how IU might be incorporated into treatment for child anxiety disorders and to examine questions about whether IU is disorder specific or transdiagnostic factor across anxiety disorders for young people.

Finally, design issues in the existing work limit the conclusions that can be made about moderators. Although there was significant unexplained heterogeneity in both associations of interest, neither age nor gender were significant moderators of either. This should be interpreted with caution given the limitations of existing work. The vast majority of studies included participants with a wide age range but didn't consider the moderating effect of age. As such, only mean age could be used in the meta-analysis to capture age differences across studies. Given the large age ranges used, mean age is not a very informative statistic. Similarly, it was unusual for studies to report effects by gender so only the proportion of female participants could be used in the moderator analysis. Overall, there was insufficient evidence to conclude whether age and/or gender moderate either association.

The most comprehensive way of addressing how age affects the association between IU and anxiety/worry would be for studies to include large enough groups of participants within narrow age bands that the association can be estimated and compared for each age group. Alternatively, smaller studies conducted with focused samples of children within narrow age bands would provide an estimate of the associations at each age group and the moderating effect of age could then be examined using meta-analytical techniques across studies. The same is true for the effects of gender; larger studies with adequate numbers of boys and girls would provide the most robust solution.

Other factors that might moderate the association of IU with anxiety and worry include methodological factors such as the assessment method of the variable of interest (questionnaire vs diagnostic interview), the informant (parent vs child), and/or factors associated with cognitive and metacognitive maturation such as negative problem orientation, positive beliefs about worry, and cognitive avoidance (Fialko et al., 2012; Kertz & Woodruff-Borden, 2013). Unfortunately there were not enough studies including these potential moderators for us to examine them in the present meta-analysis.

Strengths and Limitations

The review has a number of strengths but also some limitations that should be considered. This study is the first to provide a systematic quantitative investigation of the association between IU and both anxiety and worry in children and adolescents. A strength is that we conducted a quality assessment of all included papers. Overall, the studies were of reasonable quality; however, the quality of the future work could be improved in the following ways: more detailed description of the sample characteristics, more thorough reporting of the number of participants excluded in the analysis and the reasons for exclusion, reporting of power calculations/reasons for the sample size, detailed descriptions of main outcomes, and the use of appropriate outcome measures. For example, only 13 of the reviewed studies provided detailed descriptions of their sample characteristics (SES, ethnicity), only four of the reviewed studies reported the reason and number of participants excluded in the analysis, and none of the studies reported the reason for the sample size with reference to a power calculation. A further issue related to quality is that the studies are mainly correlational but the degree to which potential confounds are investigated is limited. By collecting rich data regarding the sample and potential moderators, as already outlined, future research will also be better placed to consider and control for potential confounds.

A strength of the present research is that we included unpublished, in-press and under-review data which were sourced by contacting corresponding authors of studies identified in our systematic review. The response rate from these authors was good (75%) which helps to address concerns about publication bias (note also that there was no evidence of publication bias from the funnel plot, rank correlation tests and regression tests). It should be considered however that not all of these studies have undergone the peer-review process. Nevertheless, where possible the methodological quality of these studies was assessed using the same criteria as for the published studies and overall, the quality assessment of these studies

showed them to have a reasonable quality, consistent with the published studies included in the review.

Considering limitations, we only included English language papers in this review for practical reasons and the focus was restricted to typically developing children, which excluded, for example the growing body of research examining IU in children with autism (Boulter et al., 2014; Chamberlain et al., 2013; Neil et al., 2016; Wigham, Rodgers, South, McConachie, & Freeston, 2015). Second, although we coded and examined a range of potential moderators for the relationship between IU and anxiety/worry, our ability to consider moderators in detail was affected by the low number of studies found overall and the relative homogeneity of the methodological factors. High heterogeneity may also arise from characteristics of the participants included in each of the studies that the study level data we extracted is unable to capture. For example, two studies could have the same mean participant age but a very different distribution of participant ages. Without individual data points from each participant within each study we are not able to capture these differences between studies (Schmid, Stark, Berlin, Landais, & Lau, 2004).

Conclusion

Given the promise of IU research in adults and the strong correlations found between IU and both anxiety and worry in this review, we conclude that the role of IU in the development and maintenance of anxiety and worry is worthy of further investigation in children and young people; however, it is premature to draw clinical implications because there is a lack of evidence that IU plays a causal or maintaining role in anxiety disorders for children and young people. Future work should consider developmental factors and incorporate longitudinal and experimental designs as well as focusing on clinical samples beyond GAD.

