ANXIETY IN AUTISM AND RARE GENETIC SYNDROMES ASSOCIATED WITH INTELLECTUAL DISABILITY

Volume 2

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List of Appendices

Appendices

Appendix 1 Chapter two search details

Appendices table 1. Scoping task search terms

	Search terms
First search field	syndrom*
Second search field	intellectual* disab* OR learning disab* OR developmental* disab* OR mental* retard* OR mental* handicap*
Third search field	anx* OR phobi* OR fear* OR panic disorder* OR worr* OR panic attack*

Appendices table 2. Syndromes identified during scoping search. Syndromes in bold were deemed appropriate for inclusion in the current review.

Genetic syndromes identified in scoping search				
1.Fragile X syndrome	**8. 3q29 deletion syndrome**	14. FOXP1 syndome	20. Turner syndrome	26. Chromosome 18 abnormalities (18q, 18p, 18p tetrasomy)
2. 22q11.22 deletion syndrome	**9. Rett syndrome**	15. Danon disease (LAMP2 gene mutation)	21. Dyskeratosis congenita	27. Moebius sequence
3. Down syndrome	10. Tourette syndrome	16. Sotos syndrome	22. Cerebrotendinous xanthomastosis	28. Potocki-Lupski syndrome
4. 7q11.23 duplication syndrome	11. Spastic peroneal flatfoot	17. MeCP2 duplication	23. Rubinstein-Taybi syndrome	29. 15q13.2q13.3 microdeletion/duplication
5. CHARGE syndrome	12. Lesch-Nyhan disease	18. Klinefelter syndrome	24. Costello syndrome	30. FG syndrome (Opitz-Kaveggia syndrome)
6. Cornelia de Lange syndrome	13. Prader-Willi syndrome	19. Alpha-mannosidosis	25. Kabuki syndrome	31. Williams syndrome
7. Cohen syndrome				

Appendices table 3. Genetic syndrome search terms and dates of searches (Wos=Web of Science)

	WoS	Dates	PsycINFO	Dates	Embase		CINAHL Plus	Dates	Search terms
Fragile X syndrome (FXS)	15/02/2019	All years (1900 - 2019)	19/02/2019	1967 to February week 1 2019	26/02/2019	1974 to 2019 February 25	28/02/2019	All years	Fragile X OR Fragile-X OR Fragile X syndrome OR FXS OR FRAXA syndrome OR AFRAX OR Martin-Bell* syndrome OR Marker X syndrome OR fraX syndrome OR fra(X) syndrome OR X-linked mental retardation OR Macroorchidism OR Escalante* syndrome OR Escalante*
22q11.2 deletion syndrome	08/03/2019	All years (1900 - 2019)	12/03/2019	1967 to March week 1 2019	15/03/2019	1974 to 2019 March 14	15/03/2019	All years	VCF OR VCFS OR Velocardiofacial syndrome OR CTAF OR Velo- cardio-facial syndrome OR DiGeorge* syndrome OR Conotruncal anomaly face syndrome OR CATCH22 OR Autosomal dominant Opitz G/BBB syndrome OR Autosomal dominant Opitz G BBB syndrome OR Cayler cardiofacial syndrome OR Deletion 22q11/2 syndrome OR 22q11/2 deletion syndrome OR 22q11/2DS OR 22q11 deletion syndrome OR Sedlackova* syndrome OR Shprintzen* syndrome
Down syndrome	08/03/2019	All years (1900	12/03/2019	1967 to March week	15/04/2019	1974 to 2019	18/04/2019	All years	Down* syndrome OR Trisomy 21 OR Trisomy G OR 47,XX,+21 OR 47,XY,+2

		- 2019)		1 2019		April 12			
Rett syndrome	04/04/2019	All years (1900 - 2019)	24/06/2019	1967 to June week 3 2019	31/05/2019	1974 to 2019 May 30	04/06/2019	All years	Rett* OR Rett* syndrome OR Rett* disorder OR RTS OR RTT OR Cerebroatrophic hyperammonemia OR Autism-dementiaataxia-loss of purposeful hand use syndrome
CHARGE syndrome	03/06/2019	All years (1900 - 2019)	07/06/2019	1967 to May week 4 2019	12/06/2019	1974 to 2019 June 11	14/06/2019	All years	CHARGE OR CHARGE syndrome OR CHARGE association OR Hall-Hittner* syndrome OR Hall* Hittner* syndrome OR Coloboma
7q11.23 duplication syndrome	20/06/2019	All years (1900 - 2019)	20/06/2019	1967 to June week 2 2019	20/06/2019	1974 to 2019 June 19	20/06/2019	All years	7q11.23* OR 7q11.23 duplication syndrome OR 7q11.23 microduplication syndrome OR chromosome 7q11.23 duplication OR chromosome 7q11.23 duplication syndrome OR dup(7)(q11.23) OR Somerville-Van der Aa syndrome OR trisomy 7q11.23 OR WBS duplication syndrome OR Williams-Beuren region duplication syndrome
3q29 microdeletion syndrome	20/06/2019	All years (1900 - 2019)	20/06/2019	1967 to June week 2 2019	21/06/2019	1974 to 2019 June 20	21/06/2019	All years	3q29* OR 3q29 mircodeletion syndrome OR 3q subtelomere deletion syndrome OR 3q29 deletion syndrome OR 3q29 recurrent deletion OR chromosome 3q29 deletion syndrome OR microdeletion

									3q29 syndrome OR monosomy 3q29
Tuberous Sclerosis Complex	26/06/2019	All years (1900 - 2019)	04/07/2019	1967 to June week 4 2019	08/07/2019	1974 to 2019 July 05	08/07/2019	All years	Tuberous sclerosis OR Tuberous sclerosis syndrome OR Bourneville* disease OR Bourneville* phakomatosis OR Cerebral sclerosis OR Cerebral sclerosis syndrome OR Epiloia OR Sclerosis tuberose OR Tuberose sclerosis OR Tuberose sclerosis syndrome OR Tuberous sclerosis complex OR TSC OR TSS

Appendices table 4. Database searching for each genetic syndrome, stages of exclusion and reasons for exclusion

[1]

	Records identified through database searching	Records after duplicates removed	Number of papers screened (Stage 1)	Excluded	Full text papers assessed for eligibility (Stage 2)	Excluded with reasons	Records identified through backward searching	Papers assessed for quality	Excluded from 'any anxiety' meta-analysis	Papers included in meta-analysis
Fragile X syndrome	5,541	4,882	4,882	4,710	172	150[1]	0	22	3[2]	19
22q11.2 deletion	1,151	1,038	1,038	896	142	118[3]	12	36	2[4]	34
Down syndrome	7,426	6,841	6,841	6,722	119	109[5]	4	14	2[6]	12
Rett syndrome	4,902	4,468	4,468	4,443	25	20[7]	1	6	0	6
CHARGE syndrome	8,882	8,370	8,370	8,360	10	7[8]	1	4	2[9]	2
7q11.23 duplication	70	68	68	59	9	6[10]	0	3	1[11]	2
3q29 deletion syndrome	74	68	68	64	4	3[12]	0	1	0	1
TSC	2,371	2,220	2,220	2,192	28	21[13]	2	9	0	9
Total	30,417	27,955	27,955	27,446	509	434	20	95	10	85

Paper exclusion reasons: 78=no reported anxiety prevalence, 50=review, 13=case study/report, 9=bias in recruitment

[2] 3 papers do not report 'any anxiety' prevalence but report specific anxiety disorders and are therefore included in the specific anxiety disorder meta-analyses

[3] Paper exclusion reasons: 42=no reported anxiety prevalence, 30=review, 21=case study/report, 25=bias in recruitment

[4] 1 paper does not report number of participants with anxiety but reports unclear percentages. Clarification not obtained following contact with author. 1 paper does not report 'any anxiety' prevalence but does report specific anxiety disorders and is therefore included in the specific anxiety disorder meta-analyses

[5] Paper exclusion reasons: 64=no reported anxiety prevalence, 22=review, 17=case study/report, 6=bias in recruitment

[6] 1 paper reports an anxiety prevalence rate of 0 and is deemed underpowered (*n*=14). 1 paper does not report 'any anxiety' prevalence but does report specific anxiety disorders and is therefore included in the specific anxiety disorder meta-analyses

[7] Paper exclusion reasons: 14=no reported anxiety prevalence, 2=review, 3=case study/report, 1=bias in recruitment

[8] Paper exclusion reasons: 5=no reported anxiety prevalence, 1=review, 1=case study/report

[9] 2 papers do not report 'any anxiety' prevalence but do report specific anxiety disorders and are therefore included in the specific anxiety disorder meta-analyses
[10] Paper exclusion reasons: 2=no reported anxiety prevalence, 3=review, 1=case study/report
[11]1 paper does not report 'any anxiety' prevalence but does report specific anxiety disorders and is therefore included in the specific anxiety disorder meta-analyses
[12] Paper exclusion reasons: 3=case study/report
[13] Paper exclusion reasons: 6=no reported anxiety prevalence, 5=review, 7=case study/report, 3=bias in recruitment

Appendix 2 Chapter two quality assessment

Appendices table 5. Quality rating criteria (adapted from Royston, Howlin, Waite and Oliver 2017).[1]

	Quality Rating			
	0 Poor	**1 Adequate**	**2 Good**	**3 Excellent**
Sample Identification	Not specified/reported	Single restricted or non-random sample e.g., a specialist clinic or previous research study[2] Single regional sample e.g., a regional parent support group	Multiple restricted or non-random samples e.g., multi-region specialist clinics National non-random sampling e.g., national parent support groups	Random or total population sample
Confirmation of syndrome[3]	Not confirmed/reported Clinical diagnosis only suspected Parent report only	Clinical diagnosis by 'generalist' e.g., General Practitioner or Paediatrician Proportion of sample has report of genetic confirmation, other part of sample not reported	Clinical diagnosis by 'expert' e.g., Clinical Geneticist or Specialist Paediatrician Parent report of genetic confirmation for all participants[4]	Genetic confirmation of diagnosis/FISH tested
Anxiety assessment	Not specified/reported Clinician judgement only Parent report only Only report of chart review	Informant report/self-report instrument e.g., SCAS, DBC-A Screening instrument e.g. PAS-ADD Clinician judgement against specified diagnostic criteria e.g., DSM-IV or ICD-10	Diagnostic instrument/interviews e.g., K-SADS, ADIS, SCID	Consensus from multiple assessments, including at least one diagnostic instrument

Spence Children's Anxiety Scale (SCAS), Developmental Behavioural Checklist-Adults (DBC-A), Psychiatric Assessment Schedule for Adults with Developmental Disabilities (PAS-ADD), Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS), Structured Clinical Interview for axis I DSM-IV (SCID)

[1] Royston, R., Howlin, P., Waite, J., & Oliver, C. (2017). Anxiety Disorders in Williams Syndrome Contrasted with Intellectual Disability and the General Population: A Systematic Review and Meta-Analysis. *J Autism Dev Disord*, *47*(12), 3765-3777. https://doi.org/10.1007/s10803-016-2909-z

[2] For individuals recruited as part of a larger *ongoing* study, if the recruitment strategy is described, it is coded. If not, it is coded as 1, indicating the sample has come from one source (i.e., the larger ongoing study).

[3] Studies can only be classified into a category if all of the participants were tested using the outlined method. For instance, if only 50% of participants were FISH tested, the study cannot receive a score of 3 and will receive a score of 2.

