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A brief psychological intervention for mothers of children with food allergy can change risk perception and reduce anxiety: outcomes of a randomised controlled trial

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Abstract

Background: Mothers of children with food allergy have increased anxiety, which may be influenced by healthcare professionals' communication of risk.

Objective: To evaluate a brief psychological intervention for reducing anxiety in mothers of children with food allergy.

Methods: Two hundred mothers of children with food allergy were recruited from allergy clinics. A computer-generated randomization list was used to allocate participants to a single-session Cognitive Behavioural Therapy intervention including a risk communication module, or standard care. Anxiety and risk perception were assessed at 6 weeks and 1 year. Primary outcome was state anxiety at 6 weeks. Secondary outcomes included state anxiety at 1 year, risk perception at 6 weeks and 1 year, and salivary cortisol response to a simulated anaphylaxis scenario at 1 year.

Results: We found no significant difference in the primary outcome state anxiety at 6 weeks, with mean 31.9 (sd 10.2) intervention, 34.0 (10.2) control; mean difference 2.1 (95%CI -0.9, 5.0; P=0.17). There was significantly reduced state anxiety at 6 weeks in the intervention group, in the subgroup of participants with moderate/high anxiety at enrolment (103/200, 52%), with mean 33.0 (sd 9.3) intervention, 37.8 (sd 10.0) control; mean difference 4.8 (95% CI 0.9, 8.7; P=0.016; Cohen's d effect size

0.50). The psychological intervention also reduced risk perception and salivary cortisol response ($P=0.032$; effect size 0.36).

Conclusion: We found evidence that a brief psychological intervention which incorporates accurate risk information may impact on anxiety, risk perception and physiological stress response in mothers of children with food allergy.

Key Words

Anxiety; food allergy; cognitive behavioural therapy; risk perception; stress response

INTRODUCTION

Food allergy is estimated to affect 6-7% of children and 1-2% of adults and may be increasing in prevalence (1). Current management is based on avoidance of allergenic foods and prompt administration of treatment for allergic reactions (2). Due to its unpredictable and potentially life-threatening nature, food allergy can provoke feelings of anxiety and stress for both sufferers and their caregivers. The dietary and social restrictions which accompany food allergy may result in children with food allergy and their parents feeling socially isolated (3). Previous studies have suggested that children with food allergy and their mothers suffer increased anxiety and stress compared with other groups (4-6). We recently found that community healthcare professionals significantly overestimate the risk of fatal anaphylaxis for children with food allergy, which may contribute to feelings of anxiety (7). Allergic comorbidities such as asthma are often present in those with food allergy, and these can also be associated with anxiety in affected children and their caregivers (8, 9). While oral and epicutaneous immunotherapy show promise as treatments to reduce immunological sensitivity in people with food allergy, there is a need for treatments

which effectively address the psychological and emotional burden of the disease. We recently developed a brief Cognitive Behavioural Therapy (CBT) intervention which includes an element of risk communication, for mothers of children with food allergy (10). The possibility that a single-session CBT intervention may reduce anxiety is supported by a recent meta-analysis of single-session interventions for young people with mental health problems, although long-term effects are unclear (11). In this manuscript we report outcomes of the first prospective randomized controlled trial of a brief CBT intervention in mothers of children with food allergy, designed to evaluate whether it can influence maternal state anxiety.

METHODS

Study design

We conducted a two-by-two factorial randomized controlled trial, on the effect of a psychological intervention on measures of maternal anxiety at 6 weeks (primary outcome) and one year after treatment, in mothers of children with food allergy (ISRCTN12504076). We simultaneously evaluated the effect of adrenaline autoinjector (AAI) device design on participants' ability to administer adrenaline in a simulated anaphylaxis scenario, and those results have been reported separately (12). There was no interaction between the AAI training intervention and the CBT intervention for the study outcomes, and no effect of AAI treatment arm on these study outcomes.

Participants

Mothers of children aged 0-18, diagnosed with food allergy by a paediatric allergist, who were deemed to need an AAI for the first time as part of their food allergy management, were eligible for inclusion. Exclusion criteria were inability to converse fluently in English or with a translator, child weight under 7.5 kg (a contraindication to AAI prescription), prior training in the use of an AAI device, and significant psychiatric problems such as current treatment for psychosis, that might be a contraindication to CBT.

Study setting

Participants were recruited from a large specialist paediatric allergy centre in an urban setting in London, UK between March 2011 and December 2012. Researchers invited eligible mothers to take part in the study, and written informed consent was obtained prior to participation in any study procedures. The study was approved by the West London Research Ethics Committee (10/H0711/76).

Randomization, treatment allocation and masking

Treatment was allocated using a computer-generated randomization list in blocks of 4, stratified by maternal State Trait Anxiety Inventory (STAI) score, generated by a statistician independent of the study team (Imperial College London Statistical Advisory Service). The randomization list was held by a clinical trials pharmacist - researchers notified the pharmacist after enrolling a participant in the trial, and the pharmacist allocated treatment based on the randomization list. It was not possible

to blind clinicians, participants or outcome assessors to treatment allocation in this trial. The primary outcome measure was a patient reported measure, state anxiety on the STAI (STAI-S), which has been used extensively in similar settings. Due to the possibility of ascertainment bias in an unblinded trial, we also evaluated objective measures of stress response using salivary samples, which were analysed by laboratory staff blind to treatment allocation.

