The impact of treatment delivery format on response to cognitive behaviour therapy for preadolescent children with anxiety disorders

Anna McKinnon,1 Robert Keers,2 Jonathan R. I. Coleman3,4 Kathryn J. Lester,5 Susanna Roberts,3 Kristian Arendt,6 Susan M. Bogels,7 Peter Cooper,8,9,10 Cathy Creswell,8 Catharina A. Hartman,11 Krister W. Fjermestad,12,13 Tina In-Albon,14 Kristen Lavallee,15 Heidi J. Lynehall,1 Patrick Smith,16 Richard Meiser-Stedman,17 Maaike H. Nauta,18 Ronald M. Rapee,1 Yasmin Rey,19 Silvia Schneider,15 Wendy K. Silverman,20 Mikael Thastum,6 Kerstin Thirwell,8 Gro Janne Wergeland,13 Thalia C. Eley,3,4,* and Jennifer L. Hudson1,1*

1Department of Psychology, Centre for Emotional Health, Macquarie University, Sydney, NSW, Australia; 2Department of Biological and Experimental Psychology, School of Biological and Chemical Sciences, Queen Mary University of London, London, UK; 3Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King’s College London, London, UK; 4NIHR Biomedical Research Centre for Mental Health, South London and Maudsley NHS Trust, London, UK; 5School of Psychology, University of Sussex, Brighton, UK; 6Department of Psychology and Behavioural Sciences, Aarhus University, Aarhus, Denmark; 7Research Institute Child Development and Education, University of Amsterdam, Amsterdam, The Netherlands; 8School of Psychology and Clinical Language Sciences, University of Reading, Reading, UK; 9Department of Psychology, Stellenbosch University, Stellenbosch, South Africa; 10Department of Psychology, The University of Cape Town, Cape Town, South Africa; 11Department of Psychiatry, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; 12Department of Clinical Psychology, Faculty of Psychology, University of Bergen, Bergen, Norway; 13Department of Child and Adolescent Psychiatry, Anxiety Disorders Research Network, Haukeland University Hospital, Bergen, Norway; 14Department of Psychology, University Landau Koblenz, Landau, Germany; 15Department of Psychology, Ruhr-Universität Bochum, Bochum, Germany; 16Department of Psychology, Institute of Psychiatry, King’s College London, London, UK; 17Department of Psychology, University of East Anglia, Norwich, UK; 18Department of Clinical Psychology and Experimental Psychopathology, University of Groningen, Groningen, The Netherlands; 19Department of Psychology, Child Anxiety and Phobia Program, Florida International University, Miami, FL, USA; 20Child Study Center, School of Medicine, Yale University, New Haven, CT, USA

Background: Several delivery formats of cognitive behaviour therapy (CBT) for child anxiety have been proposed, however, there is little consensus on the optimal delivery format. The primary goal of this study was to investigate the impact of the child’s primary anxiety diagnosis on changes in clinical severity (of the primary problem) during individual CBT, group CBT and guided parent-led CBT. The secondary goal was to investigate the impact of the child’s primary anxiety diagnosis on rates of remission for the three treatment formats. Methods: A sample of 1,253 children (5–12 years; Mage = 9.3, SD = 1.7) was pooled from CBT trials carried out at 10 sites. Children had a primary diagnosis of generalised anxiety disorder (GAD), social anxiety disorder (SoAD), specific phobia (SP) or separation anxiety disorder (SAD). Children and parents completed a semistructured clinical interview to assess the presence and severity of DSM-IV psychiatric disorders at preintervention, postintervention and follow-up. Linear mixture modelling was used to evaluate the primary research question and logistic modelling was used to investigate the secondary research question. Results: In children with primary GAD, SAD or SoAD, there were no significant differences between delivery formats. However, children with primary SP showed significantly larger reductions in clinical severity following individual CBT compared to group CBT and guided parent-led CBT. The results were mirrored in the analysis of remission responses with the exception that individual CBT was no longer superior to group CBT for children with a primary SP. The difference between individual and group was not significant when follow-up data were examined separately. Conclusions: Data show there may be greater clinical benefit by allocating children with a primary SP to individual CBT, although future research on cost-effectiveness is needed to determine whether the additional clinical benefits justify the additional resources required. Keywords: Anxiety; treatment trials; cognitive therapy.

Introduction
Up to 32% of children and adolescents attending primary care settings present with a primary anxiety disorder (Hansen, Oerbeck, Skirbekk, & Kristensen, 2016; Scott, Mughelli, & Deas, 2005). These problems are highly comorbid with one another (Rapee et al., 2013), and children and adolescents with these problems are at risk of suffering enduring disability. Cognitive behaviour therapy (CBT) is regarded as the front-line psychological treatment for child anxiety with approximately 60% of children in remission from their anxiety disorder diagnosis.
immediately after completing treatment (James, James, Cowdrey, Soler, & Choke, 2015). However, despite widespread support for CBT, the empirical data clearly indicate that a sizeable proportion of children do not recover. A clearer understanding of the limits to CBT, and correspondingly, the ideal conditions for delivery of CBT for child anxiety are essential. There are now a variety of evidence-based CBT programs defined under the broad term ‘CBT’. Some of the main programs in the field are trans-diagnostic, whereas others are disorder-specific (Schneider et al., 2013), or intensive treatments (Ollendick et al., 2009). Even though programs share some important similarities, they also differ in a number of areas; for example, duration, treatment targets and level of parental involvement.