[4] A score of 2 was given to studies that report details of genetic subtyping e.g., via informant report but did not include formal genetic confirmation within the study

Appendix 3 Chapter two anxiety prevalence analysis

Appendices table 6. Study characteristics, quality rating and reported prevalence rate of anxiety in Fragile X syndrome

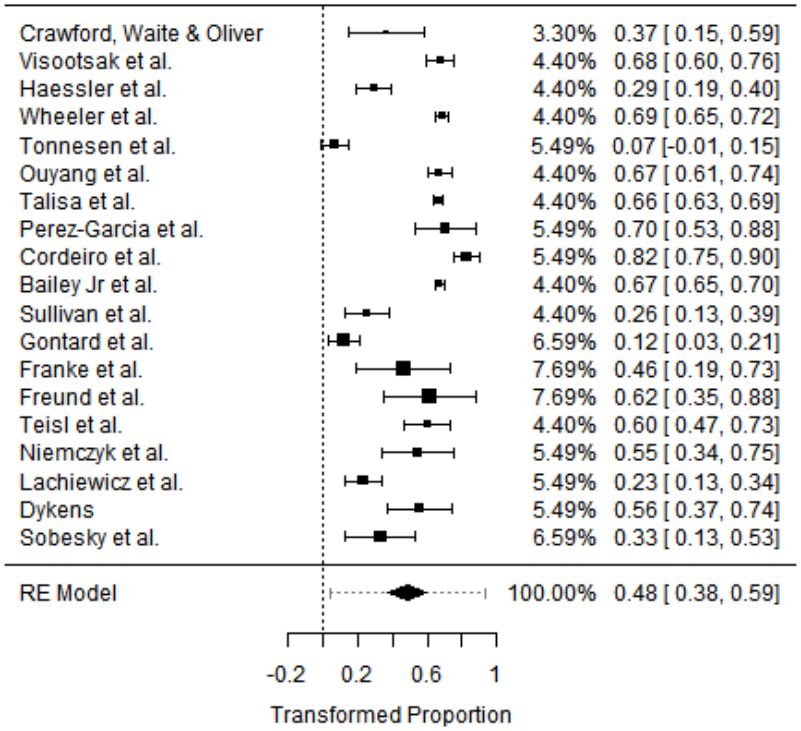
	Quality criteria								Outcome data	
Authors	Sample	Syndrome	Anxiety	N	Gender	Mean age (SD) Range	Syndrome diagnosis	Anxiety measure	% Anxiety (N)	Quality weighting
1. Crawford et al. 2017				19	19 m	24.19 (7·51), range NR	Pediatrician/clinical geneticist	SCAS-P	36.8 (7)	0.33
2. Visootsak et al. 2016				133	115 m, 18 f	6.6 (NR), 5 months-17 years	DNA testing	Medical record review	67.7 (90)	0.44
3. Haessler et al. 2016				75	63 m, 12 f	16.7 (14.5), 2-82	Genetic diagnosis confirmed	Medical record review	29.3 (22)	0.44
4. Wheeler et al. 2016				774	642 m, 132 f	19.80 (11.41), 3-67	Parent report of full mutation	Parent report	68.5 (503)[1]	0.44
5. Tonnsen et al. 2014				43	43 m	57.57 (12.13), 22-71[2]	Review of genetic reports	CBCL	7 (3)	0.56
6. Ouyang et al. 2014				189	153 m, 36 f	NR (NR), 5-17	Parent report of FXS testing	Parent report	67.2 (127)	0.44
7. Talisa et al. 2014				1027	1,027 m	19.9 (NR), 11.1-58.1[3]	Parent report of full mutation	Parent report	66.2 (680)	0.44
8. Perez-Garcia et al. 2011				27	27 m	12.4 (.71), 6-18	Genetic diagnosis confirmed	CBCL	70.4 (19)	0.56
9. Cordeiro et al. 2011				97	58 m, 39 f	12.78 (5.81), 5-33.30	Genetic diagnosis confirmed	ADIS-IV	82.5 (80)	0.56
10. Gabis et al. 2011				28	23 m, 5 f	14.2 (NR), range NR	Review of medical files from 25% (7) of sample	ECI-4/CSI-4/ASI-4	NR[4]	0.44
11. Bailey Jr et al. 2008				1235	976 m, 259 f	Not reported	Parent report of full mutation	Parent report	67.2 (830)	0.44
12. Sullivan et al. 2007				43	39 m, 4 f	10 years 3 months (NR), 6-14	Genetic diagnosis confirmed	CBCL	26 (11)	0.44

13. von Gontard et al. 2002	49	49 m	8.6 (NR), 5.7-16.10	'with full-mutation'	Kinder-DIPS	12.2 (6)	0.67
14. Teisl et al. 1999	55	32 m, 23 f	NR (NR), 10 months-18 years 10 months	Genetic diagnosis confirmed	Parent report	60 (33)	0.44
15. Niemczyk et al. 2016	22	22 m	11 (3.8), 4-17	'with full-mutation'	Kinder-DIPS	54.5 (12)	0.56
16. Franke et al. 1998	13	13 f	35.9 (10), range NR	Genetic testing	DIGS	46.2 (6)	0.78
17. Freund et al. 1993	17	17 f	12.8 (7.5), 4-27	Genetic testing	DICA	61.5 (8)[5]	0.78
18. Lachiewicz et al. 1994	60	60 f	86.5 (NR), 35-152[6]	Genetic diagnosis confirmed	Conners' Parent's Questionnaire	23.3 (14)	0.56
19. Dykens, 1989	27	27 m	38.2 (NR), 23-51[7]	Cytogenetic procedures	VABS	55.6 (15)	0.56
20. Sobesky et al. 1994	21	21 f	30.81 (7.09), 18-45	Genetic/DNA analysis	SADS-L	33.3 (7)	0.67
21. Shaw & Porter, 2013[8]	16	4 m, 12 f	24.8 (12.9), 12.1-56.1	Genetic testing confirmed	SPAI-C	53.8 (7)	0.56
22. Moss et al. 2016[9]	142	142 m	19.8 (8.6), 9-49	Not reported	SQID	17.8 (21)	0.33

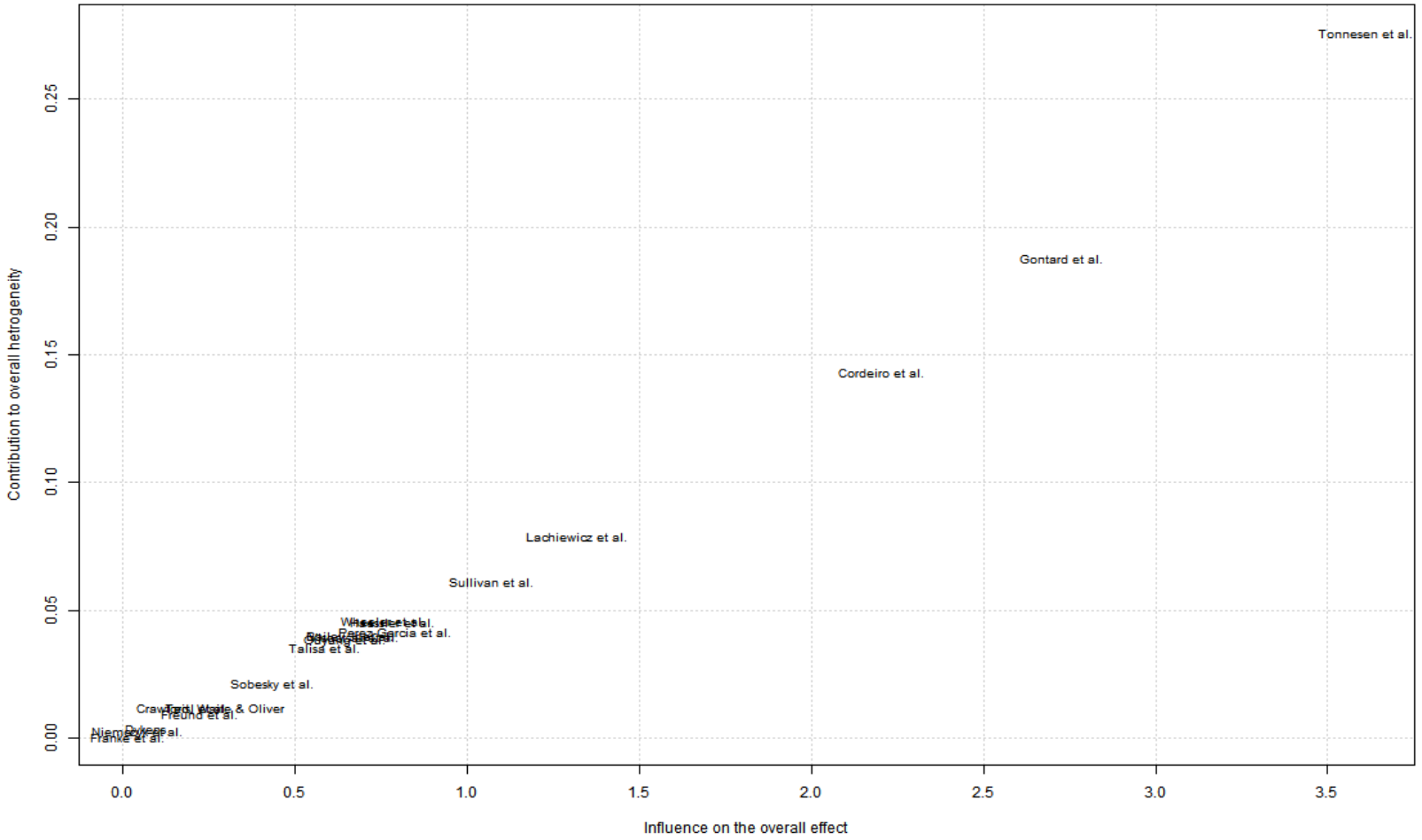
SCAS-P=Spence Children's Anxiety Scale-Parent, CBCL=Child Behaviour Checklist, ADIS-IV=Anxiety Disorders Interview Schedule for DSM-IV, ECI-4/CSI-4/ASI-4= Early Childhood Inventory-4/Child Symptom Inventory-4/Adolescent Symptom Inventory-4, DIGS=Diagnostic Interview for Genetic Studies, DICA=Diagnostic Interview for Children and Adolescents, VABS=Vineland Adaptive Behaviour Scales, SADS-L=Schedule for Affective Disorders and Schizophrenia-Lifetime version, SPAI-C=Social Phobia and Anxiety Inventory for Children, SQID=Sociability Questionnaire for People with Intellectual Disabilities

[1] Based on 734 participants
[2]Age reported in months
[3]Age means and standard deviations reported separately for children. Adolescents/adults as reported above, children: 6.6 (SD NR), 3.3-10.9
[4] Paper not included in overall anxiety disorder meta-analysis due to unknown overall n, following contact with author. Paper included in specific anxiety disorder meta-analyses e.g. specific phobia, generalised anxiety disorder
[5] Anxiety prevalence based on 13 participants with full mutation (remaining 4 participants: *n*=2 DNA analyses not available, *n*=1 premutation and *n*=1 mosaic)
[6] Age reported in months
[7] Age means and standard deviations reported separately for institutionalised and non-institutionalised group. Institutionalised group reported above. Non-institutionalised group: 14 (NR), 3-28

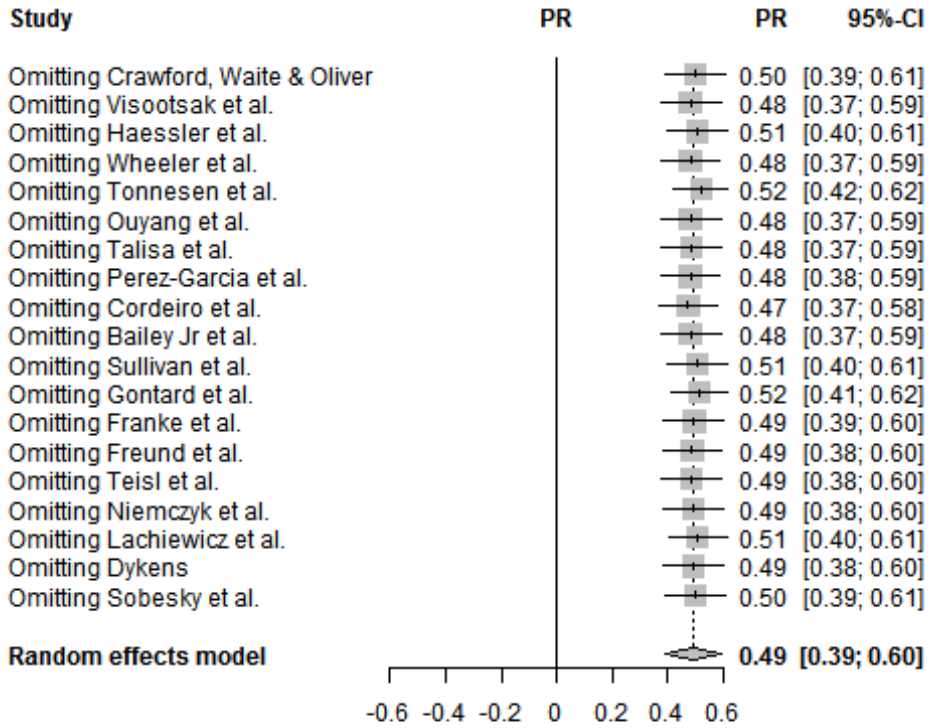
[8] Paper only considers social anxiety and therefore is not included in the 'any anxiety' meta-analysis but is included in the specific anxiety disorder meta-analyses
[9] Paper only considers selective mutism and therefore is not included in the 'any anxiety' meta-analysis but is included in the specific anxiety disorder meta-analyses. Prevalence based on 118 participants



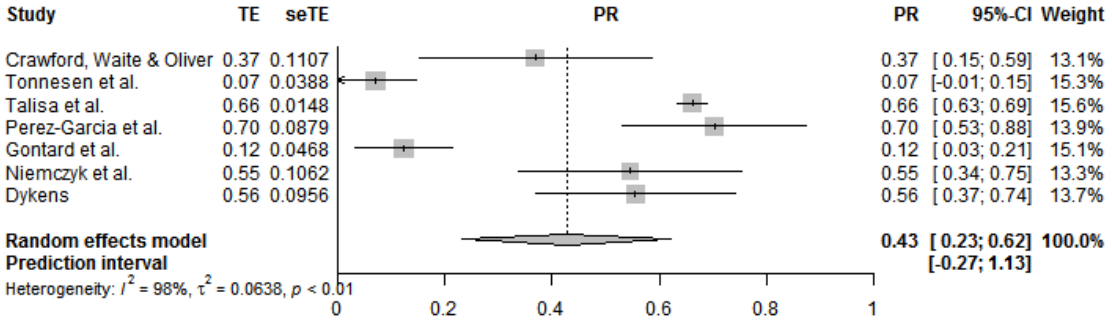
Appendices Figure 1. Forest plot for anxiety in Fragile X syndrome using a quality-effects model.