Intervention

Participants were randomized to receive either a single session of CBT, with reinforcement of CBT at a phone call 2 weeks later and a visit 6 weeks later, or no intervention. The CBT intervention was modified from existing single sessions used to treat fears and phobias (13). The CBT intervention consisted of psychoeducation, including both the risk of living with high anxiety and the risk of fatal anaphylaxis for a child with food allergy, a cognitive component (coping thoughts), and a behavioural component (relaxation technique). The initial intervention was designed to be delivered within 45 minutes, and the reinforcement at 2 weeks and 6 weeks within 15 minutes. Figures S1 A-F were used to communicate the specific information about risk of fatal anaphylaxis in the child, with estimated fatal food anaphylaxis risks of $10^{-6.0}$ for a child with food allergy aged under 5, $10^{-5.4}$ at age 5-9 years, and $10^{-5.2}$ for a young person aged 10-19. These estimates were based on our previous work (14, 15). No specific information was given about risk of non-fatal anaphylaxis or all-cause fatality. The control group received standard care with no CBT intervention. The development of the CBT intervention is described elsewhere, and the Manual for therapists is available in the Supplementary Material (10). Briefly, therapists were

trained over 3 half-day taught sessions, and provided with a training video and manual. They received weekly 2-hour supervision sessions for 4 months, then fortnightly 2-hour supervision sessions for 8 months. Supervision was structured to build skills and to model guided discovery for therapists. The supervisor was a Consultant Child Psychiatrist with a post-graduate diploma in CBT, and 10 years' experience of delivering and teaching CBT. Therapists had no prior experience or training in CBT. One therapist was a paediatrician in training (UT), two were registered nurses (KP, HH) and one was a newly-qualified psychologist (CP). The quality of delivered CBT was assessed using audiotapes CBT sessions as previously described (10). In brief, BV used the Revised Cognitive Therapy Scale (CTS-R) to rate audio tapes, and a sample was rated by an independent assessor as a reliability check.

Outcome measures

Participants were assessed at enrolment, 6 weeks after enrolment, and at 12 months. These timepoints were chosen for practical reasons, because they sometimes coincided with clinical assessments for the study participants. All 6 week outcome measures were recorded prior to the CBT reinforcement at the 6 week visit. The primary outcome measure was STAI-S score 6 weeks after enrolment. STAI is a self-evaluation questionnaire designed to assess the degree of state and trait anxiety in adults. State anxiety (STAI-S) is a transitional emotional state which refers to the feelings the patient is currently experiencing. Trait anxiety (STAI-T) is a preset level of anxiety which alludes to an individual's tendency to become anxious. STAI-S can be categorized as low (20-34), moderate (35-49) and high (50-80) anxiety.

Secondary outcomes included maternal STAI-S at 12 months, STAI-T at 6 weeks and 12 months, Perceived Stress Scale (PSS) score at 6 weeks and 12 months, Behaviour Check List (BCL), Strengths and Difficulties questionnaire (SDQ), Screen for Child Anxiety Related Emotional Disorders (SCARED), Food Allergy Impact Scale (FAIS), Food Allergy Quality of Life Questionnaire (FAQLQ) and maternal risk perception at 6 weeks and 12 months; and maternal change in salivary cortisol and alpha amylase levels following a simulated anaphylaxis scenario, at 12 months. Maternal risk perception was assessed using a Risk Ladder, developed using data from public databases and previous systematic reviews undertaken by our group (14, 15). The Risk Ladder and comparator risks used are shown in Figures S2-4. Full details of the outcome assessment methods are described in the Supplementary Material.

Sample size

Prior work showed that mothers of children with food allergy have increased STAI-S (mean 39.0, SD 12.0; control mean 32.8, SD 8.3) and 'perceived stress' (mean 25.1, SD 6.7; control mean 19.6, SD 7.5) scores compared with a control population (4). Randomising 86 participants to intervention and 86 to standard care gives 80% power at 5% 2-sided significance to detect a difference in STAI-S from 39.0 to 34.4 with SD 10. This number of participants gives the same power to detect a difference in PSS of 25.1 versus 21.9 with SD 7. We aimed to recruit 200 participants in order to allow for loss to follow up. We did not evaluate for a minimal clinically important difference in STAI-S, since a minimal clinically important difference has not been

established for mothers of children with food allergy or other chronic health conditions.

Statistical methods

For binary comparisons we used chi-squared test, or Fisher's exact test; for continuous data we used independent-group *t*-tests with effect sizes computed as Cohen's *d* (16). Where one or more data distributions deviated markedly from normal (i.e., skewness and/or kurtosis value(s) > 1), bootstrapping (bias-corrected and accelerated; based on 2000 bootstrap samples) was employed to estimate 95% confidence intervals (CI) around mean difference. Within-group changes were assessed using paired-sample *t*-tests with bootstrapping applied where distributions deviated markedly from normal. In the case of salivary markers (cortisol, amylase), where distributions of values were severely kurtotic and/or (positively) skewed at time-points, values were transformed using Box-Cox methods (17) to better approximate a normal distribution and then *t*-tests and (for adjusted analyses) analysis of covariance were used. All primary analyses used group assignment as randomized, whether or not treatment was received, and were on an available case basis without imputation for missing outcome data. One planned subgroup analysis and two *post hoc* subgroup analyses were undertaken to evaluate the effect of the intervention in specific groups – the planned analysis was for participants with moderate-to-high anxiety at baseline, defined as STAI-S ≥ 35 . *Post hoc* analyses were for participants who received 'good quality CBT'; and for participants with accurate fatal anaphylaxis risk estimates post-intervention. 'Good quality CBT' was defined as a mean item score ≥ 3 on the CTS-R for those participants with a

recorded therapy session - 46 sessions were recorded, of which 31 (67%) had a CTS-R score ≥ 3 ; effective risk information was defined as an estimated 'risk of fatal anaphylaxis' VAS at 6 weeks within 1 log of the true fatal anaphylaxis risk for their child – 33 of 91 (34%) participants in the intervention group who completed the VAS at 6 weeks met this criterion. To control for the possibility of false-positives because of multiple outcome testing, the false discovery rate approach was applied to each set of comparisons concerning participant-reported outcomes other than the primary outcome, with control set to 5% (18). All statistical analyses used SPSS v22.0 (IBM, Armonk, NY, USA).