**Efficacy of CBT treatment formats**

Decisions regarding the best way to allocate children to child anxiety treatments are currently poorly understood. Our goal in the current study was to investigate whether clinical responses to individual CBT, group CBT and guided parent-led CBT are influenced by the child’s primary anxiety diagnosis.\(^1\) There are very few published evaluations of the costs of CBT treatments for child anxiety, but it is typically presumed that whilst individual CBT allows for extensive tailoring of treatments to the individual, it is most expensive. Group CBT may be slightly cheaper and there are invaluable opportunities for peer normalisation, positive peer modelling, reinforcement and social support (Manassis et al., 2002). Three trials have concluded that treatment responses were no different for individual CBT and group CBT (Liber et al., 2008; Manassis et al., 2002; Wergeland et al., 2014). In contrast, one meta-analysis showed that individual CBT for child anxiety led to superior effect sizes (on a child reported self-report symptom measure) compared to group CBT (Reynolds, Wilson, Austin, & Hooper, 2012). Guided parent-led CBT (i.e. delivered directly to children via their parents) can be delivered remotely thereby increasing the chances that it is cost-effective (Creswell et al., 2017; Lyneham & Rapee, 2006; Silverman, Pettit, & Lebowitz, 2016; Thirlwall et al., 2013). A recent Cochrane review indicated that there were no differences in the efficacy of individual CBT, group CBT and family/parental CBT\(^2\) (James et al., 2015).

Despite having important implications for clinical decision making, previous meta-analyses (James et al., 2015; Reynolds et al., 2012) are yet to elucidate if there is a clinical need to allocate children presenting with a primary anxiety problem to a particular treatment format. There are very plausible reasons that there could be disorder-specific responses to different treatment formats. For example, in social anxiety disorder (SoAD) the group situation may provide important opportunities for practicing exposure skills, but it could also prove to be too anxiety provoking, making it difficult for children to engage with their therapist and learn core CBT skills. It may be more difficult to deliver group CBT to children with a specific phobia (SP) due to the amount of psychoeducation and in-session exposure typically needed to treat these cases. As such, establishing whether individual CBT, group CBT or guided parent-led CBT leads to similar improvements for the range of child anxiety disorders is an empirical question with important implications for the development of stepped care models.

**Diagnosis and clinical responses to CBT treatment formats**

Three small RCTs (Liber et al., 2008; Manassis et al., 2002; Wergeland et al., 2014) have investigated the impact of having an SoAD diagnosis on clinical outcomes following group or individual therapy. Manassis et al. (2002) reported a significant interaction effect between type of anxiety disorder and treatment approach in that children with high levels of social anxiety symptoms improved significantly more with individual CBT compared with group CBT. A second trial showed no difference in outcomes for children with a primary SoAD (Wergeland et al., 2014). A third trial showed that when the child had an SoAD diagnosis in their profile, greater reductions in internalising symptoms (according to father’s report) were achieved with group CBT compared to those achieved by individual CBT (Liber et al., 2008). These mixed findings are at odds with some findings in the adult SoAD field that have shown individual CBT is associated with more improvement in clinical severity than group CBT (Ingul, Aune, & Nordahl, 2014; Stangier, Heidenreich, Peitz, Lauterbach, & Clark, 2003). Taken together, these findings underscore the need to investigate interactions between treatment format and diagnosis in a large well-powered sample.

The literature on the differential effect of individual CBT and group CBT for response to different CBT treatment formats in generalised anxiety disorder (GAD), SP and separation anxiety disorder (SAD) is sparse. Manassis et al. (2002) found greater reductions in mother-rated anxiety symptoms for children with a primary GAD across both formats compared with children with SAD, SoAD or SP. Another study found that participants with a primary GAD diagnosis showed significantly greater reductions in parent-rated anxiety and depressive symptoms in individual CBT relative to group CBT, but children with SAD benefitted equally (Wergeland et al. (2014). The only trial that evaluated the impact of having a primary SP on treatment responses found no differences between individual CBT and group CBT (Manassis et al., 2002). Reasons contributing to the variable pattern of results include the fact that treatment responses were not always evaluated with
respect to changes in symptom severity and remis-
sion (Liber et al., 2008; Manassis et al., 2002). Some
studies assessed differences across primary prob-
lems (Wergeland et al., 2014), whereas others looked
differences according to having a diagnosis in the
overall profile (Liber et al., 2008), some trials had
very small sample sizes that limited conclusions
(Liber et al., 2008; Manassis et al., 2002), and all
previous studies have used either a parent- or child-
rated self-report measure to measure symptom
change.

The present study investigated whether clinical
responses to treatment formats are influenced by the
child’s primary anxiety diagnosis. This will be the
first comparison of individual CBT, group CBT and
guided parent-led CBT within individual anxiety
disorder categories in the child anxiety field. We
used the Genes for Treatment dataset, which is a
pooled sample of children taking part in CBT treat-
ments for child anxiety (Hudson et al., 2015; Keers
et al., 2016). The dataset employed in this study was
significantly larger than previous RCT’s that have
assessed questions in the field. The use of pooled
individual-level data in this study allows for
greater precision when controlling for covariates and
in the examination of potential treatment modera-
tors. This is also the first study to evaluate treatment
responses in a robust manner using a clinician-rated
composite measure derived from ratings on a struc-
tured clinical interview. Children were split into
diagnostic groups based on their primary anxiety
diagnosis. This is very relevant to both research and
routine clinical practice where it is commonplace for
the clinician to assess all presenting problems and
focus treatment on the disorder leading to the
highest levels of impairment.

