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Online supplement

Sample characteristics and site specific trial details

Unless otherwise specified, clinical trials included all primary anxiety disorder diagnoses. All sites made secondary anxiety disorder diagnoses where appropriate.

Sydney, Australia (n = 293**).** Participants aged 6-18 were recruited from the Centre for Emotional Health, Macquarie University, Sydney. All participants completed the Cool Kids program (1), with 10-12 family sessions involving the parents (the majority of which were conducted in groups; 8% of the sample's DNA were collected retrospectively). Variations on this treatment program include a subgroup from previous randomised trials who received group, individual or phone-based CBT sessions (2, 3); participants from a guided self-help trial with phone support for children in rural Australia (4); a group from a trial with additional parental anxiety management (5); and those recruited from an ongoing randomised trial of progressive allocation to treatment (Stepped Care).

Reading and Oxford (n = 199**), UK** Participants aged 5-18 were recruited jointly from Reading and Oxford from eight trials at the Berkshire Child Anxiety Clinic (University of Reading) and the Oxfordshire Primary Child and Adolescent Mental Health Service. Participants received treatment in three main themes; one focussing on children with anxious mothers; a set of trials using a parent-guided self-help CBT program; and an online CBT program for adolescents.

The Mother and Child (MaCh) project (6). Children whose mother also had a current anxiety disorder completed an 8 session manual-based CBT treatment based on the Cool Kids program (7). The mothers of these children also received extra sessions focussing on their own anxiety and on mother-child interactions.

Overcoming. Children were treated with a parent-guided self-help CBT program, comprised of the same primary components as the Cool Kids program (7, 8). This consisted of 2-4 in-person sessions and 2-4 telephone sessions. A sub-set of this group with a primary anxiety disorder diagnosis of Social Phobia also received targeted Cognitive Bias Modification Training (CBM-I, (9)). Additionally, participants with highly anxious parents (screened using DASS or by meeting ADIS criteria) were randomised to groups in a trial including additional sessions for the parents which focussed on strategies for tolerating children's negative emotions. In Oxford, treatment was based on the same basic program, and delivered by primary health workers as part of a feasibility trial (10).

BRAVE. The final treatment group completed a therapist-supported online CBT program for adolescents (BRAVE), consisting of 10 sessions, half with 5 additional parent sessions and half without parent sessions.

Aarhus, Denmark (n = 112**).** Participants aged 7-17 years were recruited from the Department of Psychology and Behavioural Sciences, Aarhus University, and all anxiety disorder diagnoses were included. Participants received CBT using the Cool Kids manual (including the adolescent version where appropriate (7, 11)). Participants came from two groups; one aged 7-17, from a trial including treatment and waitlist conditions; and another

group aged 7-12 from a trial comparing efficacy of traditional group-based treatment with Cool Kids versus a guided self-help version with clinician support (bibliotherapy). In both trials only participants that received in-person CBT were included.

Bergen, Norway (n = 35**).** Participants aged 5-13 were recruited from the child part of the "Assessment and Treatment – Anxiety in Children and Adults" study, Haukeland University Hospital, Bergen. Patients referred to outpatient mental health clinics in Western Norway, with a primary diagnosis of separation anxiety, social phobia, or generalized anxiety, received group or individual treatment with the FRIENDS program (4^{th} edition (12, 13)) in a randomised control trial comparing active treatment with a waitlist condition (14).

Bochum, Germany (n = 50**).** Participants aged 5-18 were recruited from the Research and Treatment Centre for Mental Health, Ruhr-Universität Bochum. Participants received either exposure-based CBT (8-25 sessions, with sessions occurring at least every 2 weeks), the Coping Cat program (15), or a family-based version of CBT specifically designed to target separation anxiety disorder (TAFF (16, 17)). Diagnoses were provided separately for parent- and child-report. The primary diagnosis was selected as being the most severe from either reporter. If the most severe disorder reported by each was of equal severity but was a different diagnosis, the parent-reported diagnosis was selected.

Basel, Switzerland (n = 46**).** Participants aged 5-13 (all with a primary diagnosis of Separation Anxiety Disorder) were recruited from the Faculty of Psychology, University of Basel. All participants took part in a randomised control trial comparing a family-based version of CBT specifically designed to target separation anxiety disorder (TAFF(16, 17)) with Coping Cat (15). All participants received 16 sessions over 12 weeks.

Florida, USA (n = 36**).** Participants aged 7 to 16 (including all primary anxiety disorder diagnoses except PTSD) were recruited from the Child Anxiety and Phobia Program, Florida International University, Miami. All participants received 12 to 14 hour-long sessions of individual manualised CBT. Additionally, two conditions included parental involvement focussing on different parent skills (Relationship Skills Training or Reinforcement Skills Training).

Groningen, the Netherlands (n = 35**).** Participants aged 8 to 17 were recruited from the Department of Child and Adolescent Psychiatry, University of Groningen. All participants were treated within a randomised control trial of Coping Cat (Dutch version (18) including 12 individual child sessions and 2 parent sessions.