RESULTS

We enrolled and randomized 200 participants between 8th March 2011 and 10th December 2012. Participant flow is shown in Figure 1. Overall 182 (91%) participants were assessed for the primary outcome at six weeks; 165 (83%) at one year. Characteristics of study participants at enrolment are shown in Table 1. Fifty-three per cent of participants had a university degree, 59% were of non-white ethnicity, 10% had a previous mental health problem. The index child was mean 4 years old, allergic to a mean 2.8 foods, 76% had eczema, 22% had asthma, and 31% had a history of anaphylaxis. Baseline maternal STAI-S was mean 36.3, similar to our previous study of mothers of children with food allergy (5). The randomized groups were similar at baseline, and had a similar number of stressful life events during the one year follow up (mean 1.13 intervention, 1.22 control $P=0.64$).

Effect of the psychological intervention on maternal anxiety, stress and risk perception

The primary outcome STAI-S did not differ between groups at six weeks but was significantly reduced in the intervention group at one year, with mean difference 3.5 points (95% CI 0.3, 6.7; $d=0.33$) (Table 2). When analysed as within group changes, we found a significant decrease in STAI-S at 6 weeks in both groups - intervention mean difference 4.4 (1.6, 7.3; $P=0.003$; $d=0.42$), control mean difference 3.2 (0.7, 5.6; $P=0.013$; $d=0.26$). At 1 year the within group change in STAI-S was only significant in the intervention group – intervention mean difference 5.0 (2.2, 7.8; $P<0.001$; $d=0.44$), control mean difference 2.2 (-1.0, 5.4; $P=0.17$). There was no significant difference between groups in STAI-T, PSS or FAQLQ at either time point, but there was weak evidence for reduced FAIS at 6 weeks (and not at 1 year). When we assessed specific domains of the FAIS at 6 weeks, there was a significant reduction in meal preparation (mean difference 0.67 95% CI 0.08, 1.27; $P=0.029$; $d=0.31$) and parental stress (mean difference 0.51 95% CI 0.05, 1.00; $P=0.042$; $d=0.29$) domains, but no significant difference in other domains of FAIS. We found clear evidence that the risk communication component of the intervention resulted in lasting changes to participant risk perception. The active intervention group estimated anaphylaxis and fatal anaphylaxis as less likely than the control group at 6 weeks, by mean 13.5-fold (mean difference on $\log_{10}$ scale was -1.13 95%CI -1.77, -0.49; $d=0.52$) and 11.0-fold (mean difference on $\log_{10}$ scale was -1.04 95%CI -1.70, -0.37; $d=0.46$) respectively. This difference was still present at one year, but at this timepoint the active intervention group also estimated all-cause fatality as less likely than the control group, and the differences in risk perception for fatal outcomes at one year were not significant after adjustment for false discovery.

Effect of the psychological intervention in specific subgroups of participating mothers

We analysed the same outcomes in those participants with moderate/high STAI-S (≥ 35) at enrolment (Table 3). This analysis showed a significant reduction in the primary outcome STAI-S at 6 weeks with mean difference 4.8 (0.9, 8.7; $P=0.016$; $d=0.50$), but not at 1 year; and a significant reduction in STAI-T at 1 year (but not 6 weeks) – with mean difference 4.5 (0.2, 8.7; $P=0.038$; $d=0.43$). Other measures of maternal anxiety, stress, quality of life or food allergy impact were not significantly different in the intervention group at either time-point, and risk perception differed significantly at 1 year, but not at 6 weeks. The differences in STAI-T and risk perception for fatal outcomes at one year were not significant after adjustment for false discovery. We conducted *post hoc* analyses to assess whether participants who received higher quality CBT, or who showed evidence of accurately recalling the risk perception information at 6 weeks, had different outcomes to the total population. The results of these analyses are shown in the Supplementary Material (Tables S1-3). Analysis of participants who received higher quality CBT showed no significant difference in measures of maternal anxiety, stress, quality of life or food allergy impact (Table S1), and there was no significant relationship between CTS-R score or CBT session duration, and change in maternal anxiety or stress at 6 weeks or 1 year (Table S2). Analysis of participants who accurately recalled risk perception information at 6 weeks showed significantly reduced STAI-S at 1 year, but not at 6 weeks, with mean difference 5.3 (1.0, 9.4; $P=0.013$ $d=0.58$) at 1 year. Maternal perceived stress was also reduced at 1 year, but not at 6 weeks, with mean difference 3.0 points (0.1, 6.0; $P=0.047$; $d=0.44$; Table S3), although this was not significant after adjustment for false discovery.

Effect of the psychological intervention on maternal report of child adjustment and anxiety

Maternally reported child outcomes are shown in Table S4. Analyses were limited by small numbers available for any single outcome measure, due to heterogeneity in the instruments available for children of different ages. There was no evidence that the psychological intervention affected child adjustment at 6 weeks, or child adjustment or anxiety at 1 year.