The primary aim of this study was to investigate
the changes in clinical severity associated with
individual CBT, group CBT and parent-led CBT in
four separate primary anxiety disorder categories -
SoAD, GAD, SAD and SP. The secondary aim was to
assess these questions using rates of remission (i.e.
absence/presence of the primary diagnosis at the
end of treatment) as the core dependent variable of
interest. If significant relationships were found in
the main analyses, interactions between diagnosis and
treatment format would be explored. The current
state of the literature precluded any a priori hypothe-
ses regarding these interactions in the present
study.

Method

Sample

Data for 1,253 children\(^3\) aged between 5 and 12 years
\(M_{\text{age}} = 9.3, SD = 1.7\) was pooled from centres in Sydney,
Australia \((n = 619; 49.40\%)\), Reading, United Kingdom
\((n = 209; 23.86\%),\) Bergen, Norway \((n = 84; 6.70\%),\) Aarhus,
Denmark \((n = 82; 6.54\%),\) Bochum, Germany \((n = 38; 3.03\%),\)
Basel, Switzerland \((n = 48; 3.83\%),\) Miami, Florida \((n = 40;
3.19\%),\) Groningen, the Netherlands \((n = 21; 1.68\%),\) Oxford
\((n = 20; 1.60\%)\) and Amsterdam, the Netherlands \((n = 2;
0.16\%). The process of patient recruitment and the pooling of
data has been described in greater detail elsewhere (Hudson
et al., 2015; Lester et al., 2016; Roberts et al., 2015).

The inclusion criteria were: meeting DSM-IV criteria for a
primary diagnosis of GAD, SoAD, SP or SAD based on the
composite report of the parent and the child; having a sample
of DNA available for analysis, and taking part in a manualised
CBT treatment protocol. Exclusion criteria were a diagnosis
of significant intellectual impairment, a neurological disorder or
psychosis for the child.

Each study received ethical approval from their local hospita-
|l/university recruitment site. Informed consent was obtained
from adult carers/parents and assent from young people. The
demographic characteristics of the sample are presented in
Table 1. A description of the interventions carried out at the
different sites is reported elsewhere (Hudson et al., 2015) and
is summarized in Appendix S1.

Measures

The DSM-IV anxiety disorders were measured pre- and
postintervention via semistructured clinical interviews carried
out with parents and children. Across individual trials, follow-
up data were collected at variable time points (3, 6 or
12 months). All interviews were carried out by graduate level
staff or trainee psychologists.

The primary outcome, absolute change in clinical severity of
the child’s primary problem across treatment, was established
using clinician severity rating (CSR) scores on the Anxiety
Disorders Interview Schedule Child/Parent (ADIS-C/P; Silver-
man & Albano, 1996). In giving a CSR rating, the assessor
makes a single assessment of function on a scale from 0
(absent) to 8 (very severely disturbing/disabling) by consider-
ing the symptom severity, avoidance and interference with the
child’s functioning in core areas (e.g. school, family, friends,
peers). The secondary outcome, rates of remission (absence of
primary diagnosis) following treatment was determined
according to whether the child endorsed the requisite symp-
toms in line with the DSM criteria measured on the ADIS-C/P
(Silverman & Albano, 1996). A child’s diagnosis was assumed
to be in remission if he/she no longer presented with the
requisite symptoms required for the DSM diagnosis, which
corresponds to a CSR score of <4.

The vast majority of postassessments were blinded,
although for some trials and a minority of nontrial cases in
the sample this was not possible (see supplementary material
in Appendix S1 for references to individual trials and a
description of methods). Inter-rater reliability was assessed
and found to be satisfactory (see supplementary details in
Appendix S1 for references to individual trials).

In Bochum, the diagnosis was made using the Diagnostis-
ches Interview bei psychischen Störungen im Kindes- und
Jugendalter (Kinder-DIPS; Neuschwander, In-Albon, Ador-
netto, Roth, & Schneider, 2013; Schneider, Unnewehr, &
Margraf, 2009). The Kinder-DIPS is based on the ADIS-C/P
and provides the same data as the ADIS.

Data analysis

All analyses were conducted in STATA Version 14 (StatCorp,
College Station, TX). As we were most interested in differences
in the efficacy of treatment formats within each disorder, linear
mixture models were carried out separately for each diagnostic
category. The primary dependent variable of interest was the
absolute change in clinical severity of the primary anxiety
problem. The secondary aim was to assess these questions

© 2018 The Authors. Journal of Child Psychology and Psychiatry published by John Wiley & Sons Ltd on behalf of Association for
Child and Adolescent Mental Health.
using rates of remission (i.e. absence/presence of the primary diagnosis at the end of treatment) as the core-dependent variable of interest. The main analysis was carried out using outcome data pooled across post and follow-up time points (3, 6 or 12 months) as the dataset was underpowered to examine fixed effects across time points due to the variable follow-up time points (i.e. 3, 6 and 12 months) employed in individual studies.