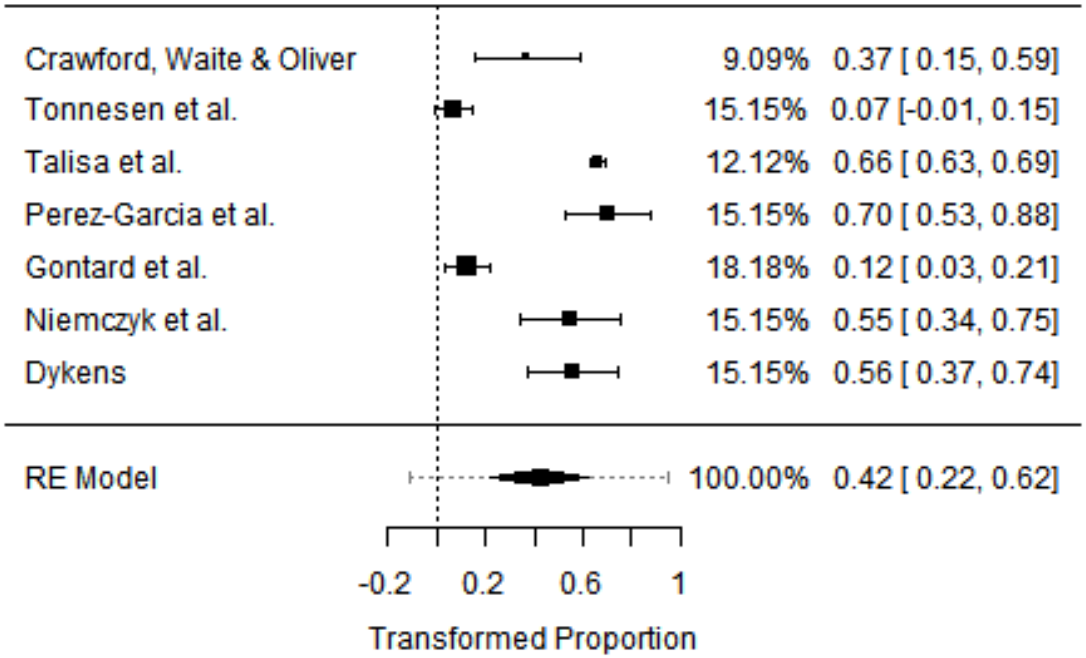
Appendices Figure 2. Baujat chart used to identify sources of heterogeneity: Fragile X syndrome.



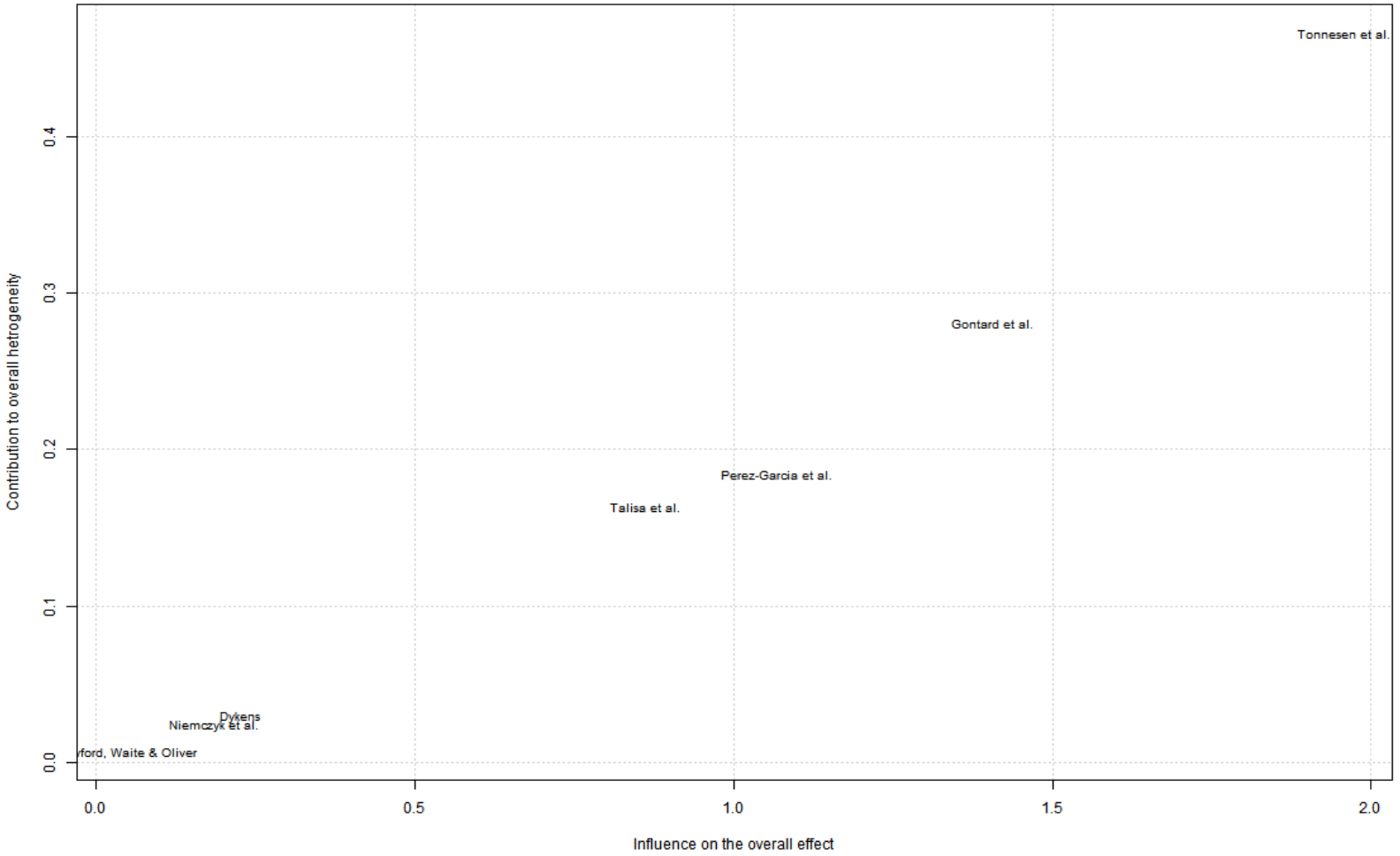
Appendices Figure 3. “Leave one out” analysis for Fragile X syndrome.



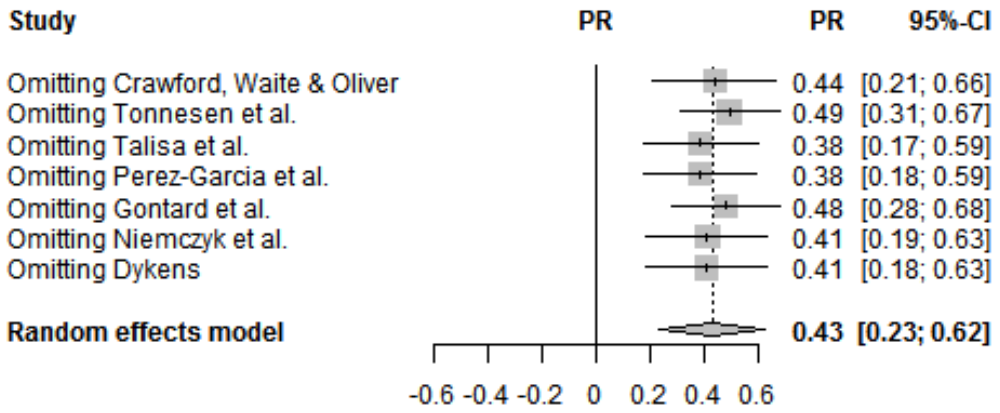
Appendices Figure 4. Forest plot for anxiety in Fragile X syndrome using a random-effects model (only males).



Appendices Figure 5. Forest plot for anxiety in Fragile X syndrome using a quality-effects model (only males).



Appendices Figure 6. Baujat chart used to identify sources of heterogeneity: Fragile X syndrome (only males).



Appendices Figure 7. “Leave one out” analysis for Fragile X syndrome (only males).

Appendices Table 7. Study characteristics, quality rating and reported prevalence rate of anxiety in 22q11.2 deletion syndrome

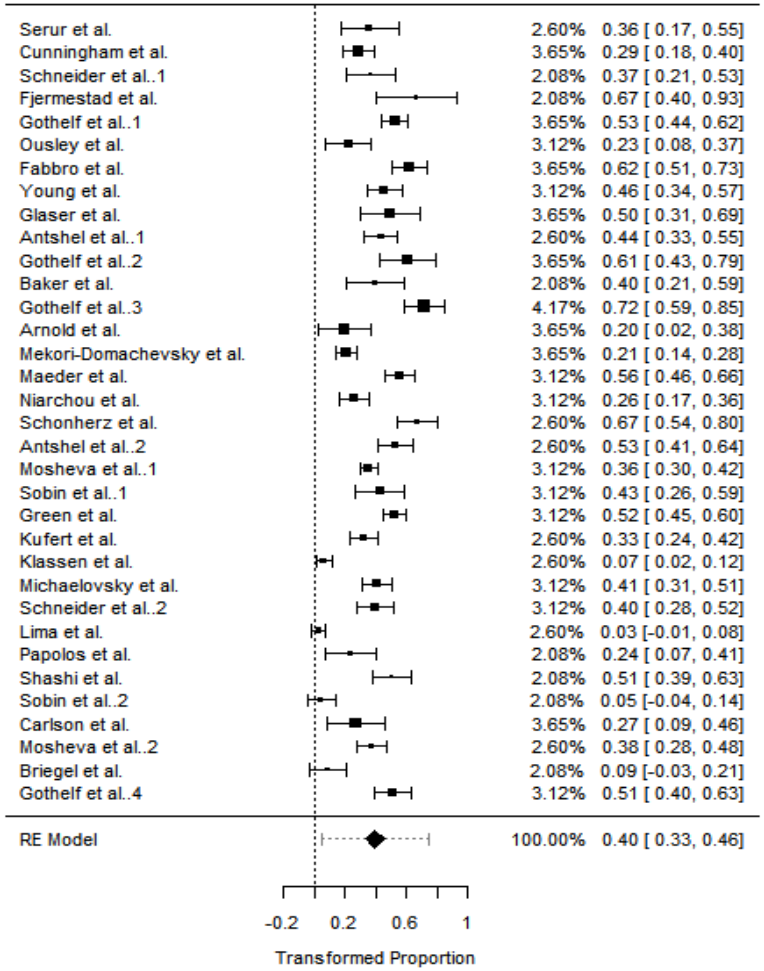
	Quality criteria								Outcome data	
Authors	Sample	Syndrome	Anxiety	N	Gender	Mean age (SD) Range	Syndrome diagnosis	Anxiety measure	% Anxiety (N)	Quality weighting
1.Serur et al. 2019				25	18 m, 7 f	5.57 (1.55), 3-8	Genetic testing	K-SADS	36 (9)	0.56
2. Cunningham et al. 2018				70	41 m, 29 f	11.2 (2.2), 6.2-14.87	Genetic testing	CAPA	29 (20)[10]	0.78
3. Schneider et al. 2017				35	14 m, 21 f	18.06 (3.40), NR	Genetic testing	Not reported	37.1 (13)	0.44
4. Fjermestad et al. 2015				12	3 m, 9 f	14.5 (1.4), 12-17	Not reported	K-SADS-PL	66.7 (8)	0.44
5. Gothelf et al. 2013				125	59 m, 66 f	15.1 (8.4), 5-49	Genetic testing	K-SADS-PL/SCID/DICA-IV	52.8 (66)	0.78
6. Ousley et al. 2013				31	14 m, 17 f	19.3 (4.1), 14-29	Genetic testing	SCID-I	22.6 (7)	0.67
7. Fabbro et al. 2012				74	36 m, 38 f	11.9 (3.35), 6-18	Genetic testing	DICA-IV	62.2 (46)	0.78
8. Young et al. 2011				72	NR	10.49 (2.6), 6-16	Genetic testing	C-DISC	45.8 (33)	0.67
9. Glaser et al. 2010				26	9 m, 17 f	12.36 (NR), 8-15	DNA analysis/Genetic testing	K-SADS-PL/SCID/DICA-IV	50 (13)	0.78
10. Antshel et al. 2010				80	NR	11.9 (2.2), range NR	Not reported	K-SADS-PL	43.8 (35)	0.56
11. Gothelf et al. 2007				28	18 m, 10 f	12.5 (3.9), range NR	Genetic testing	C-DISC & K-SADS-PL	60.7 (17)	0.78