Effect of the psychological intervention on maternal salivary stress response

Valid salivary cortisol and α -amylase response data at more than one time point were available from 120 participants (intervention $n = 56$, control $n = 64$). Summary findings are shown in Figure 2A and 2B, and Table S5. Salivary cortisol was significantly increased at 30 minutes post anaphylaxis scenario in the control group ($d=0.26$), but not in the intervention group, and the rise in the control group was significantly greater than in the intervention group ($P=0.054$ unadjusted; $d=0.36$; $P=0.032$ when adjusted for successful adrenaline administration in anaphylaxis scenario). Salivary cortisol levels at earlier time-points did not differ significantly from pre-scenario, although there was weak evidence for raised cortisol in the control group (but not the intervention group) at 20 minutes post anaphylaxis scenario. Salivary α -amylase was significantly raised at all time-points in the control group ($d=0.28$, 0.21 , and 0.26 for 10, 20 and 30 minute time-points, respectively), but only at 10 minutes post anaphylaxis scenario in the intervention group ($d=0.27$) – differences between intervention and control group salivary α -amylase responses were not statistically significant at any time-point. In 49 participants paired salivary

cortisol/ α -amylase measurements were available from 24 hours (+/- 1 hour) prior to the anaphylaxis scenario and just prior to anaphylaxis scenario. Analysis of these samples showed a significant increase in salivary cortisol prior to the anaphylaxis scenario in both groups - mean change 1.64 nmol/l (0.05, 3.19; d=0.31) intervention; 2.43 (0.46, 4.67; d=0.51) control with no significant difference between groups in this change (P = 0.86 unadjusted; 0.92 adjusted). Salivary α -amylase was not significantly different pre-scenario compared with 24 hours previously (P = 0.70 unadjusted, 0.91 adjusted; data not shown).

DISCUSSION

In this prospective randomized controlled trial in mothers of children with food allergy, we found that a brief psychological intervention which incorporated quantitative information about the risks associated with food allergy did not significantly change maternal state anxiety score at 6 weeks. There were however positive findings in several other analyses of the intervention versus control group – in particular for the primary outcome in mothers with moderate/high baseline anxiety scores, and for an objective measure of stress response to a simulated anaphylaxis scenario at 1 year. We also found evidence that mothers' estimation of risks for their child was significantly reduced 1 year after the brief intervention, compared with the control group. Overall our data suggest that this brief psychological intervention for mothers of children with food allergy can reduce feelings of anxiety and reduce perception of the level of risk that food allergy carries for their child.

To our knowledge this is the first randomized controlled trial of an intervention aimed at addressing the psychological consequences of childhood food allergy in a routine allergy clinic setting. While many of our outcome measures relied on maternal report

in this non-blinded study, the positive findings for anxiety were supported by an objective measure of maternal salivary stress response, which was analysed by blinded laboratory technicians. The intervention was delivered by personnel with no prior training in CBT, who received regular supervision by a CBT trainer (10). Food allergy is a common condition, and the intervention was designed to be practical and feasible for delivery in a routine allergy clinic setting, taking a median 45 minutes to complete in this study. We did not find positive effects on maternal report of child anxiety and adjustment, but numbers included in these analyses were small due to the age restrictions of the instruments available, and further work is needed to assess the interactions between maternal and child anxiety in the context of childhood food allergy (5, 6). A limitation of the trial is that only parent perception of child anxiety and adjustment were evaluated. The intervention included components of psychoeducation, relaxation training and cognitive restructuring – as such it is not possible to specify which component(s) of the intervention led to reduced anxiety and stress response. *Post-hoc* analysis suggests that psychoeducation (risk information), or at least retention of such information, may have played a key part. The intervention may have reduced longer-term anxiety through altering risk perception, which is thought to be influenced by the evaluation of probability of a negative outcome (19). These *post hoc* findings require separate confirmation, especially since the primary outcome at 6 weeks was negative. We previously identified exaggerated risk perception in relation to childhood food allergy, in a sample of community healthcare professionals – our new findings suggest that accurate risk information at the time of first adrenaline prescription may be important for longer term maternal psychological health.

Previous work has identified increased anxiety in parents of children with food allergy (4, 5, 20), especially mothers (4). This is also seen in other childhood illnesses (21) and may be harmful for mother and child, especially if high level anxiety is sustained in the long term (22). CBT is a well-established treatment for people with anxiety disorders (23), where it has been shown to reduced State Trait Anxiety Inventory scores, but can also be effective when used for prevention of anxiety disorders in a non-psychological setting (24). We previously reported that CBT-competency in this setting increased with supervision over time (10, 25). Our work provides proof of principle that paediatric staff with no prior experience of CBT can be trained to deliver CBT to mothers of children with food allergy, resulting in a significant reduction in anxiety at one-year follow-up. A randomized controlled trial in mothers of children with other chronic illnesses suggested that peer-to-peer support programs can also have positive effects on maternal well-being including reduced anxiety (26). In the setting of food allergy we are not aware of other randomized trials to address the emotional and psychological components of the condition, but observational studies suggest that passing an oral food challenge, and peer-to-peer support, may both have positive effects on maternal or child quality of life or psychological health (27, 28).

Our findings in a representative UK paediatric allergy clinic population of young children being prescribed an AAI for the first time, may not be generalizable without reproducing the close CBT supervision received by allergy clinic staff in this study. Generalizability may also be influenced by inter-cultural variations in the psychological impact of childhood food allergy on mothers (30), and differential effects on other care-givers such as fathers, extended family and guardians. Long

term effects on maternal psychological well-being and child adjustment, and cost-effectiveness of this intervention, remain unexplored. The decision to include all mothers, rather than just those with moderate or high baseline anxiety scores, may have reduced our ability to detect a treatment effect, due to floor effects caused by participants with low baseline anxiety. The specific time-points for outcome evaluation in this trial relate to 6 weeks and 1 year after an allergist assessment with first AAI prescription and training.

To summarize we found that a brief CBT intervention which included a risk communication module failed to change STAI-S at 6 weeks, unless mothers already had a raised anxiety level. However 1 year after the intervention there was a significant reduction in maternal anxiety for all participants, supported by a reduction in stress response to a simulated anaphylaxis scenario. These findings suggest that the information given at the time of food allergy diagnosis, and any associated psychological intervention, can have significant long-term effects on maternal psychological well-being.