Cambridge, UK (n = 9**).** Participants aged 8-17 were recruited from the MRC Cognition and Brain Sciences Unit, Cambridge, UK. Participants were taking part in the ASPECTS trial, which recruited individuals exposed to a recent (i.e. in the previous six months) traumatic stressor (i.e. any event that involve the threat of death, severe injury, or threat to bodily integrity, or witnessing such an event). Those that developed PTSD were randomised to a 10-week waitlist or individual PTSD-specific CBT (19), which consisted of up to 10 sessions over a 10 week period. Only participants that received treatment were included

Amsterdam, the Netherlands (n = 3**).** Participants aged 10-14 were recruited from the Academic Treatment Centre for Parent and Child, University of Amsterdam UvA Minds and received either 12 weeks of CBT in individual sessions or 8 weeks of CBT in group sessions, according to the Dutch protocol Discussing + Doing = Daring (20). Diagnoses were provided

separately for parent- and child-report with the primary diagnosis selected from these data by the trial manager.

Table DS1: White Subset Cohort 2 results; categorical remission and change in symptom severity at post-treatment and follow-up for primary anxiety diagnosis, and remission from all anxiety disorder diagnoses at post and follow-up.

Cohort 2 – White Subset		Remission						Response – Change in CSR		
		Primary Anxiety Disorder (n = 550)			All Anxiety Diagnoses (n = 516)			Primary Anxiety Disorder (n = 529)		
Time-point	Predictor Variable	**OR**	**β**	**β**	**OR**	**95% CI**	**P**	**β**	**95% CI**	**P**
Post-Treatment	Genotype	0.92	-0.06	-0.06	1.16	0.80-1.68	0.421	-0.06	-0.15-0.02	0.124
	Time							-1.37	-1.44--1.30	0.000
	Baseline severity	1.12	0.27	0.27	1.22	0.96-1.31	0.136	0.27	0.24-0.31	0.000
	Age	1.04	0.02	0.02	0.99	0.92-1.07	0.806	0.02	0.00-0.03	0.040
	Sex	1.13	0.04	0.04	1.41	1.03-1.92	0.030	0.04	-0.03-0.11	0.294
		Primary Anxiety Disorder (n = 442)			All Anxiety Diagnoses (n = 411)			Primary Anxiety Disorder (n = 421)		
Time-point	Predictor Variable	**OR**	**β**	**β**	**OR**	**95% CI**	**P**	**β**	**95% CI**	**P**
Follow-up	Genotype	1.11	-0.01	-0.01	0.94	0.43-2.04	0.875	-0.01	-0.12-0.09	0.781
	Time	0.00	-1.09	-1.09	0.00	0.00-0.05	0.000	-1.09	-1.16--1.01	0.000
	$Time^2$	2.61	0.16	0.16	2.19	1.53-3.12	0.000	0.16	0.14-0.18	0.000
	Baseline severity	1.84	0.24	0.24	1.82	1.22-2.70	0.003	0.24	0.20-0.28	0.000
	Age	0.91	-0.01	-0.01	1.01	0.86-1.19	0.889	-0.01	-0.03-0.02	0.621
	Sex	0.87	0.05	0.05	1.37	0.71-2.65	0.348	0.05	-0.03-0.13	0.240

Note. 5HTTLPR genotype is defined using a recessive model, where SS=1 and LL/LS=0. Age and baseline severity are centred at the mean

Table DS2: White Subset Mega-analyses; results combined Cohorts 1 & 2. Outcome measures; primary anxiety disorder remission at follow-up, change in primary anxiety CSR from pre-treatment to follow-up, all anxiety disorder diagnoses remission at follow-up

White Subset Mega-analyses		Remission						Response – Change in CSR		
		Primary Anxiety Disorder (n = 722)			All Anxiety Diagnoses (n = 701)			Primary Anxiety Disorder (n = 691)		
		OR	**95% CI**	**P**	**OR**	**95% CI**	**P**	**β**	**95% CI**	**P**
Follow-up	Genotype	0.58	0.25-1.32	0.52	0.52	0.25-1.07	0.074	-0.06	-0.14-0.02	0.140
	Time	0.00	0.00-0.01	0.00	0.00	0.00-0.02	0.000	-0.97	-1.03--0.92	0.000
	$Time^2$	2.65	1.89-3.74	2.18	2.18	1.66-2.86	0.000	0.14	0.13-0.15	0.000
	Baseline severity	2.21	1.43-3.41	2.29	2.29	1.53-3.42	0.000	0.26	0.22-0.29	0.000
	Age	0.87	0.73-1.03	1.00	1.00	0.86-1.15	0.973	-0.01	-0.03-0.01	0.295
	Sex	1.28	0.67-2.44	1.66	1.66	0.93-2.97	0.085	0.08	0.02-0.15	0.010
	Cohort	0.66	0.30-1.47	0.49	0.49	0.24-0.99	0.047	-0.06	-0.14-0.02	0.116

Note. 5HTTLPR genotype is defined using a recessive model, where SS=1 and LL/LS=0. Age and baseline severity are centred at the mean

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