Absolute changes in clinical severity and remission rates during the study period, and the extent of changes between diagnostic categories for the Genes for Treatment sample, have previously been reported (Hudson et al., 2015). A preliminary analysis was carried out to show the results of this previous study are replicated in this subsample of Genes for Treatment dataset. A Linear Mixture Model was fitted using the linear and quadratic effects of time, age, gender, baseline severity, treatment format and diagnostic category as fixed effects and clinical severity (i.e. CSR scores) as the dependant variable. In a second similar set of analyses, a logistic regression model was fitted with the same fixed effects and the dependent variable was the presence/absence of the primary anxiety disorder diagnosis.

For the main analyses investigating diagnosis-specific effects, four separate Linear Mixture Models were carried out to investigate the primary research questions regarding the efficacy of treatment format within each diagnostic category (GAD, SoAD, SP and SAD). All models included individual random intercepts in order to account for the correlation of repeated measures. Trials were nested within sites. Trial was entered in the model as a higher order random effect to account for possible differences by trial or site. The model included the linear and quadratic effects of time, age, gender, baseline severity, treatment format and diagnostic category as fixed effects and CSR scores as the dependant variable of interest. Supplementary analyses are also presented showing outcomes for these analyses at post and follow-up time points. In a second similar set of analyses, we used logistic regression models to investigate remission of the primary diagnosis following treatment in each of the four diagnostic categories.

Bonferroni corrections were employed and a p value of at least .006 (.05/8) was set on each of the linear models to indicate a significant result, based on eight analyses (four linear regression models, four logistic regression models) being conducted in the main analyses.

In addition to the separate analyses above for each diagnosis, we also conducted a formal test of the interaction between diagnosis and treatment format on clinical severity with the whole sample. Interactions were only investigated within a diagnostic category if a significant result was found in the main results. Given the exploratory nature of these analyses, a p value of <.05 was set to indicate significance. To determine whether there was an interaction of disorder and treatment format on change in clinical severity and remission rates, variables were dummy coded (SP vs. Other anxiety disorders, individual CBT vs. Other CBT treatments) and then entered as covariates in the model. Due to the nonrandomised nature of the study, we also carried out a post-hoc logistic regression analysis to see whether the proportions of children allocated to treatment formats significantly differed within each diagnostic category.

Results

Sample characteristics

Table 1 shows the baseline descriptive characteristics across the four diagnostic categories. The majority of the sample had a primary diagnosis of GAD (n = 508), followed by SAD (n = 319), SoAD (n = 283) and finally SP (n = 143). Across the samples, 9.4% of children had a comorbid internalising disorder (a nonanxiety internalising disorder) and 19.4% of children had a comorbid externalising disorder. The most common treatment format was group CBT (52.0%; n = 652), followed by individual CBT.

Table 1 Demographic and sample characteristics across diagnosis

<table>
<thead>
<tr>
<th></th>
<th>GAD</th>
<th>SoAD</th>
<th>SP</th>
<th>SAD</th>
<th>Total</th>
<th>Test statistic</th>
<th>Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of total sample (n)</td>
<td>40.5 (507)</td>
<td>22.6 (283)</td>
<td>11.4 (143)</td>
<td>25.5 (319)</td>
<td>100 (1,253)</td>
<td>χ²(3) = 216.63, p &lt; .001</td>
<td>–</td>
</tr>
<tr>
<td>% Female participants (n)</td>
<td>48.9 (248)</td>
<td>45.2 (128)</td>
<td>53.8 (77)</td>
<td>55.2 (176)</td>
<td>50.2 (629)</td>
<td>H(3) = 7.04, p = .07</td>
<td>–</td>
</tr>
<tr>
<td>Age (M, SD)</td>
<td>9.4 (1.7)</td>
<td>9.5 (1.6)</td>
<td>9.4 (1.6)</td>
<td>9.0 (1.7)</td>
<td>9.3 (1.7)</td>
<td>F(3) = 4.9, p = .002</td>
<td>GAD, SoAD, SP &gt; SAD</td>
</tr>
<tr>
<td>CSR severity at baseline (M, SD)</td>
<td>6.2 (9.4)</td>
<td>6.1 (1.0)</td>
<td>6.4 (1.1)</td>
<td>6.3 (1.0)</td>
<td>6.1 (1.0)</td>
<td>F(3) = 2.4, p = .17</td>
<td>–</td>
</tr>
<tr>
<td>% Comorbid externalising disorder (n)</td>
<td>21.8 (107)</td>
<td>21.1 (53)</td>
<td>8.4 (19)</td>
<td>20.8 (47)</td>
<td>19.4 (226)</td>
<td>H(3) = 7.04, p = .07</td>
<td>–</td>
</tr>
<tr>
<td>% Comorbid internalising disordera (n)</td>
<td>10.6 (52)</td>
<td>13.6 (34)</td>
<td>3.5 (5)</td>
<td>6.7 (19)</td>
<td>9.4 (110)</td>
<td>H(3) = 14.1, p = .003</td>
<td>SoAD &gt; SP, SAD</td>
</tr>
<tr>
<td>% CBT treatment (n)</td>
<td>Individual (n)</td>
<td>15.3 (78)</td>
<td>29.3 (83)</td>
<td>32.2 (46)</td>
<td>42.0 (134)</td>
<td>27.2 (341)</td>
<td>H(3) = 73.6, p &lt; .001</td>
</tr>
<tr>
<td></td>
<td>Group (n)</td>
<td>65.7 (333)</td>
<td>50.2 (142)</td>
<td>41.3 (59)</td>
<td>37.0 (118)</td>
<td>52.1 (652)</td>
<td>H(3) = 73.1, p &lt; .001</td>
</tr>
<tr>
<td></td>
<td>Parent-led (n)</td>
<td>19.1 (97)</td>
<td>20.5 (58)</td>
<td>26.6 (38)</td>
<td>21.0 (67)</td>
<td>20.8 (260)</td>
<td>H(3) = 14.1, p = .28</td>
</tr>
</tbody>
</table>