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REFERENCES

1. Turner PJ, Gowland MH, Sharma V, Ierodiakonou D, Harper N, Garcez T, et al. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: an analysis of United Kingdom national anaphylaxis data, 1992-2012. *The Journal of allergy and clinical immunology*. 2015;135(4):956-63 e1.
2. Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. Guidelines for the Diagnosis and Management of Food Allergy in the United States: Summary of the NIAID-Sponsored Expert Panel Report. *Journal of Allergy and Clinical Immunology*. 2010;126(6):1105-18.
3. Ravid NL, Annunziato RA, Ambrose MA, Chuang K, Mullarkey C, Sicherer SH, et al. Mental Health and Quality-of-Life Concerns Related to the Burden of Food Allergy. *Immunology and Allergy Clinics of North America*. 2012;32(1):83-95.
4. King RM, Knibb RC, Hourihane JO. Impact of peanut allergy on quality of life, stress and anxiety in the family. *Allergy*. 2009;64(3):461-8.
5. Lau GY, Patel N, Umasunthar T, Gore C, Warner JO, Hanna H, et al. Anxiety and stress in mothers of food-allergic children. *Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology*. 2014;25(3):236-42.

6. Shanahan L, Zucker N, Copeland WE, Costello EJ, Angold A. Are children and adolescents with food allergies at increased risk for psychopathology? *Journal of psychosomatic research*. 2014;77(6):468-73.
7. Hanna H, Emmanuel J, Naim S, Umasunthar T, Boyle RJ. Community-based healthcare professionals overestimate the risk of fatal anaphylaxis for food allergic children. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology*. In Revision.
8. Szabo A, Mezei G, Kovari E, Cserhati E. Depressive symptoms amongst asthmatic children's caregivers. *Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology*. 2010;21(4 Pt 2):e667-73.
9. Stauder A, Kovacs M. Anxiety symptoms in allergic patients: identification and risk factors. *Psychosomatic medicine*. 2003;65(5):816-23.
10. Vickers B, Boyle RJ, Umasunthar T, Smith JA, Hodes M. Therapy competence in delivering a brief cognitive behavioural therapy intervention to reduce maternal anxiety associated with child food allergy. *Journal of health psychology*. Under Review.
11. Schleider JL, Weisz JR. Little Treatments, Promising Effects? Meta-Analysis of Single-Session Interventions for Youth Psychiatric Problems. *J Am Acad Child Adolesc Psychiatry*. 2017;56(2):107-15.
12. Umasunthar T, Procktor A, Hodes M, Smith JG, Gore C, Cox HE, et al. Patients' ability to treat anaphylaxis using adrenaline autoinjectors: a randomized controlled trial. *Allergy*. 2015;70(7):855-63.

13. Thom A, Sartory G, Johren P. Comparison between one-session psychological treatment and benzodiazepine in dental phobia. *J Consult Clin Psychol.* 2000;68(3):378-87.
14. Umasunthar T, Leonardi-Bee J, Hodes M, Turner PJ, Gore C, Habibi P, et al. Incidence of fatal food anaphylaxis in people with food allergy: a systematic review and meta-analysis. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology.* 2013;43(12):1333-41.
15. Umasunthar T, Leonardi-Bee J, Turner PJ, Hodes M, Gore C, Warner JO, et al. Incidence of food anaphylaxis in people with food allergy: a systematic review and meta-analysis. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology.* 2015;45(11):1621-36.
16. Cohen J. Statistical power analysis for the behavioral sciences: Lawrence Erlbaum Associates; 1988.
17. Sakia RM. The Box-Cox transformation technique: a review. *The Statistician.* 1992;41:169-78.
18. Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *J R Statist Soc B.* 1995;57(1):289-300.
19. Lennart Sjöberg B-EM, Torbjørn Rundmo. Explaining risk perception. An evaluation of the psychometric paradigm in risk perception research: Rotunde publikasjone; 2004.
20. Primeau MR, Kagan R, Joseph L, Lim H, Dufresne C, Duffy C, et al. The psychological burden of peanut allergy as perceived by adults with peanut allergy and the parents of peanut-allergic children. *Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology.* 2000;30(8):1135-43.

21. van Oers HA, Haverman L, Limperg PF, van Dijk-Lokkart EM, Maurice-Stam H, Grootenhuis MA. Anxiety and depression in mothers and fathers of a chronically ill child. *Maternal and child health journal*. 2014;18(8):1993-2002.
22. Bollinger ME, Dahlquist LM, Mudd K, Sonntag C, Dillinger L, McKenna K. The impact of food allergy on the daily activities of children and their families. *Ann Allergy Asthma Immunol*. 2006;96(3):415-21.
23. Hunot V, Churchill R, Silva de Lima M, Teixeira V. Psychological therapies for generalised anxiety disorder. *Cochrane Database Syst Rev*. 2007(1):CD001848.
24. Forneris CA, Gartlehner G, Brownley KA, Gaynes BN, Sonis J, Coker-Schwimmer E, et al. Interventions to prevent post-traumatic stress disorder: a systematic review. *Am J Prev Med*. 2013;44(6):635-50.
25. Mannix KA, Blackburn IM, Garland A, Gracie J, Moorey S, Reid B, et al. Effectiveness of brief training in cognitive behaviour therapy techniques for palliative care practitioners. *Palliative medicine*. 2006;20(6):579-84.
26. Ireys HT, Chernoff R, DeVet KA, Kim Y. Maternal Outcomes of a Randomized Controlled Trial of a Community-Based Support Program for Families of Children With Chronic Illnesses. *Arch Pediatr Adolesc Med*. 2001;155(7):771-7.
27. van der Velde JL, Flokstra-de Blok BM, de Groot H, Oude-Elberink JN, Kerkhof M, Duiverman EJ, et al. Food allergy-related quality of life after double-blind, placebo-controlled food challenges in adults, adolescents, and children. *The Journal of allergy and clinical immunology*. 2012;130(5):1136-43 e2.
28. Knibb RC, Hourihane JO. The psychosocial impact of an activity holiday for young children with severe food allergy: a longitudinal study. *Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology*. 2013;24(4):368-75.