12. Baker et al. 2005	25	15 m, 10 f	16.4 (2.0), range NR	Not reported	CAPA	40 (10)	0.44
13. Gothelf et al. 2004	43	25 m, 18 f	18.3 (10.6), 6-40	Genetic testing	K-SADS-PL/SCID-P/Y-BOCS	72.1 (31)	0.89
14. Arnold et al. 2001	20	9 m, 11 f	11 (NR), 6-20	Genetic testing	K-SADS-E & OCHS-R	20 (4)	0.78
15. Mekori-Domachevsky et al. 2017	119	75 m, 44 f	16.51 (2.71), 12.1-22	Genetic testing	NIMH K-SADS-PL/SCID	21 (25)	0.78
16. Maeder et al. 2016	95	45 m, 50 f	12.80 (4.23), range NR	Genetic testing	DICA-R/SCID-I	55.8 (53)	0.67
17. Niarchou et al. 2014	80	40 m, 40 f	10.2 (2.1), 6.6-14.1	Genetic testing confirmed	CAPA	26.3 (21)	0.67
18. Schonherz et al. 2014	49	27 m, 22 f	10.9 (4.9), 5.5-20.9	Genetic testing	K-SADS-PL/SCID	67.3(33)	0.56
19. Antshel et al. 2013	72	37 m, 35 f	15 (2.1), range NR	Genetic testing	K-SADS-PL	52.8 (38)	0.56
20. Mosheva et al. 2019	260	134 m, 126 f	21.3 (10.8), 5-59	Genetic testing	K-SADS-PL/SCID	35.8 (93)	0.67
21. Sobin et al. 2009	51	26 m, 25 f	9.4 (2.8), 5.3-17.2	Genetic testing	DISC-IV	42.9 (15)[11]	0.67
22. Green et al. 2009	172	90 m, 82 f	15.9 (9.1), 5-54	DNA analysis/Genetic testing	K-SADS-PL/SCID/DICA	52.3 (90)	0.67
23. Kufert et al. 2016	128	77 m, 51 f	12.9 (11), 1-55	Genetic testing	K-SADS-PL/SCID	32.7 (34)[12]	0.56
24. Klaassen et al. 2012	90	36 m, 54 f	3.47 (1.31), 1.42-5.99	Genetic testing	CBCL	6.7 (6)	0.56
25. Michaelovsky et al. 2012	142	78 m, 64 f	16.1 (9.7), range NR	Genetic testing	K-SADS-PL/SCID	40.8 (38)[13]	0.67

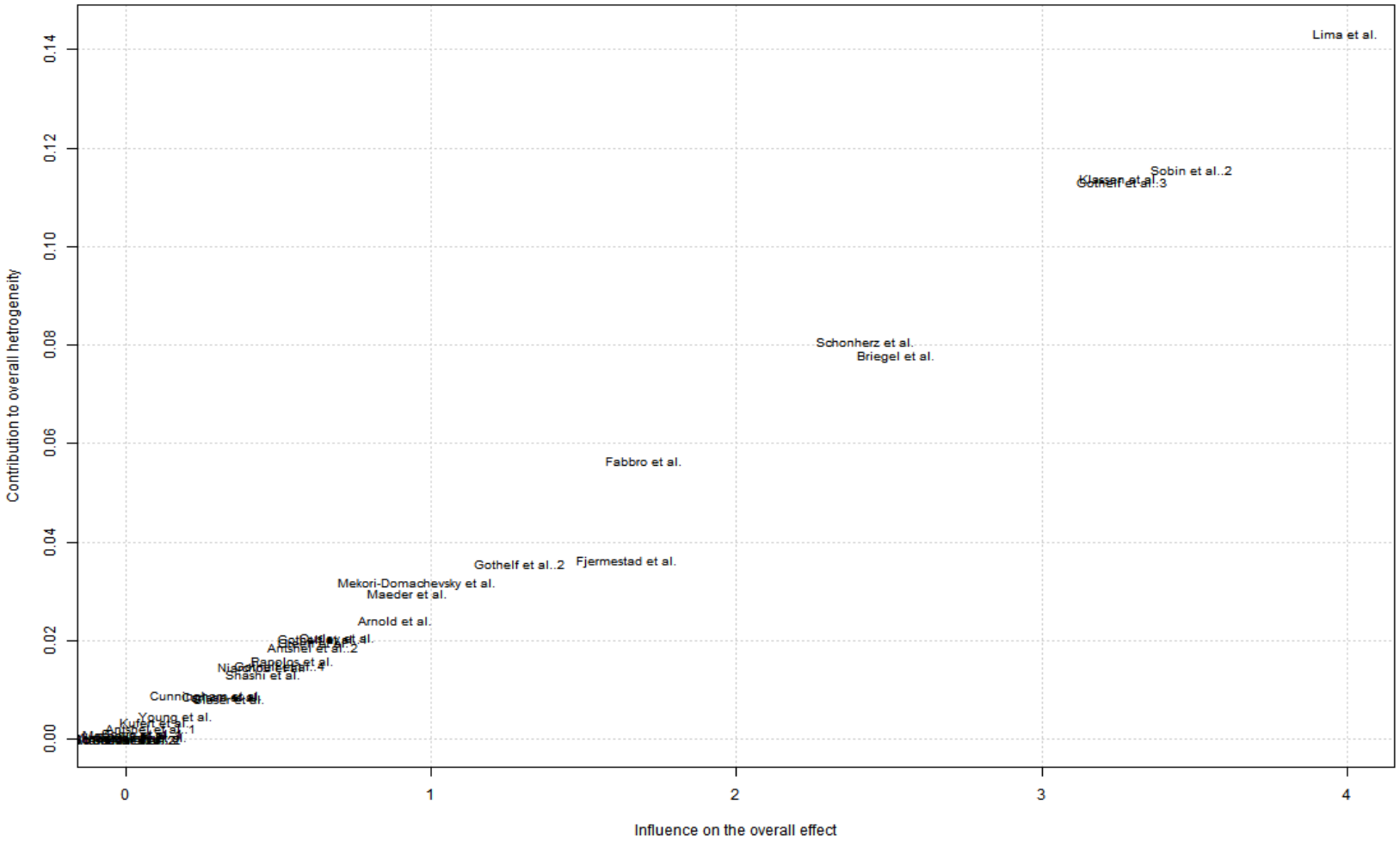
26. Kates et al. 2003	10	7 m, 3 f	10.1 (1.8), range NR	Genetic testing	DICA-IV	18%/18%/54%[14]	0.67
27. Schneider et al. 2014	63	30 m, 33 f	16.96 (4.17), 10-28	Genetic testing	DICA-R/SCID-I	39.7 (25)	0.67
28. Lima et al. 2010	60	28 m, 32 f	Median age: 9, 1-54	Genetic testing	Not reported	3.3 (2)	0.56
29. Papolos et al. 1996	25	13 m, 12 f	15.64 (NR), 5-34	Not reported	DICA-R/SCID	24 (6)	0.44
30. Feinstein et al. 2002	28	18 m, 10 f	12.31 (3.89), 6-19	Genetic testing	CBCL/DICA-P	NR[15]	0.78
31. Shashi et al. 2010	65	34 m, 31 f	10.2 (2.6), range NR	Not reported	CDISC-IV	51 (33)	0.44
32. Sobin et al. 2005	21	10 m, 11 f	10.55 (2.8), range NR[16]	Genetic testing	CSI-4 & DISC-IV	4.8 (1)	0.44
33. Carlson et al. 1997	26	13 m, 13 f	15.5 (NR), 5-34	Genetic testing	DICA/SCID	27.3 (6)[17]	0.78
34. Mosheva et al. 2017	90	48 m, 42 f	29.8 (10.3), 18-67	Genetic testing	SCID	37.8 (34)	0.56
35. Briegel et al. 2006	22	12 m, 10 f	2 years 9 months (NR), 1 year 8 months-3 years 11 months	Genetic testing	CBCL	9.1 (2)[18]	0.44
36. Gothelf et al. 2007	79	50 m, 29 f	15.1 (11), 1.5-55	Genetic testing	K-SADS-PL/SCID	51.4 (36)[19]	0.67

NR=Not reported, K-SADS=Kiddie Schedule of Affective Disorders and Schizophrenia, CAPA=Child and Adolescent Psychiatric Assessment Interview, NR=not reported, K-SADS-PL=Kiddie Schedule of Affective Disorders and Schizophrenia-Present and Lifetime Version, SCID=Structured Clinical Interview for Axis I DSM-IV, DICA-IV=Diagnostic Interview for Children and Adolescents-Revised, C-DISC=Computerized Diagnostic Interview Schedule for Children, Y-BOCS=Yale-Brown Obsessive Compulsive Scale, K-SADS-E=Kiddie Schedule of Affective Disorders and Schizophrenia-Epidemiological Version, OCHS-R=Ontario Child Health Study-Revised, NIMH K-SADS=NIMH Genetic Epidemiology Research Branch Kiddie-SADS

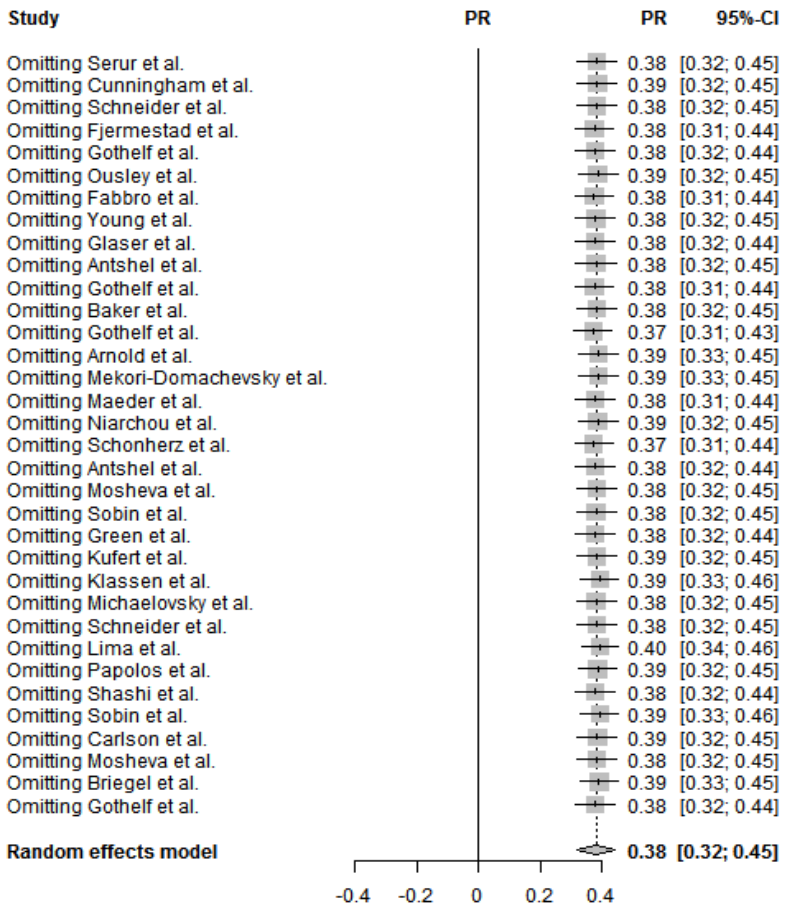
[10] Based on 69 participants
[11] Based on 35 participants
[12] Based on 104 participants
[13] Based on 93 participants
[14] Paper not included in meta-analysis due to (n) for anxiety being unknown after contact with author. Percentages for generalised anxiety disorder, obsessive-compulsive disorder and simple phobias respectively
[15] Paper does not report 'any anxiety' prevalence and so is not included in the 'any anxiety' analysis. However, the paper is included in the specific anxiety disorder meta-analyses
[16] Means and standard deviations reported separately for males and females. Males as reported above. Females: 10.34 (2.4), range NR
[17] Based on 22 participants due to bias in recruitment of 4 participants
[18] Although 1 participant was identified as a 'borderline clinical case', they were included in the analysis due to the display of anxiety symptomatology
[19] Based on 70 participants, psychiatric assessment included only subjects with age ≥ 4 years



Appendices Figure 8. Forest plot for anxiety in 22q11.2 deletion syndrome using a quality-effects model.



Appendices Figure 9. Baujat chart used to identify sources of heterogeneity: 22q11.2 deletion syndrome.



Appendices Figure 10. “Leave one out” analysis for 22q11.2 deletion syndrome.