GAD, generalised anxiety disorder; SoAD, social anxiety disorder; SP, specific phobia; SAD, separation anxiety disorder; CSR, Clinician severity rating score.

*aComorbid internalising problem refers to a nonanxious internalising disorder.
(27.2%; n = 341) and then guided parent-led CBT (20.8%; n = 260). The proportion of cases at each site within each treatment format for each primary diagnostic category is reported in Table S1.

Average CSR severity scores ranged from 6.1 (SD = 1.0) to 6.4 (SD = 1.1) across categories. The proportions of females in the four groups ranged from 45.2% in primary SoAD to 55.2% in children with primary SAD. The mean age of children across diagnostic categories ranged from 9.0 years in the SAD group to 9.5 years in the SoAD group. Of note, children with primary SPs were the least likely to have a comorbid nonanxiety internalising problem (3.5%) and externalising problem (8.4%). In contrast, rates of comorbid externalising problems were highest in the GAD group (21.8%) and rates of comorbid nonanxiety internalising problems were highest in the SoAD group (13.6%).

Changes in clinical severity and remission rates for CBT treatment in the full sample

As reported previously (Hudson et al., 2015), there was a significant reduction in clinical severity scores (i.e. CSR scores; p < .001) during the study period (Table S2). Children with a primary SoAD (p < .001) diagnosis had significantly smaller reductions in clinical severity during the study period relative to GAD (p < .001), SP (p = .001), and SAD (p < .001). Reductions in clinical severity were comparable for GAD, SP and SAD (Table S2). Similarly, for the full sample there were improvements in remission rates (p < .001) during the study period (Table S2). Children with a primary SoAD (p < .001) diagnosis were also less likely to lose their diagnosis relative to GAD (p = .001), SP (p = .003) and SAD (p < .001).

Improvements in remission rates were comparable for GAD, SP and SAD.

Change in symptom level and remission rates for CBT treatment formats across primary anxiety disorder categories

Table 2 summarises the results of linear mixed models evaluating changes in CSR scores over treatment formats for the four diagnostic categories. Treatment format did not have a significant effect on changes in clinical severity for those with a primary diagnosis of GAD, SoAD or SAD. These findings were replicated in supplementary analyses carried out on response data when postintervention (Tables S4a and S4b) and follow-up (Tables S5a and S5b) data were considered separately.

However, treatment format was significantly associated with outcomes for children with SP. Individual CBT was associated with significantly larger improvements in clinical severity than both group CBT (p < .001) and guided parent-led CBT (p < .001). Figure 1 shows the change in CSR scores for children with a primary SP over the three assessment time points in each of these treatment formats. These results suggest a 1.58-point greater reduction in CSR scores for individual CBT over group CBT and a 1.54-point greater reduction in CSR scores for individual CBT in comparison to guided parent-led CBT.

This result remained when outcomes were limited to the post-treatment time point (Table S4a). At follow-up, individual CBT was no longer more effective than guided parent-led CBT (p = .17) or group CBT (p = .007) once Bonferroni corrections were employed. This provides some evidence that the significant advantage of individual CBT over both

<table>
<thead>
<tr>
<th>Group</th>
<th>Severity of primary diagnosis at baseline&lt;sup&gt;a&lt;/sup&gt;</th>
<th>CBT treatment</th>
<th>CBT treatment format</th>
<th>GAD</th>
<th>SoAD</th>
<th>SP</th>
<th>SAD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Age</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Gender</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

GAD, generalised anxiety disorder; SoAD, social anxiety disorder; SP, specific phobia; SAD, separation anxiety disorder; CBT, cognitive behaviour therapy.

<sup>a</sup>Standardised regression coefficients (β) significantly different than zero indicate association with clinical severity after treatment.

<sup>b</sup>Reference category.

<sup>c</sup>Standardised regression coefficients (β) significantly different than zero indicate higher (negative value) or lower (positive value) changes in clinical severity compared to the reference category.
CBT treatment reduces at follow-up, although this finding should be interpreted cautiously in light of the smaller sample size at the follow-up analysis.