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Table 1. *Reviewed Studies, Sample Characteristics, Anxiety/Worry/IU Measures, Effect Sizes, and Quality Ratings*

[illegible]

[illegible]

Cervin et al. (under review)	Clinical	52	8-18	13.78	SCARED	PSWQ	items	IU and anxiety (r = .62) IU and worry (r = .58)	
Lunderg et al. (under review)	Community	509	9-16	11.61	Beck Youth Inventory - Anxiety	PSWQ	IUS -5 items	IU and anxiety (r = .57) IU and worry (r = .61)	

Note: PSWQ=Penn State Worry Questionnaire, WTQ= Worry Tendency Questionnaire, WAQ= Worry and Anxiety Questionnaire, MASC= Multidimensional Anxiety Scale for Children, GHQ= General Health Questionnaire – Anxiety Scale, RCMAS= Revised Child's Manifest Anxiety Scale, ACS=Affective Control Scale, SAS-A= Social Anxiety Scale for Adolescents, SCAS= Spence Child Anxiety Scale, SCARED= Screen for Anxiety-Related Emotional Disorders, STAI-C= State-Trait Anxiety Inventory for Children, CBCL= Child Behaviour Checklist, SPAI-C= Social Phobia and Anxiety Inventory, SPIN= Social Phobia Inventory, IUS= Intolerance of Uncertainty Scale, IUS-C= Intolerance of Uncertainty Scale for Children.