29. Koman E, Raver E, Frome H, Adams M, Aisleen K, Hourihane J, et al. An examination of the Food Allergy Quality of Life Questionnaire performance in a Countrywide American Sample of Children: Cross cultural differences in age and impact in the US and Europe. The journal of allergy and clinical immunology In practice. (in press).
30. DunnGalvin A, Koman E, Raver E, Frome H, Adams M, Keena A, et al. An Examination of the Food Allergy Quality of Life Questionnaire Performance in a Countrywide American Sample of Children: Cross-Cultural Differences in Age and Impact in the United States and Europe. The journal of allergy and clinical immunology In practice. 2017;5(2):363-8 e2.
31. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF, Jr., Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. The Journal of allergy and clinical immunology. 2006;117(2):391-7.

Table 1. Participant characteristics at baseline

	Intervention (<i>n</i> = 101)	Control (<i>n</i> = 99)	P
Maternal age	35.9 (6.3)	36.2 (6.1)	0.72
Age left full time education (years)	23.0 (5.8)	22.4 (5.2)	0.47
Living with partner	75 (77.3)	74 (77.9)	0.92
University degree	53 (56.4)	53 (58.2)	0.80
Non-white ethnicity	60 (61.2)	56 (59.6)	0.82
Previous mental health problem	10 (10.9)	9 (9.8)	0.81
Number of children in household:			
One child	39 (40.2)	46 (48.4)	
Two children	40 (41.2)	31 (32.6)	0.43
Three or more children	18 (18.6)	18 (18.9)	
Child age (years)	4.2 (3.4)	3.7 (3.3)	0.33
Male child	59 (58.4)	63 (63.6)	0.45
No. food allergies	2.8 (1.9)	2.8 (1.7)	0.79
Eczema in child	76 (80.0)	75 (80.6)	0.91
Eczema severity (POEM)	9.8 (7.3)	9.4 (7.0)	0.72
Asthma in child	25 (26.0)	19 (20.7)	0.38
Partially controlled/uncontrolled	19 (19.8)	14 (15.4)	0.43
Allergic rhinitis in child	28 (29.5)	29 (31.9)	0.72
Moderate/Severe allergic rhinitis	26 (27.4)	25 (27.5)	0.99
History of anaphylaxis*	32 (32.7)	29 (30.2)	0.71
Maternal State Anxiety (STAI-S)	36.2 (11.4)	36.4 (11.7)	0.89
Maternal Trait Anxiety (STAI-T)	37.5 (9.4)	37.2 (9.1)	0.85
Perceived Stress Scale	14.7 (6.0)	15.1 (7.3)	0.71
General Health Questionnaire	1.97 (2.91)	2.14 (3.07)	0.71
Food Allergy Impact Scale	3.18 (1.50)	3.19 (1.53)	0.98
Perceived risk of food anaphylaxis†	-2.94 (1.94)	-2.64 (1.85)	0.28
Perceived risk of fatal anaphylaxis†	-5.05 (2.21)	-5.11 (2.11)	0.85
Frequency of thoughts about child's food allergy			

Infrequent‡	21 (22.1)	18 (20.0)	
Moderately frequent	19 (20.0)	25 (27.8)	0.46
Frequent‡	55 (57.9)	47 (52.2)	
Randomised to Anapen¥	40 (39.6)	39 (39.4)	
Randomised to EpiPen	39 (38.6)	40 (40.4)	0.95
Non-randomly allocated to EpiPen	22 (21.8)	20 (20.2)	
Days since treatment at primary outcome assessment	57.2 (20.9)	52.9 (16.1)	0.13

Continuous data are presented as mean (sd), categorical data as n (%).

STAI = State Trait Anxiety Inventory; POEM = Patient-Oriented Eczema Measure.

*Anaphylaxis was defined according to NIH/NIAID guidance (31)

† Risk perception is measured on a log₁₀ scale for example -3 equates to a 1 in 1000

risk.

‡ Infrequent was defined as ≤ once per week, and frequent as ≥ once per day.

¥ There was no interaction between CBT intervention and Adrenaline Autoinjector allocation for maternal anxiety, stress or risk perception.

Table 2. Effect of the psychological intervention on maternal anxiety, stress, quality of life and risk perception

	6 weeks – primary outcome					1 year – secondary outcome				
	Intervention (<i>n</i> = 92)	Control (<i>n</i> = 90)	<i>P</i>	Mean difference (95% CI)	Effect size	Intervention (<i>n</i> = 80)	Control (<i>n</i> = 85)	<i>P</i>	Mean difference (95% CI)	Effect size
Maternal State Anxiety (STAI-S)	31.9 (10.2)	34.0 (10.2)	0.17	2.1 (-0.9, 5.0)	0.21	31.5 (10.5)	34.9 (10.3)	0.033	3.5 (0.3, 6.7)	0.33
Maternal Trait Anxiety (STAI-T)	35.9 (10.1)	37.2 (9.1)	0.38	1.3 (-1.6, 4.1)	0.14	37.0 (9.7)	39.2 (9.9)	0.14	2.3 (-0.8, 5.3)	0.22
Perceived Stress Scale	14.5 (6.5)	15.3 (6.1)	0.39	0.8 (-1.1, 2.7)	0.13	15.3 (6.8)	15.8 (7.1)	0.65	0.5 (-1.6, 2.6)	0.07
FAQLQ	2.48 (1.40)	2.61 (1.45)	0.54	0.13 (-0.26, 0.50)	0.09	2.73 (1.53)	2.78 (1.60)	0.86	0.04 (-0.45, 0.54)	0.03
Food Allergy Impact scale	3.10 (1.40)	3.50 (1.46)	0.058	0.41 (-0.01, 0.83)	0.28	3.15 (1.51)	3.49 (1.51)	0.15	0.34 (-0.13, 0.80)	0.23
Perceived risk of food anaphylaxis*	-4.63 (2.19)	-3.50 (2.14)	0.001	-1.13 (- 1.77, -0.49)	0.52	-4.91 (2.09)	-3.56 (1.90)	<0.001	-1.35 (- 1.97, -0.74)	0.68