Appendices Table 8. Study characteristics, quality rating and reported prevalence rate of anxiety in Down syndrome

	Quality criteria								Outcome data	
Authors	Sample	Syndrome	Anxiety	N	Gender	Mean age (SD) Range	Syndrome diagnosis	Anxiety measure	% Anxiety (N)	Quality weighting
1. Esbensen et al. 2018				88	54 m, 34 f	11.35 (3.02), 6-18	Not reported	CBCL	24.6 (17)[20]	0.33
2. Moss et al. 2016[21]				117	50 m, 67 f	22.6 (13), 4-62	Not reported	SQID	7.5 (8)[22]	0.33
3. Tasse et al. 2016				291	154 m, 137 f	33.7 (12.5), 18-79	Parent report of genetic confirmation	Parent/self-report	6.8 (20)	0.44
4. Mantry et al. 2008				186	91 m, 95 f	41.1 (11.8), 16-74	"Almost all had cytogenetic testing"	PPS-LD & clinical consensus	2.7 (5)	0.78
5. Mallardo et al. 2014				49	28 m, 21 f	26.75 (NR), 20.3-31.3	Not reported	PAS-ADD	18.4 (9)	0.22
6. Patti & Tsiouris, 2006[23]				206	115 m, 91 f	47.4 (10.41), 20-71	Chromosomal studies	DSM-IV criteria	43.2 (89)	0.44
7. Glenn et al. 2013				125	62 m, 63 f	30 years 5 months (7), 18-43	Not reported	ICD-10 criteria	9.6 (12)	0.33
8. Myers & Pueschel, 1991				497	288 m, 209 f	19.4 (13.3), 1-72	97% (483) had cytogenetic/chromosome analysis	DSM-III-R criteria	1.8 (9)	0.56

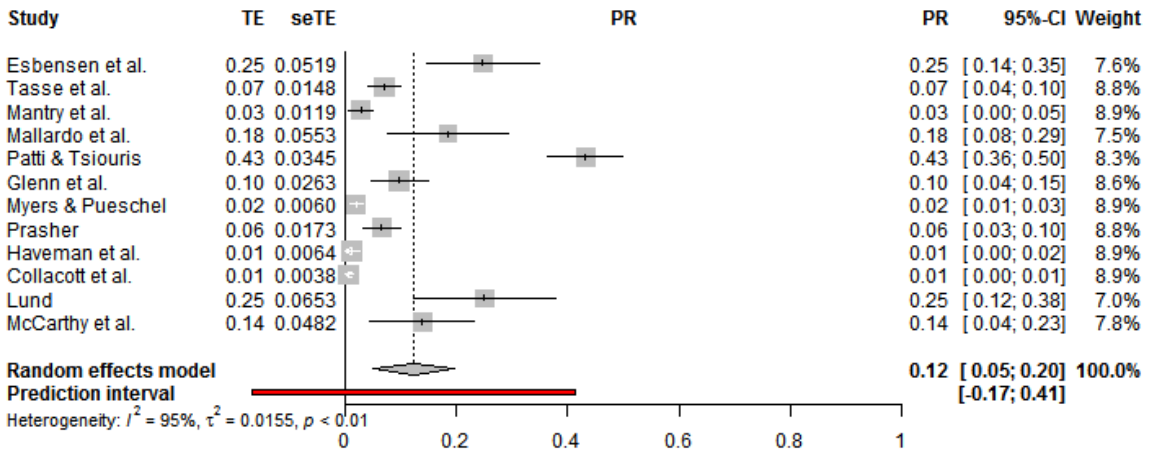
[20] Based on 69 participants data
[21] Paper not included in 'any anxiety' meta-analysis as not reported. Paper included specific anxiety disorder meta-analysis (selective mutism)
[22] Selective mutism prevalence based on 106 participants
[23] Paper identified as highly heterogeneous with the rest of the literature and having a disproportionate influence on the overall effect (top right-hand corner of the Baujat chart: see below). Paper re-reviewed and potential bias identified that may have an impact on reported anxiety prevalence. Recruitment based on referral to a clinic due to changes in behaviour/functioning. Paper removed from final meta-analysis.

9. Prasher, 1995	201	102 m, 99 f	40.9 (11.64), 16-72[24]	85.1% (171) had cytogenetic testing	DCR-10	6.5 (13)	0.56
10. Way & Rojahn, 2012[25]	14	3 m, 11 f	9.8 (1.9), 6.3-11.8	Karyotype analysis	Parent report	0 (0)	0.44
11. Haveman et al. 1994	268	Not reported	Not reported	Medical checklist by GP	Medical checklist by GP	1.1 (3)	0.33
12. Collacott et al. 1992	371	53% male	36.34 (11.25), 16-78	Health service records	Based on records and ICD-9 criteria	0.3 (1)[26]	0.33
13. Lund, 1988	44	23 m, 21 f	Not reported	Diagnosed on a clinical or chromosomal basis	Research psychiatric diagnostic criteria	25 (11)	0.44
14. McCarthy et al. 2001	52	28 m, 24 f	26.63 (3.45), 22-33	Not reported	PAS-ADD based on ICD-10 criteria	13.7 (7)[27]	0.22

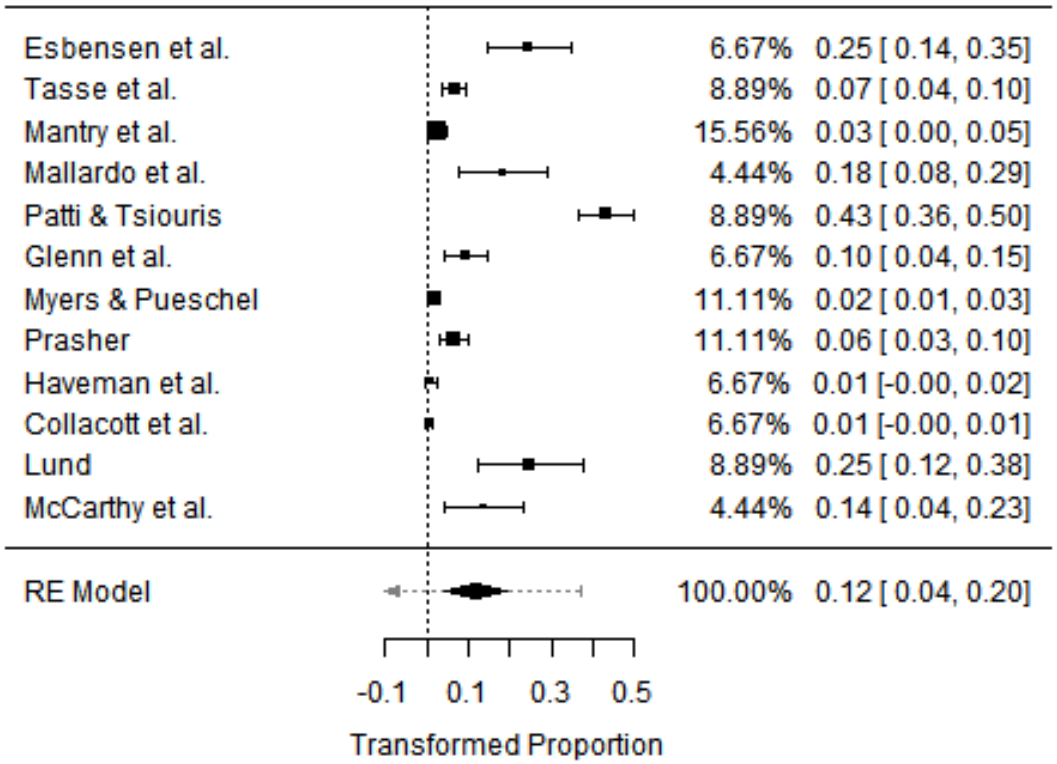
PPS-LD=Present Psychiatric State for Adults with Learning Disability, PAS-ADD=Psychiatric Assessment Schedule for Adults with Developmental Disabilities, DCR-10=Diagnostic Criteria for Research

[20] Based on 69 participants data
[21] Paper not included in 'any anxiety' meta-analysis as not reported. Paper included specific anxiety disorder meta-analysis (selective mutism)
[22] Selective mutism prevalence based on 106 participants
[23] Paper identified as highly heterogeneous with the rest of the literature and having a disproportionate influence on the overall effect (top right-hand corner of the Baujat chart: see below). Paper re-reviewed and potential bias identified that may have an impact on reported anxiety prevalence. Recruitment based on referral to a clinic due to changes in behaviour/functioning. Paper removed from final meta-analysis.
[24] Age means and standard deviations reported separately for males and females. Males as reported above. Females: 43.6 (13.26), 16-76

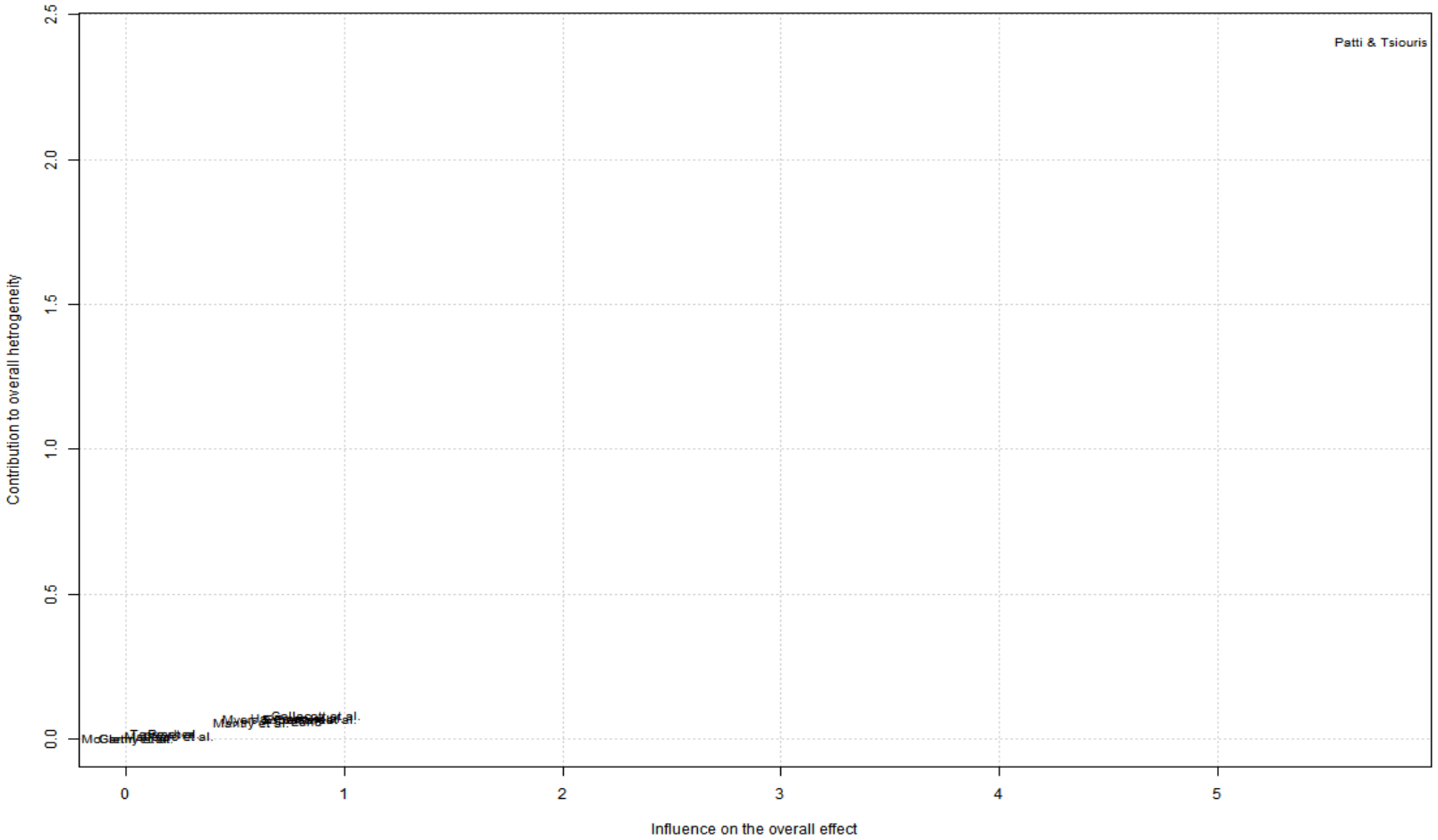
[25] Paper not included in meta-analysis due to potential underpowered sample that failed to detect an effect, anxiety prevalence was 0% based on *n*=14
[26] A continuity correction of 0.5 was added to the event rate to avoid division by zero errors, as the sample size was deemed sufficient to provide a valid estimation of anxiety prevalence
[27] Prevalence based on 51 participants



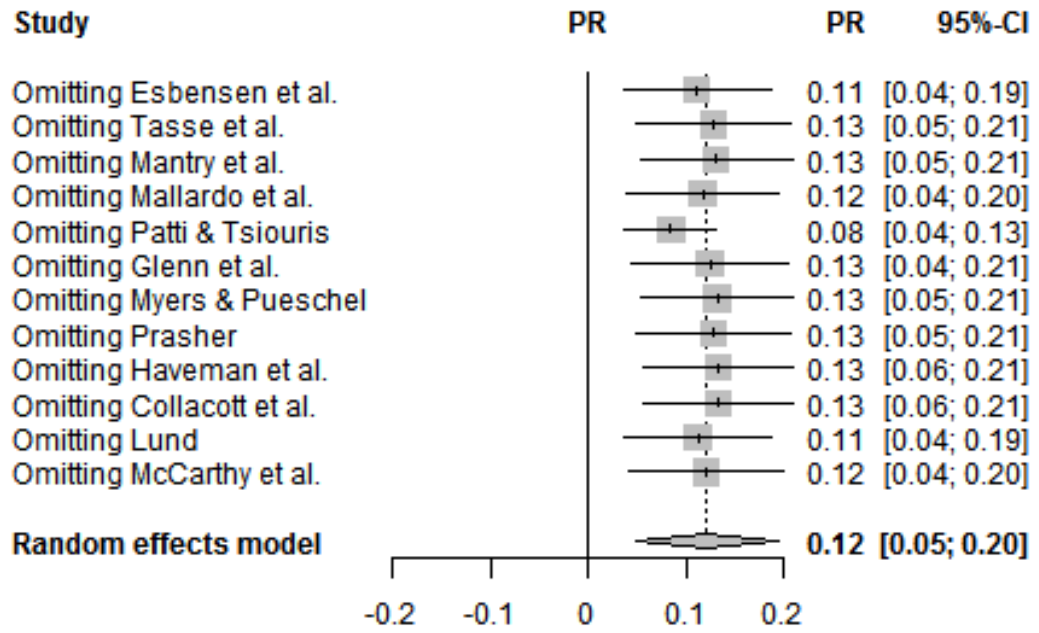
Appendices Figure 11. Forest plot for anxiety in Down syndrome using a random-effects model.