A similar pattern of results was observed in the analysis of remission. Table 3 summarises the results of logistic mixed models examining remission rates over the three treatment formats within each psychiatric condition. The mean severity scores of the three treatment formats within each psychiatrist condition are presented in Table S3. Treatment format did not have a significant effect on improvements in remission for GAD, SoAD and SAD. In contrast, children with a primary SP who received individual CBT were significantly more likely to lose their SP diagnosis compared to children in guided parent-led CBT (p = .005). There were no significant differences in remission rates for individual CBT and group CBT (p = .04) after correction for multiple testing. This finding was replicated in the supplementary analysis carried out on the postintervention data (Table S4b). There were no significant differences in remission rates between individual CBT, group CBT and guided parent-led CBT for SP when the follow-up data were analysed separately (Table S5b).

To determine whether there was a diagnosis (SP vs. Other Anxiety Disorders) by treatment format (Individual CBT vs. Other CBT treatments) interaction on clinical severity, variables were dummy coded and then entered as covariates in the regression model. Preliminary analysis of baseline differences between SP and Other Anxiety Disorders groups showed there were no differences with respect to baseline CSR scores, age, gender or presence of a comorbid externalising problems (p > .05). Children in the SP group were less likely than children in the other categories to have a comorbid nonanxious internalising problem (χ² (1) = 6.59 p = .01), however, this variable was not controlled for in the analysis as a high correlation of anxiety and mood problems in youth is expected, and partialling out this variable may remove an important element of the anxiety construct of interest. The statistical interaction between diagnosis (SP vs. Other Anxiety Disorders) and treatment format (Individual CBT vs. Other CBT treatments) on CSR scores was significant (p = .003; based on a threshold of p < .05). Figure 2 summarises this interaction. Individual CBT was more effective than the other treatments for children with primary SP (β = .63; CI95: [0.35, 0.89]; p < .001). In contrast, individual CBT was no more effective than other treatment formats for children with other primary anxiety disorders (β = −.04; CI95: [−0.24, 0.16]; p = .71). Post-hoc analyses also suggested this result was not an artefact of biases in treatment allocation. Children with a primary SP were no more likely to receive individual CBT compared to any other sort of treatment (β = .33; CI95: [−0.02, 0.68];

Table 3 Results of logistic mixed models examining the relationship between primary diagnosis and treatment format on change in diagnostic frequency (remission) using all follow-up points

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>OR (SE)</th>
<th>95% CI</th>
<th>OR (SE)</th>
<th>95% CI</th>
<th>OR (SE)</th>
<th>95% CI</th>
<th>OR (SE)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAD</td>
<td></td>
<td></td>
<td>SoAD</td>
<td></td>
<td>SP</td>
<td></td>
<td>SAD</td>
<td></td>
</tr>
<tr>
<td>Severity</td>
<td>0.75 (0.13)</td>
<td>[0.52, 1.0]</td>
<td>0.45* (0.09)</td>
<td>[0.30, 0.68]</td>
<td>0.70 (0.22)</td>
<td>[0.38, 1.3]</td>
<td>0.35* (0.19)</td>
<td>[0.21, 0.61]</td>
</tr>
<tr>
<td>of primary diagnosis at baseline*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBT treatment</td>
<td>Individual</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group-basedc</td>
<td>0.75 (0.61)</td>
<td>[0.15, 30.7]</td>
<td>0.64 (0.46)</td>
<td>[0.16, 20.6]</td>
<td>0.15 (0.15)</td>
<td>[0.02, 10.0]</td>
<td>0.47 (0.42)</td>
<td>[0.08, 20.7]</td>
</tr>
<tr>
<td>Guided parent-ledc</td>
<td>10.4 (10.4)</td>
<td>[0.20, 90.5]</td>
<td>0.70 (0.65)</td>
<td>[0.11, 40.3]</td>
<td>0.05* (0.05)</td>
<td>[0.01, 0.32]</td>
<td>0.08 (0.09)</td>
<td>[0.01, 0.69]</td>
</tr>
<tr>
<td>Age</td>
<td>10.0 (10.0)</td>
<td>[0.88, 10.2]</td>
<td>0.94 (0.11)</td>
<td>[0.74, 10.2]</td>
<td>0.87 (0.16)</td>
<td>[0.60, 10.3]</td>
<td>10.0 (10.0)</td>
<td>[0.77, 10.4]</td>
</tr>
<tr>
<td>Gender</td>
<td>0.66 (0.19)</td>
<td>[0.37, 10.2]</td>
<td>0.82 (0.29)</td>
<td>[0.41, 10.6]</td>
<td>10.7 (0.97)</td>
<td>[0.54, 50.2]</td>
<td>0.43 (0.20)</td>
<td>[0.17, 10.1]</td>
</tr>
</tbody>
</table>

GAD, generalised anxiety disorder; SoAD, social anxiety disorder; SP, specific phobia; SAD, separation anxiety disorder; CBT, cognitive behaviour therapy.

*Odds ratios of variables predicting a higher likelihood of remission are significantly greater than one, whereas variables predicting a lower likelihood of remission have odds ratios of significantly <1.

†Reference category.

‡Odds ratios of variables predicting a higher likelihood of remission relative to the reference category are greater than one, whereas variables predicting a lower likelihood of remission relative to the reference category have odds ratios of <1.

p < .006.

© 2018 The Authors. Journal of Child Psychology and Psychiatry published by John Wiley & Sons Ltd on behalf of Association for Child and Adolescent Mental Health.
The same pattern of significant and non-significant comparisons was replicated when remission rates were investigated.