Perceived risk of fatal anaphylaxis*	-6.25 (2.02)	-5.21 (2.48)	0.002	-1.04 (-1.70, -0.37)	0.46	-6.00 (1.90)	-5.28 (2.12)	0.023⁺	-0.72 (-1.34, -0.10)	0.36
Perceived risk of any fatality*	-4.92 (1.75)	-4.59 (2.00)	0.24	-0.33 (-0.89, 0.22)	0.18	-4.77 (1.89)	-4.10 (1.75)	0.021⁺	-0.66 (-1.22, -0.10)	0.37

STAI = State Trait Anxiety Inventory. FAQLQ = Food Allergy Quality of Life Questionnaire. STAI = State Trait Anxiety Inventory. FAQLQ = Food Allergy Quality of Life Questionnaire, calculated using the FAQLQ parent form (age 0-12), where higher scores indicate increased quality of life impact. *Risk perception is measured on a $\log_{10}$ scale for example -3 equates to a 1 in 1000 risk. Effect size = Cohen's *d*: small effect size = 0.2; medium = 0.5; large = 0.8 (16). Outcome measures showing significant differences are highlighted in bold. ⁺Difference not statistically significant, after adjustment for false discovery.

Table 3. Effect of the psychological intervention on maternal outcomes in participants with moderate/high STAI-S at baseline

	6 weeks – primary outcome					1 year – secondary outcome				
	Intervention (<i>n</i> = 49)	Control (<i>n</i> = 47)	P	Mean difference (95% CI)	Effect size	Intervention (<i>n</i> = 44)	Control (<i>n</i> = 45)	P	Mean difference (95% CI)	Effect size
Maternal State Anxiety (STAI-S)	33.0 (9.3)	37.8 (10.0)	0.016	4.8 (0.9, 8.7)	0.50	33.5 (11.8)	35.9 (9.2)	0.28	2.5 (-2.2, 7.1)	0.23
Maternal Trait Anxiety (STAI-T)	37.9 (9.9)	40.5 (8.5)	0.16	2.7 (-1.1, 6.4)	0.28	37.9 (11.0)	42.4 (8.9)	0.038†	4.5 (0.2, 8.7)	0.43
Perceived Stress Scale	15.3 (6.0)	16.9 (5.6)	0.19	1.6 (-0.8, 3.9)	0.28	16.3 (7.3)	17.3 (5.9)	0.46	1.0 (-1.8, 3.8)	0.15
FAQLQ	2.51 (1.37)	2.71 (1.34)	0.48	0.20 (-0.35, 0.71)	0.15	2.92 (1.58)	2.74 (1.40)	0.59	-0.18 (- 0.82, 0.47)	-0.12
Food Allergy Impact scale	3.27 (1.32)	3.70 (1.35)	0.13	0.43 (-0.12, 0.97)	0.32	3.49 (1.62)	3.64 (1.33)	0.63	0.15 (-0.47, 0.77)	0.10

Perceived risk of food anaphylaxis*	-4.48 (2.21)	-3.77 (2.17)	0.12	-0.72 (-1.62, 0.18)	0.32	-5.25 (1.85)	-3.65 (1.82)	<0.001	-1.60 (-2.37, -0.83)	0.87
Perceived risk of fatal anaphylaxis*	-6.27 (2.21)	-5.47 (2.29)	0.089	-0.81 (-1.68, 0.10)	0.36	-6.11 (1.98)	-5.29 (1.90)	0.051†	-0.81 (-1.63, 0.05)	0.42
Perceived risk of any fatality*	-5.01 (1.85)	-4.78 (2.02)	0.57	-0.23 (-1.03, 0.57)	0.12	-4.73 (1.85)	-3.90 (1.41)	0.019†	-0.83 (-1.53, -0.14)	0.51

Participants scoring ≥ 35 on the state anxiety component of the State Trait Anxiety Inventory (STAI) were classified as moderate/high.