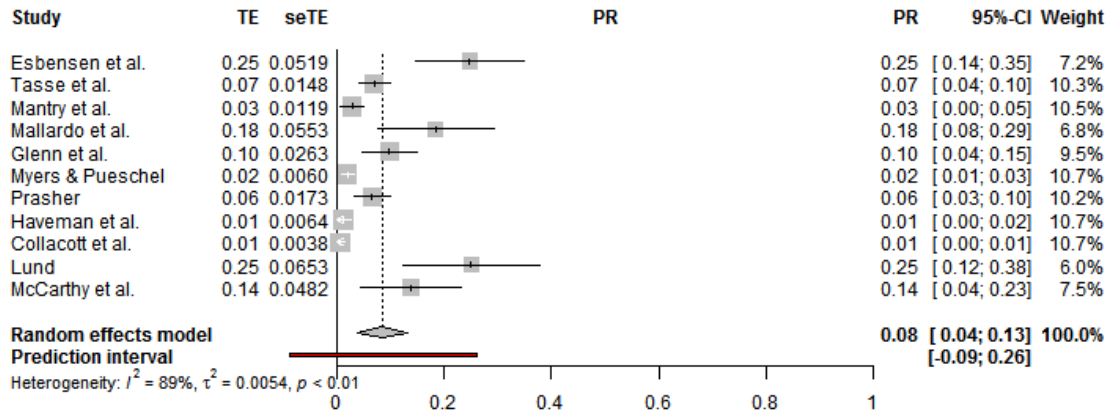
Appendices Figure 12. Forest plot for anxiety in Down syndrome using a quality-effects model



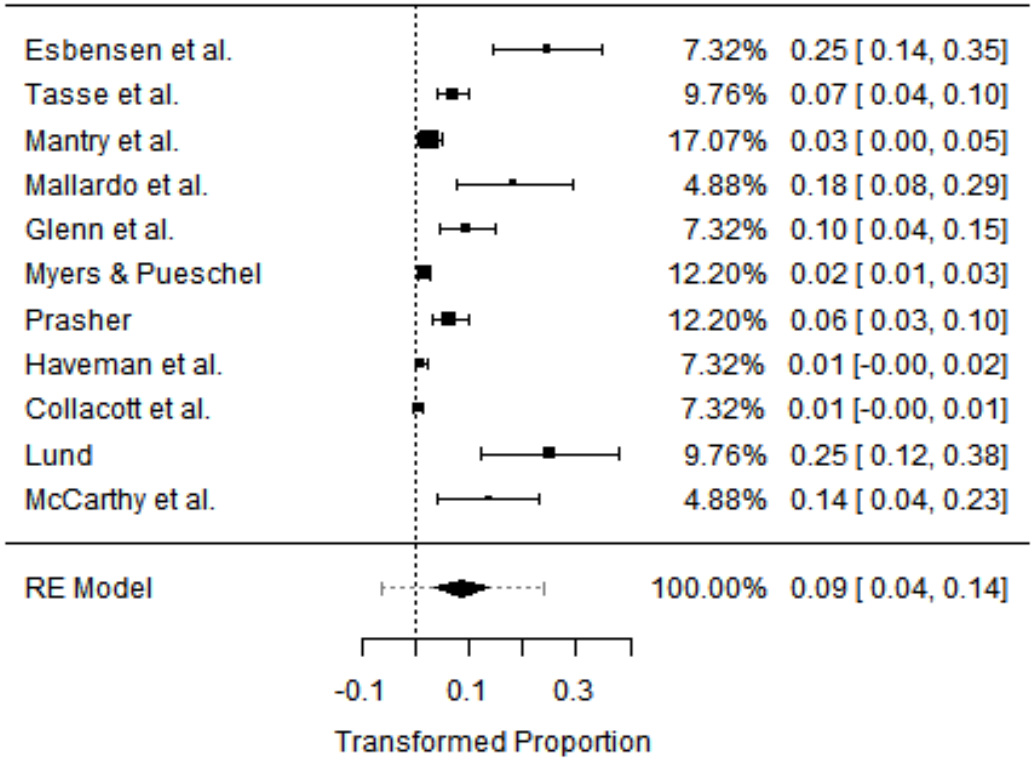
Appendices Figure 13. Baujat chart used to identify sources of heterogeneity: Down syndrome.



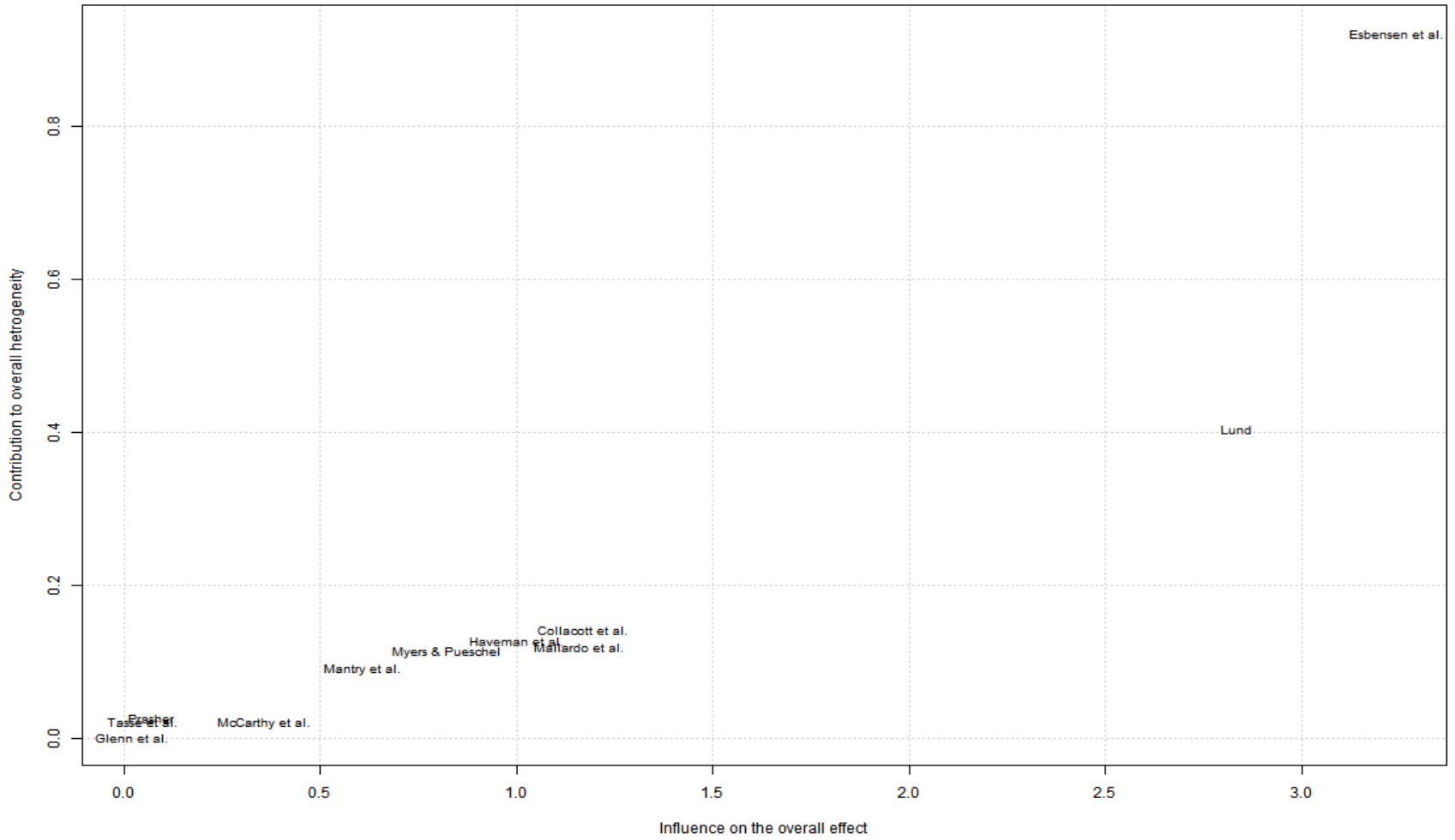
Appendices Figure 14. “Leave one out” analysis for Down syndrome.



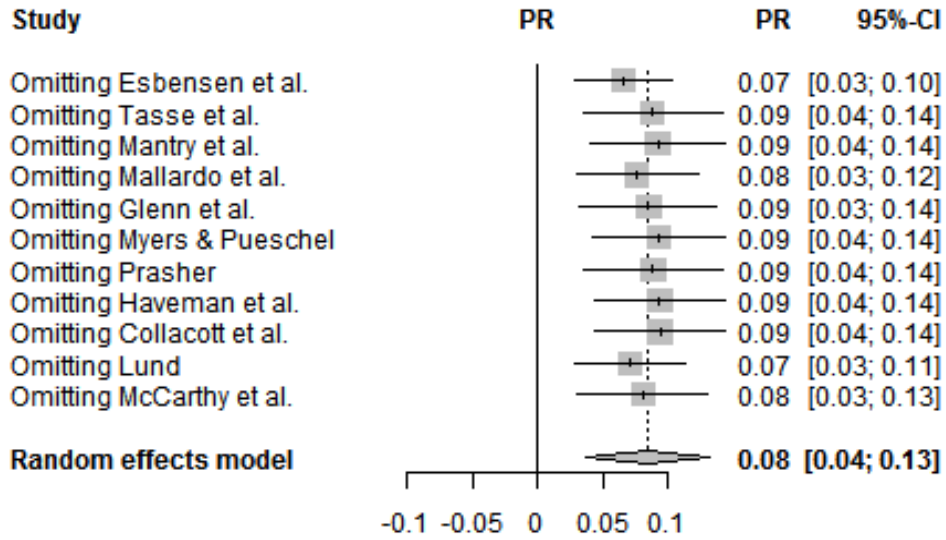
Appendices Figure 15. Forest plot for anxiety in Down syndrome using a random-effects model (final analysis with removal of Patti & Tsiouris)



Appendices Figure 16. Forest plot for anxiety in Down syndrome using a quality-effects model (final analysis with removal of Patti & Tsiouris)



Appendices Figure 17. Baujat chart used to identify sources of heterogeneity: Down syndrome (final analysis with removal of Patti & Tsiouris)



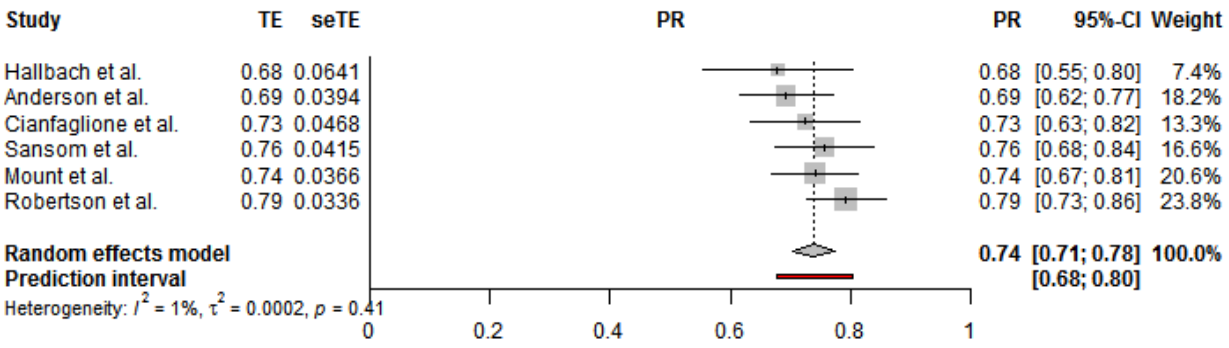
Appendices Figure 18. “Leave one out” analysis for Down syndrome (final analysis with removal of Patti & Tsiouris)

Appendices Table 9. Study characteristics, quality rating and reported prevalence rate of anxiety in Rett syndrome