**Discussion**

In the present study, we evaluated the treatment responses associated with individual CBT, group CBT and guided parent-led CBT in a pooled sample of children with a primary anxiety disorder diagnosis. Our results indicated there were no differences across the three treatment formats for children with primary SoAD, GAD or SAD. However, individual CBT was better than guided parent-led CBT for SP in terms of both improvement in symptoms and remission rates. Individual CBT also performed better than group CBT for SP in the clinical severity change analysis, but not in the remission analysis (after correction for multiple testing). The interaction between diagnosis (SP vs. Other anxiety disorders) and treatment format (Individual CBT vs. Other CBT treatments) on changes in clinical severity was significant, with the analyses suggesting this was not due to baseline severity of symptoms, site differences, or biases in treatment allocation.

The inability to replicate the significant differences between individual and group CBT for SP in the remission model could be explained by the fact that remission outcomes rely on cutoffs and are less well powered. Our approach of applying Bonferroni corrections to control for multiple comparisons may have been overly restrictive. This finding is also at odds with the Manassis et al. (2002) study, which was limited by its small sample size. Whilst the result found here was obtained in a large sample that used a clinician-rated measure, it is also important to acknowledge that our pooled analysis did not have the same tight experimental controls as a single RCT. In the present study, the statistics performed on the primary outcome of interest are based on pooled data from postintervention and follow-up measures time points (3, 6 and 12 months), meaning that the time point at which the significant effects took place in this study is less clear than in the Manassis et al. (2002) study. The difference between individual and group for SP was observed when examining postdata separately but not follow-up data. These differences also offer potential explanations for the discrepant results across the two studies.

Our results suggest that children with SPs can improve in parent-led, group and individual CBT, but they do significantly better in individual CBT. It was particularly noteworthy that although SP tends to be considered less pervasive and more amenable to treatment, individual CBT produced better outcomes than either group CBT or guided parent-led approaches. Children present with a range of SP’s in clinical settings. In individual CBT, therapists tailor protocols by providing specific psychoeducation surrounding the fear (e.g. education about dog safety) as well as in-session-guided exposure to feared situations, and training parents to be efficacious in guiding their child through the exposure process. In group CBT and guided parent-led CBT, such specificity to target avoidance behaviours may not be possible, and this explanation may account for the superiority of individual CBT here. The data here show a stronger clinical benefit is associated with the allocation of children with SPs to individual CBT. However, decisions regarding the allocation of children to a treatment format are complex, and influenced by multiple factors including pragmatic concerns (e.g. ability of parents to bring child to appointments, demand for service, waiting lists etc.), patient preferences and therapist preferences. Furthermore, an analysis of the cost-effectiveness of individual CBT for SP relative to the other treatment formats is needed, given the additional resources required per patient to deliver individual CBT.

These results are consistent with previous studies showing individual CBT and group CBT are comparable for GAD (Manassis et al., 2002), SoAD (Wergeland et al., 2014) and SAD (Wergeland et al., 2014). Our findings are at odds with other studies that found outcomes with individual CBT to be better than those with group CBT for children with GAD.
Finally, a study to assess these questions among cognitive and biological processes that could be driving these disorders. These studies should also measure important cognitive and biological processes that could be driving differential responses to CBT treatment formats. Finally, a study to assess these questions among adolescents is needed. This is the first study to compare outcomes from guided parent-led CBT, group CBT and individual CBT among children with four primary anxiety disorder diagnoses. Individual CBT was superior to group CBT and guided parent-led CBT for children with a primary SP. With variable CBT programs being delivered in the community, further research is needed to understand the optimal conditions for allocating anxious children to different forms of CBT.

Supporting information
Additional Supporting Information may be found in the online version of this article:
Appendix S1. References to individual trials and a description of methods.
Table S1. Percentage of cases per site for treatment formats within diagnostic categories.
Table S2. Results of linear and logistic mixed models examining the relationship between primary diagnosis and treatment format in the full sample using all follow-up points.
Table S3. Means (standard errors) of the relationship between primary diagnosis and treatment format on severity scores (CSR) at pre, post and follow-up.
Table S4a. Results of linear mixed models examining the relationship between primary diagnosis and treatment format on severity scores (CSR) using the post time point only.
Table S4b. Results of logistic mixed models examining the relationship between primary diagnosis and treatment format on severity scores (CSR) using the post time point only.
Table S5a. Results of linear mixed models examining the relationship between primary diagnosis and treatment format on severity scores (CSR) using the post time point only.
Table S5b. Results of logistic mixed models examining the relationship between primary diagnosis and treatment format on severity scores (CSR) using the follow-up time point only.
Figure S1. Mean clinician severity rating (CSR) scores over time across individual CBT, group CBT and parent-led CBT for children with GAD, SAD, SoAD.