***unpublished data

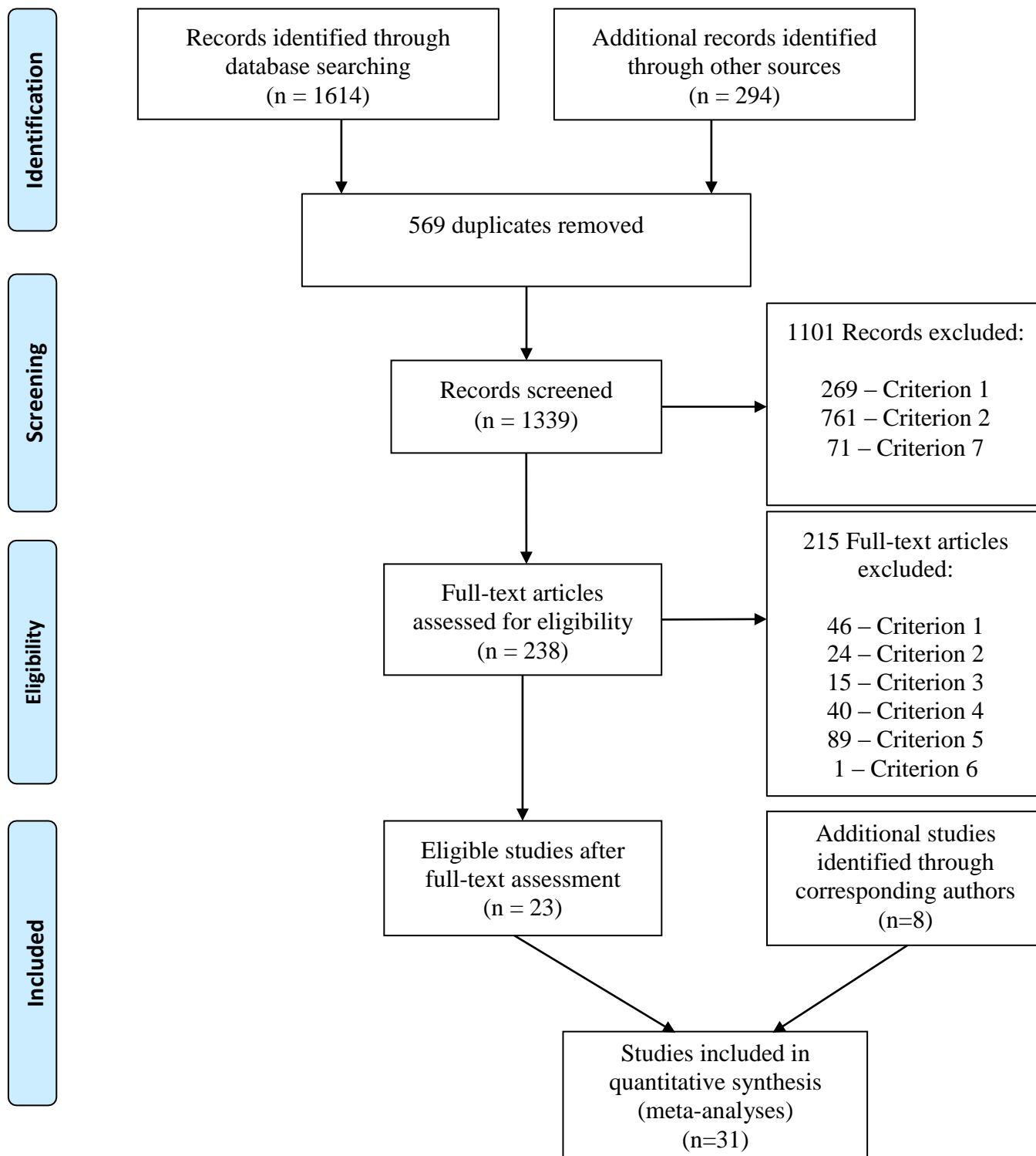


Figure 1. Flow chart of the studies accepted through the eligibility screening process
(criterion1: not empirical research, criterion 2: outside of age range, criterion3: atypical
development, criterion 4: no anxiety measure, criterion 5: no IU measure, criterion 6:
effect size not available, criterion 7: foreign language)

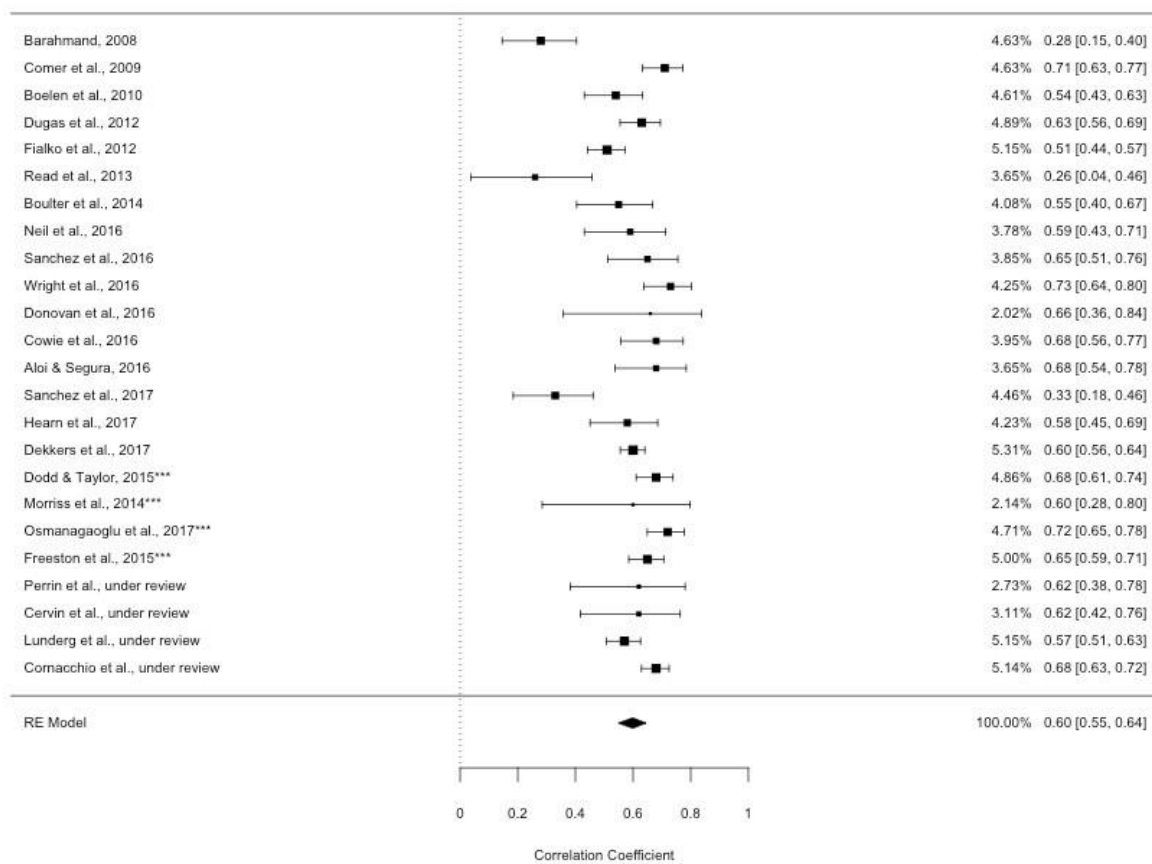


Figure 2. Forest plot showing correlation coefficients (r) for the association between IU and anxiety with confidence intervals and study weights for contribution to overall effect size.