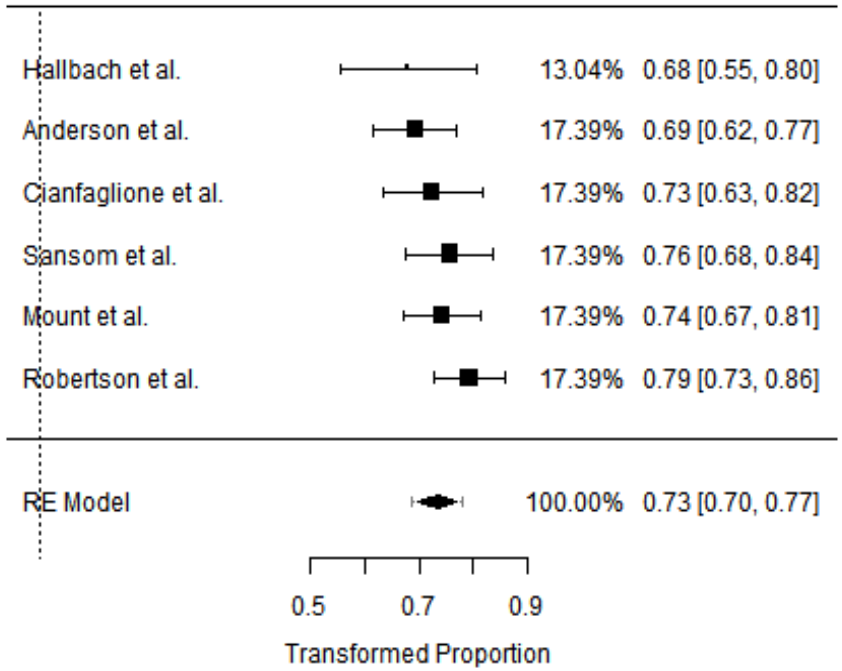
	Quality criteria								Outcome data	
Authors	Sample	Syndrome	Anxiety	N	Gender	Mean age (SD) Range	Syndrome diagnosis	Anxiety measure	% Anxiety (N)	Quality weighting
1. Halbach et al. 2008				53	53 f	26.9 (7.85), 16-53	All with clinical diagnosis confirmed by experienced clinicians 70% (37) had genetic analysis	Parent report	67.9 (36)	0.33
2. Anderson et al. 2014				423	423 f	Mean & SD NR, Median: 24.9, 18-54.3	Confirmed using consensus diagnostic criteria or genetic testing	RSBQ	69.3 (95)[28]	0.44
3. Cianfaglione et al. 2015				91	91 f	20.5 (NR), 4-47	Pediatrician, clinical geneticist, another professional	RSBQ	72.5 (66)	0.33
4. Sansom et al. 1993				107	107 f	10.6 (5.4), 2.2-28	Confirmed by specialist pediatricians	Parent report	75.7 (81)	0.44
5. Mount et al. 2002				143	143 f	10.3 (4.7), range NR	Specialist pediatrician, clinical geneticist	RSBQ	74.1 (106)	0.44
6. Robertson et al. 2006				145	145 f	14.1 (6.2), 2.8-27.4[29]	Genetic testing in 93% (135) of sample	RSBQ	79.3 (115)	0.44

RSBQ=Rett Syndrome Behaviour Questionnaire

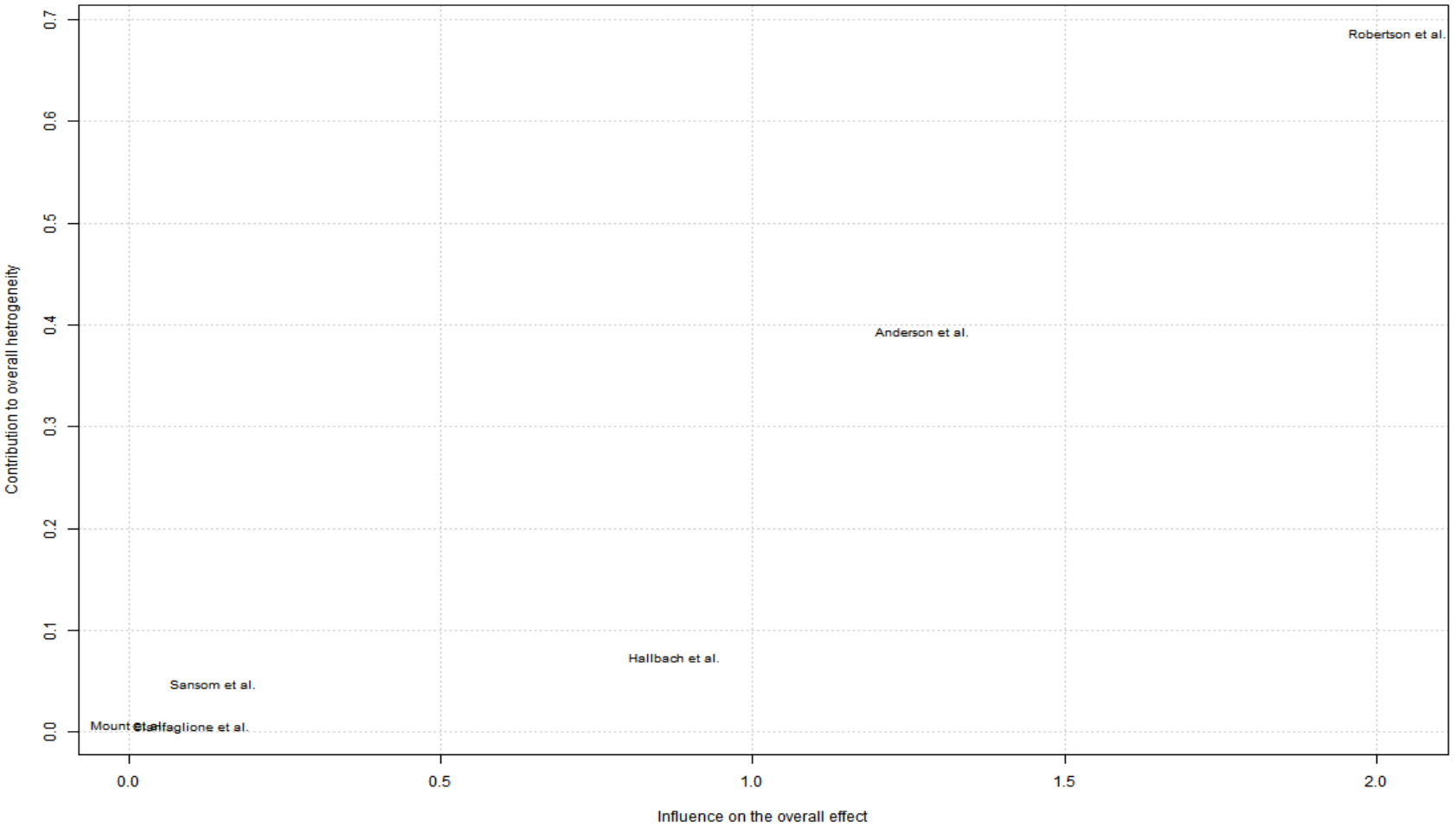
[28] Anxiety prevalence based on 137 participants
[29] Based on 135 participants



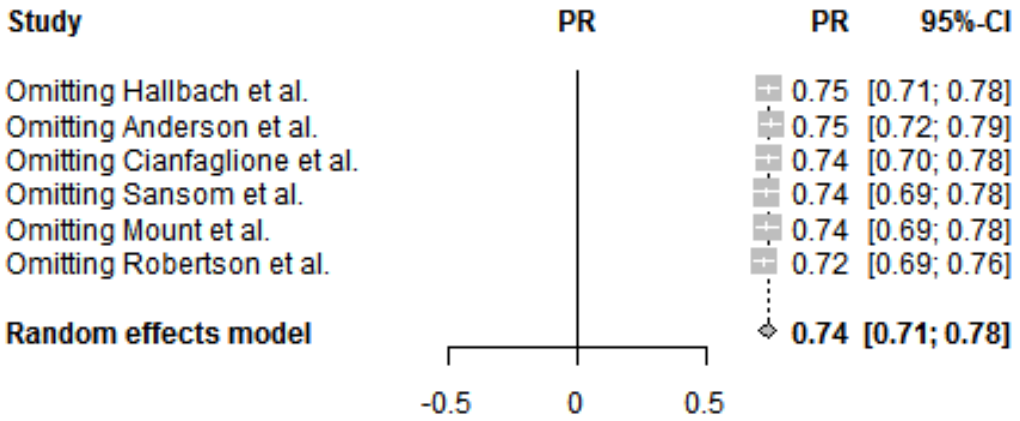
Appendices Figure 19. Forest plot for anxiety in Rett syndrome using a random-effects model.



Appendices Figure 20. Forest plot for anxiety in Rett syndrome using a quality-effects model.



Appendices Figure 21. Baujat chart used to identify sources of heterogeneity: Rett syndrome.

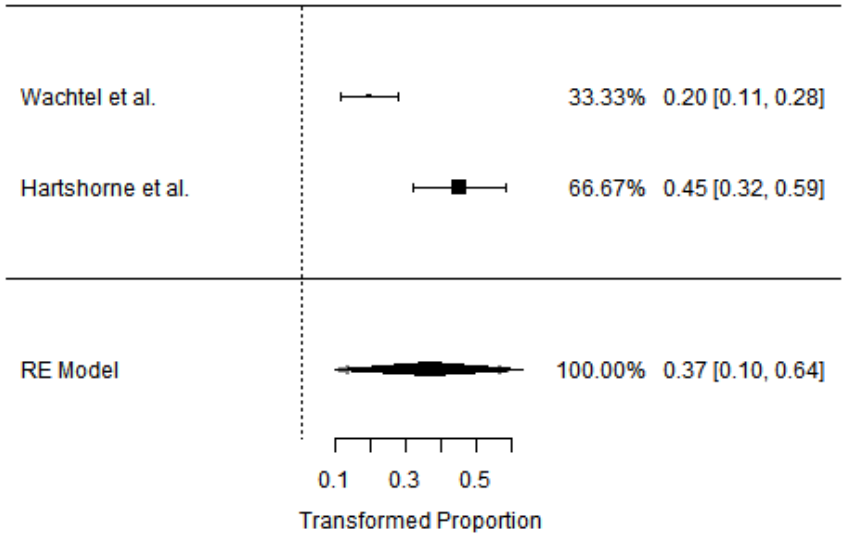


Appendices Figure 22. “Leave one out” analysis for Rett syndrome.

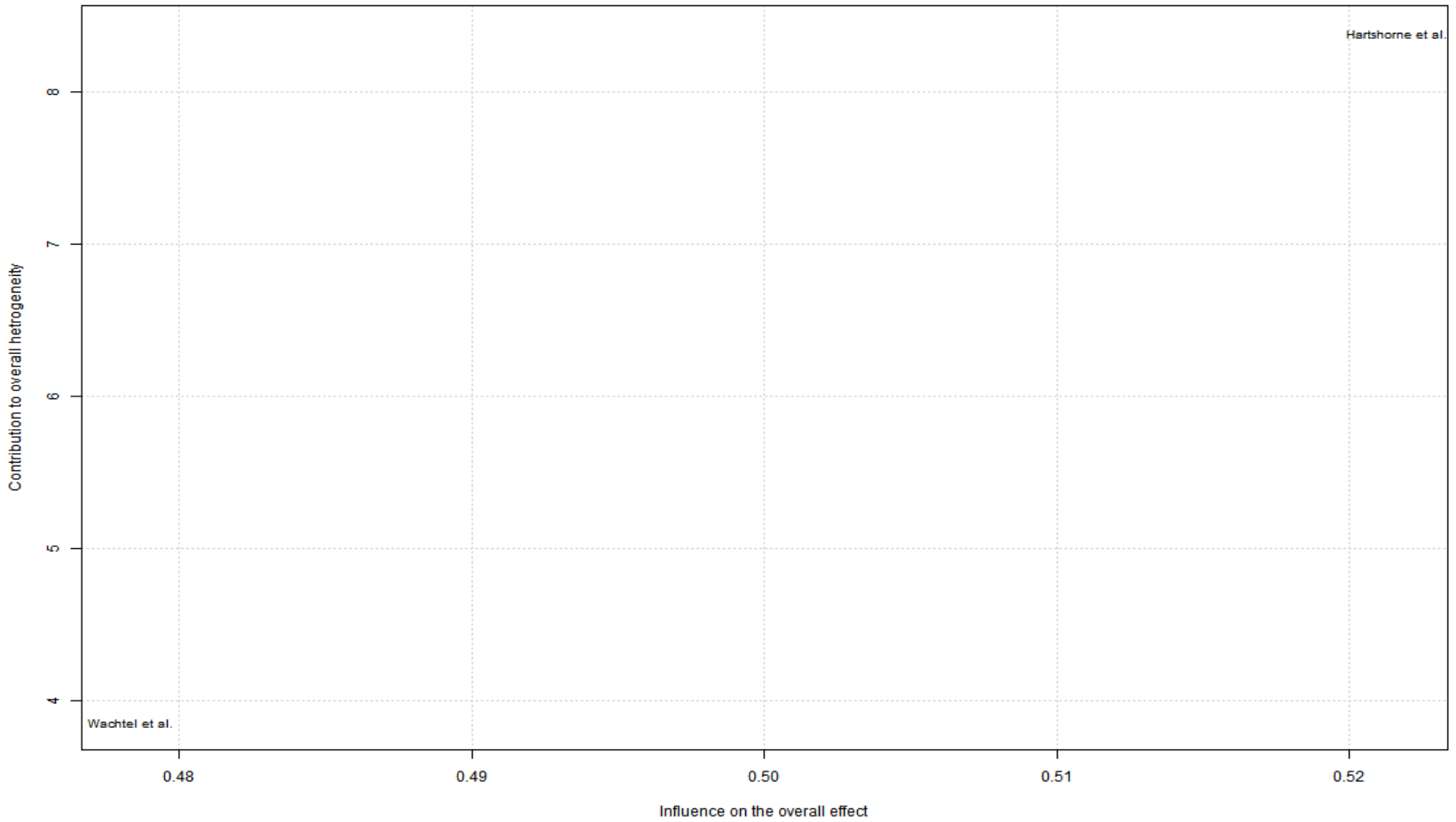
Appendices Table 10. Study characteristics, quality rating and reported prevalence rate of anxiety in CHARGE syndrome