Acknowledgements
Aarhus: TrygFonden grant 7-10-1391 (MT and Hougaard*) and Edith og Godtfred Kirk Christiansens Fond grant 21-5675 (MT); Basel: Swiss National Science Foundation grant 105314-116517 (SS); Western Norway: Regional Health Authority grants 911253 (Odd E. Havik*) and 911366 (Einar R. Heiervang*); Cambridge: UK MRC Clinician Scientist Fellowship G0802821 (RM-S); Florida: National Institute of Mental Health R01MH079943 (WKS); London: UK MRC grants G0901874/1 (TCE) and MR/J011762/1 (TCE & KJL); Reading: UK MRC grants 09-800-17 (PC and CC), G0802326 (KT, PC and CC), and G0601874 (CC), and; Sydney: Australian Research Council grant DP0878609 (JLH, RMR and TCE); Australian National Health and Medical Research Council grants 1027556 (RMR, JLH, HJL and Cathy Mihalopolous*), 488505 (HJL, JLH and RMR) and 382008 (JLH and RMR).
This study presents independent research partly funded by the NIHR. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

RK served as the statistical expert for this research. The authors thank the following for their contributions: Aarhus: Marianne Bjerregaard Madsen, Hjalti Jonsson, and Lisbeth Jorgensen; Amsterdam: Nynke Wagenaar; Basel: Carmen Adornetto, Judith Meunier-Blatter, Chantal Herren; Bergen: Einar R. Heiervang, Kristine Fonnes Griffin and Odd E. Havik; Bochum: Elisa Kulewski, Jonas Großekathöfer, Nora Dirks, Evelyn Kmelnitski, Sabrina Heuser, Katrin Hötzel and Karen Krause; Cambridge: Adrian Boyle, Clare Dixon and Tim Dalgleish; Florida: Luci Motoca, Yesenia Rodriguez, Klaudia Perreira, Erin Hedemann and Carla Marin; Groningen: Harma Moorlag, Nienke Boersma and Sanne M. Hogendoorn; Oxford and Reading: Francoise Hentges and Liz White; Reading: Sue Cruddace, Marie Weber, Zoe Hughes and Kiri Clarke; Sydney: Irma Knuistingh Neven, Talia Morris and Sophie C. Schneider.

JLH is an author of the Cool Kids program but receives no direct payment from it. CC is joint author of a book used in treatment within the Overcoming trial and receives royalties from sales of the book. HJL is an author of the Cool Kids program but receives no direct payment from it. RMR is an author of the Cool Kids program but receives no direct payment from it. SS is an author of the Diagnostisches Interview bei psychischen Störungen im Kindes- und Jugendalter from which she receives royalties. WKS is an author of the Anxiety Disorders Interview Schedule for Children from which she received royalties. MHN is an author of the Dutch version of the Coping Cat manual and receives no direct payment from it. Silvia Schneider and Kristen Lavallee are joint authors of a book based on the TAFF treatment used in their trial and they receive royalties from sales of the book. PS is joint author of a book used in treatment within the ASPECTS trial, and receives royalties from sales of the book. AM, RK, JRIC, KJL, SR, KA, CAH, KWF, TI-A, RM-S, YR, KT, and GJW, and SB, PC, WKS, MT and TCE have declared that they have no competing or potential conflicts of interest.

Some authors have changed institutions since carrying out their trials. Prof Schneider and Dr Lavallee carried out their trial at the Department of Psychology, University of Basel. Dr Meiser-Stedman carried out the ASPECTS trial at the Medical Research Council Cognition & Brain Sciences Unit, University of Cambridge. Prof Silverman and Dr. Rey carried out their trial at the Department of Psychology, Florida International University. Dr Keers and Dr Lester were based at the SDGP during coordination of the Genes for Treatment Study. *Was involved as lead investigators for the grant funding used to collect the data.

Correspondence
Jennie L. Hudson, Centre for Emotional Health, Department of Psychology, Macquarie University, NSW 2109, Australia.; Email: jennie.hudson@mq.edu.au; Thalia C. Eley, SGDP Centre, Institute of Psychiatry, Psychology and Neuroscience, King’s College London, De’Crespigny Park, London SE5 8AF, UK; Email: thalia.eley@kcl.ac.uk

Key points

- The impact of CBT treatment format on response to treatment was investigated in a sample of children with a primary GAD, SAD, SP and SoAD.
- In children with a primary GAD, SAD or SoAD, there were no differences between individual CBT, group CBT and guided parent-led CBT.
- In children with a primary SP, individual CBT led to greater reductions in clinical severity and higher remission rates than guided parent-led CBT.
- In children with a primary SP, individual CBT led to greater reductions in the clinical severity of primary problems than group CBT.
- Allocation of children with SPs to individual CBT may have a stronger clinical benefit than allocation to group or guided parent-led CBT.
- For children with GAD, SoAD and SAD decisions about treatment format can incorporate cost considerations and patient choice.

Notes

1. The primary problem is the disorder deemed by the clinician to be the most impairing of all the child’s psychiatric diagnoses. This judgement is made by consideration of symptom severity, avoidance, and interference with core aspects of functioning for each psychiatric diagnosis.

2. In this study, ‘family parental CBT’ was defined as treatment with the direct involvement of parents. In some instances, the whole family was involved, in others the parents were present for conjoint or separate sessions, and sometimes the parents were cotherapists.

3. Please note, whilst there were some cases taking part in computer/internet CBT and some children
with additional primary disorders (e.g. obsessive compulsive disorder, posttraumatic stress disorder, etc.) within the Genes for Treatment dataset, these occurred with low frequency in the dataset and were hence excluded from the analysis. Additionally, all adolescents were excluded from the dataset as there were no adolescents that took part in parent-led CBT.

References