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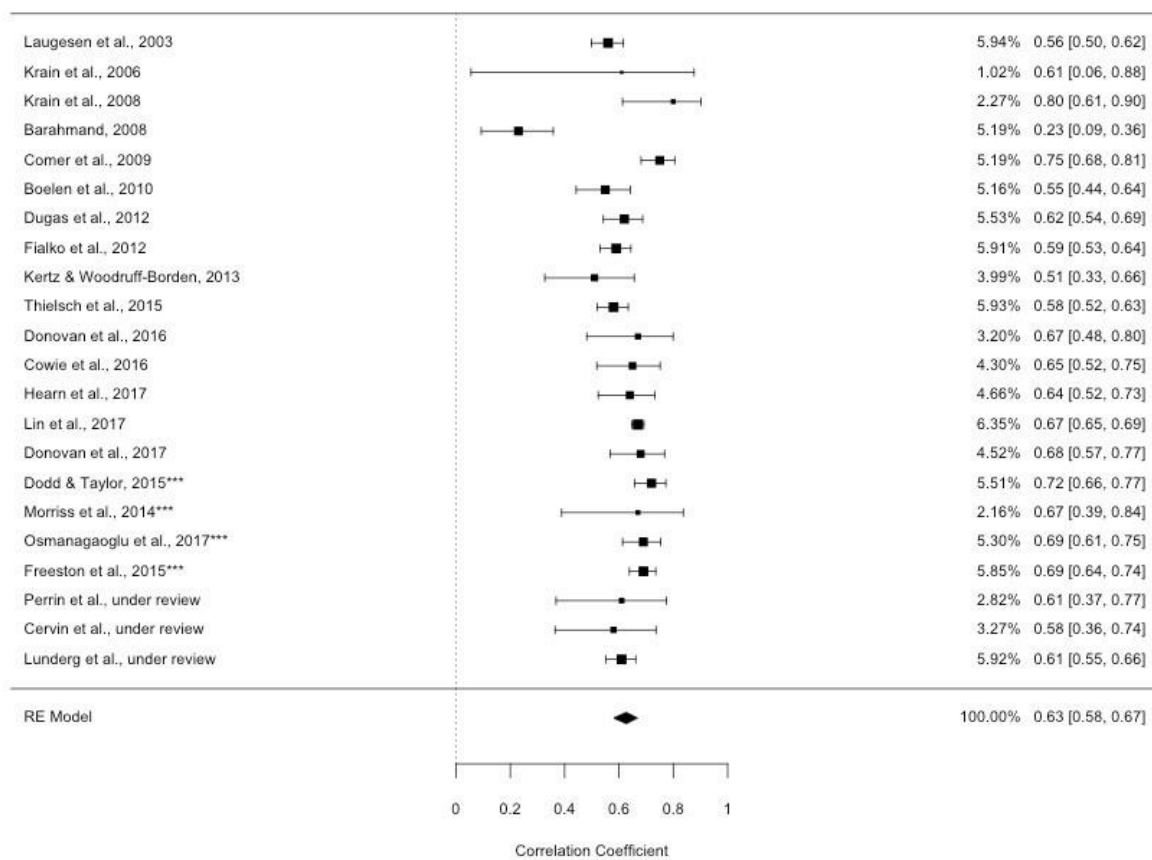


Figure 3. Forest plot showing correlation coefficients (r) for the association between IU and worry with confidence intervals and study weights for contribution to overall effect size.

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Author disclosure

Contribution of authors

NO conducted the searches and analyses and produced the first and final draft of the paper. HD developed the initial idea, advised on the search criteria, supervised the search process and edited the paper. CC advised on the search criteria, supervised the search process and edited the paper.

All authors approved the final version of the manuscript for submission.

Role of Funding Source

NO was supported by a Turkish Government PhD scholarship (ref.537635). HD is supported by an ESRC Future Research Leaders grant ES/L010119/1. CC is supported by an NIHR Research Professorship (RP_2014-04-018).

Acknowledgements

We would like to thank Mariel Thottam and Charlotte Lewis-Pryde for assistance with study selection, quality assessment, and data extraction.

Limitations

- We only included English language papers in this review for practical reasons.
- The focus was restricted to typically developing children, which excluded, for example the growing body of research examining IU in children with autism (Boulter, Freeston, South, & Rodgers, 2014; Chamberlain et al., 2013; Neil et al., 2016; Wigham, Rodgers, South, McConachie, & Freeston, 2015).
- Although we coded and examined a range of potential moderators for the relationship between IU and anxiety/worry, our ability to consider moderators

in detail was affected by the low number of studies found overall and the relative homogeneity of the methodological factors.