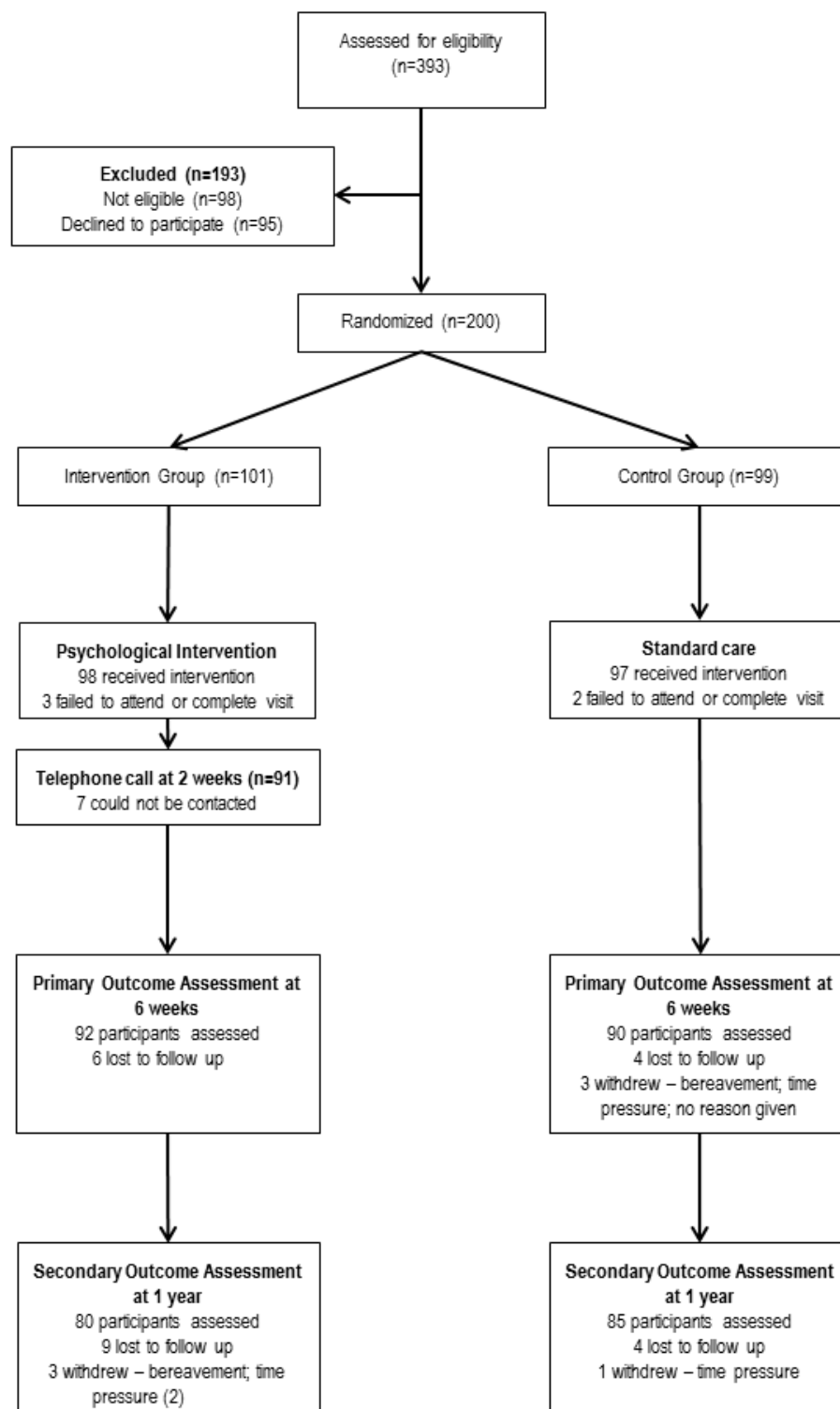
STAI = State Trait Anxiety Inventory. FAQLQ = Food Allergy Quality of Life Questionnaire, calculated using the FAQLQ parent form (age 0-12), where higher scores indicate increased quality of life impact.

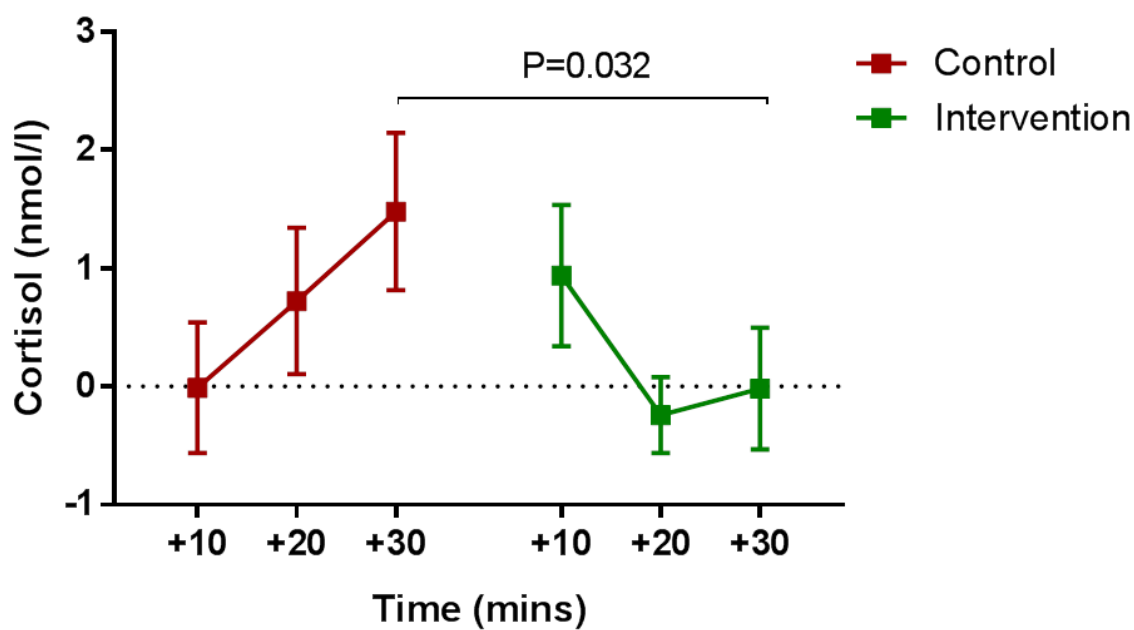
*Risk perception is measured on a $\log_{10}$ scale for example -3 equates to a 1 in 1000 risk. Effect size = Cohen's d : small effect size = 0.2; medium = 0.5; large = 0.8 (16). Outcome measures showing significant differences are highlighted in bold. †Difference not statistically significant, after adjustment for false discovery.

FIGURE LEGENDS

Figure 1. CONSORT flow diagram

Figure 2. Effect of the intervention on salivary stress response to a simulated anaphylaxis scenario. Data shown are mean ($\pm$ SEM) change in salivary cortisol (A) and amylase (B) levels at 10, 20 and 30 minutes post scenario.



A**B**