	Quality criteria								Outcome data	
Authors	Sample	Syndrome	Anxiety	N	Gender	Mean age (SD) Range	Syndrome diagnosis	Anxiety measure	% Anxiety (N)	Quality weighting
1. Bernstein & Denno, 2005				29	29 m, 15 f	Mean & SD NR, 3-21	Not reported	Author judgment	72.4 (21)[30]	0.22
2. Wachtel et al. 2007				87	52 m, 35 f	11.1 (3.66), 6-18	Not reported	Parent report	19.5 (17)	0.11
3. Hartshorne et al. 2016				53	33 m, 20 f	Mean & SD NR, 13-39	Not reported	Parent report	45 (24)	0.22
4. Hartshorne et al. 2004				100	43 m, 56 f	Mean & SD NR, Median: 7, 1-30	Not reported	Parent report	3 (3)[31]	0.22

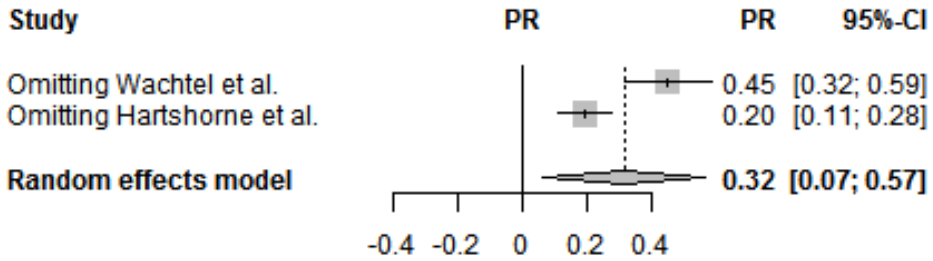
[30] Anxiety prevalence is based on obsessive-compulsive disorder (OCD) prevalence only. No other anxiety disorder diagnoses were reported. Only included in OCD meta-analysis.
[31] Anxiety prevalence is based on obsessive-compulsive disorder (OCD) prevalence only. No other anxiety disorder diagnoses were reported. Only included in OCD meta-analysis.



Appendices Figure 23. Forest plot for anxiety in CHARGE syndrome using a quality-effects model.



Appendices Figure 24. Baujat chart used to identify sources of heterogeneity: CHARGE syndrome.



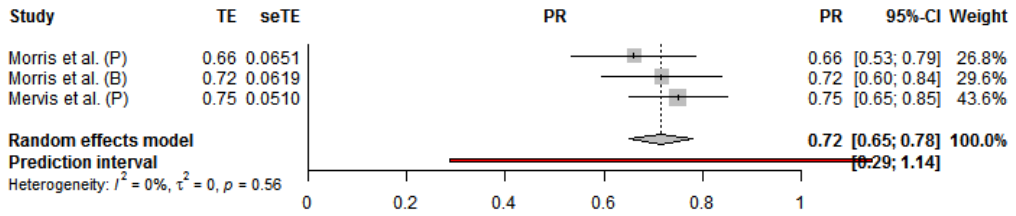
Appendices Figure 25. “Leave one out” analysis for CHARGE syndrome.

Appendices Table 11. Study characteristics, quality rating and reported prevalence rate of anxiety in 7q11.23 duplication syndrome

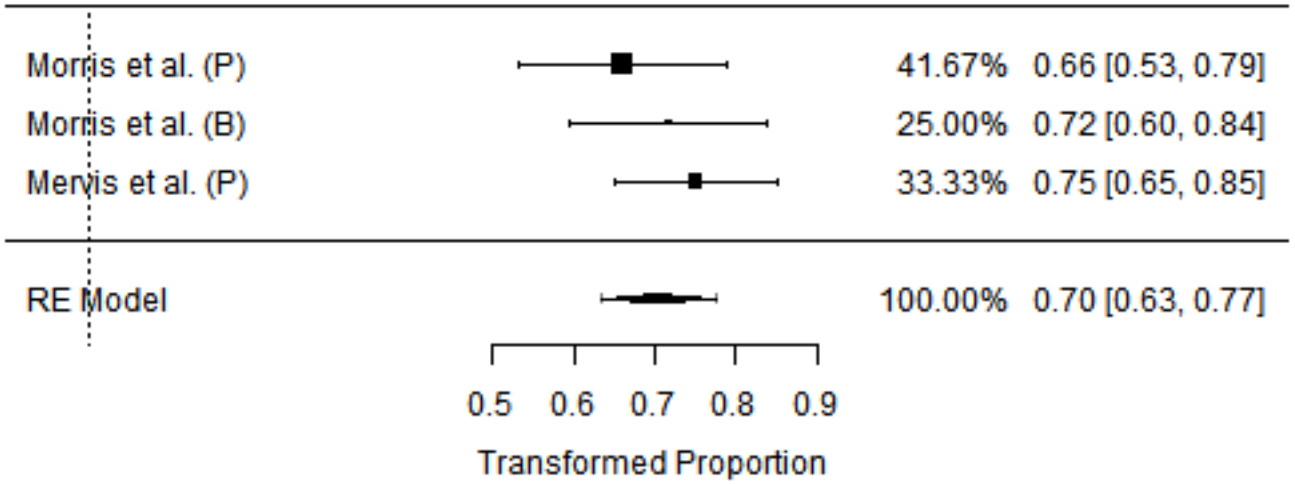
	Quality criteria								Outcome data	
Authors	Sample	Syndrome	Anxiety	N	Gender	Mean age (SD) Range	Syndrome diagnosis	Anxiety measure	% Anxiety (N)	Quality weighting
1. Morris et al. 2015[32]				64	30 m, 34 f	8.12 (4.87), 1.25-21.25[33]	Genetic testing	Parent report	71.7 (38)[34]	0.33
1b. Morris et al. 2015				64	30 m, 34 f	8.12 (4.87), 1.25-21.25	Genetic testing	ADIS-P/ADIS-IV	66 (35)[35]	0.56
2. Mervis et al. 2015				75	41 m, 34 f	8.80 (3.68), 4.01-17.76[36]	Genetic testing for "almost all"	ADIS-P/ADIS-IV	75 (54)[37]	0.44
3. Mervis et al. 2012[38]				27	15 m, 12 f	7.78 (2.78), 4.03-12.93	Genetic testing	ADIS-P and CBCL	30 (8)	0.67

ADIS-P=Anxiety Disorders Interview Schedule Parent interview

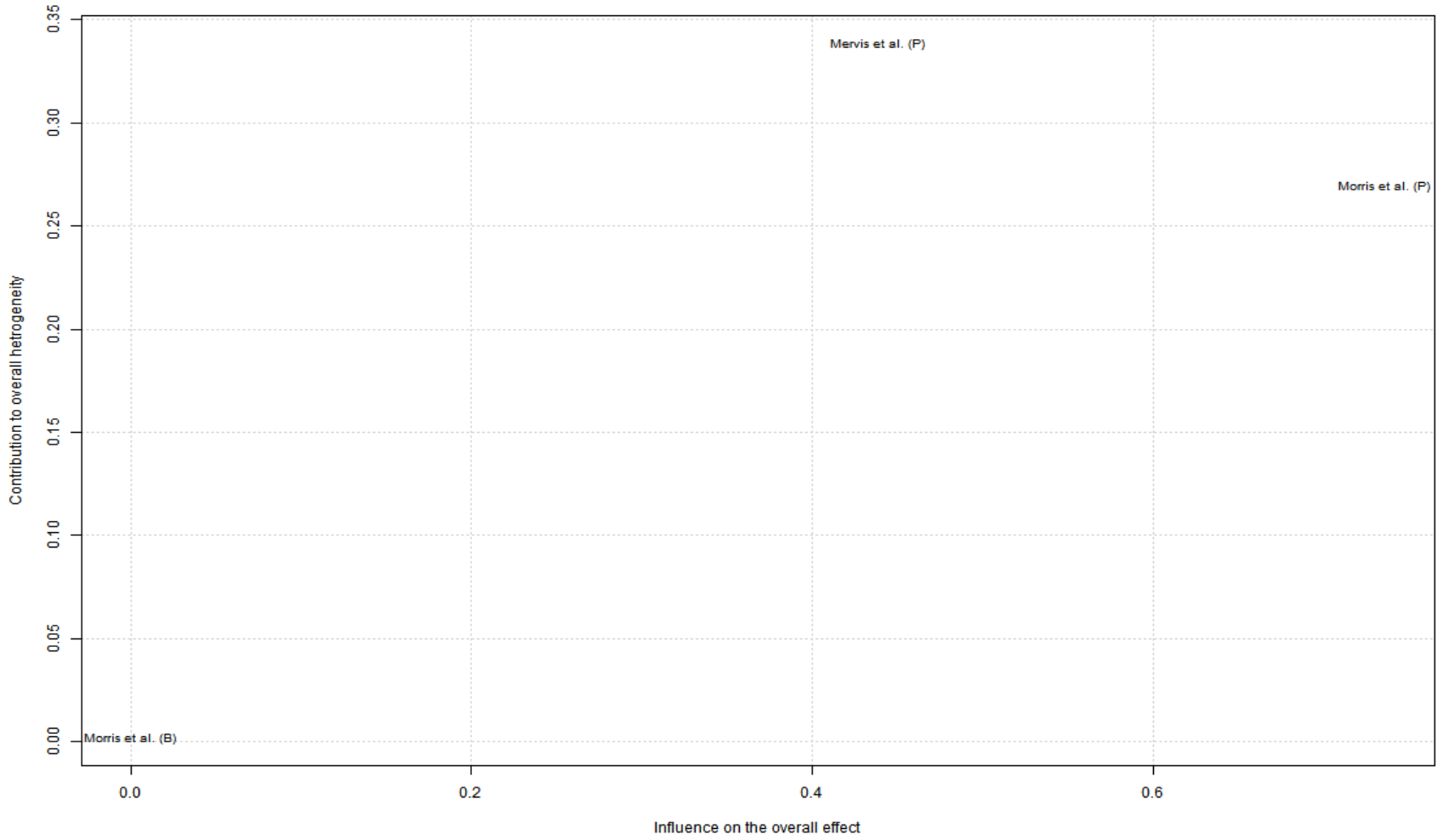
[32] Paper reports anxiety prevalence on a behavioural (1) and psychiatric level (1b). Separate meta-analyses were conducted for behavioural and psychiatric prevalence
[33] Age means and standard deviations only reported for children in the sample (*n*=53). Not reported for adults (*n*=11)
[34] Anxiety prevalence calculated based on 53 participants (parent report of anxiety based on participants aged 21 years or younger)
[35] Anxiety prevalence calculated based on 53 participants (psychiatric report of anxiety from 46 parents of children and 7 adults with 7q11 duplication syndrome)
[36] Age means and standard deviations reported separately for children (*n*=63) and adults (*n*=12). Child data reported above. Adult: 36.39 (9.13), 27.47-61.05
[37] Anxiety prevalence calculated based on 72 participants (children: *n*=62; adults: *n*=10)
[38] Paper only included in specific anxiety disorder meta-analysis (separation anxiety disorder) as no prevalence reported for 'any anxiety'



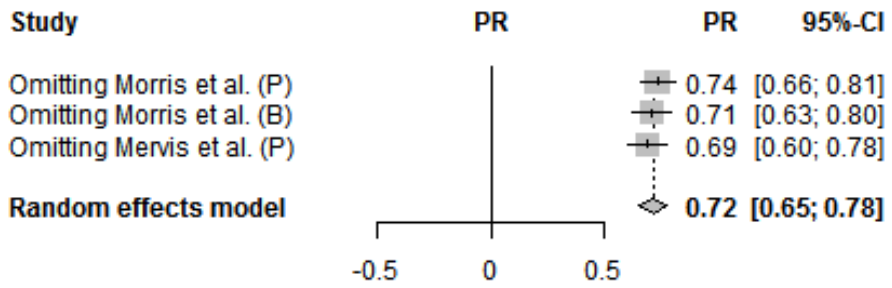
Appendices Figure 26. Forest plot for anxiety in 7q11.23 duplication syndrome using a random-effects model.



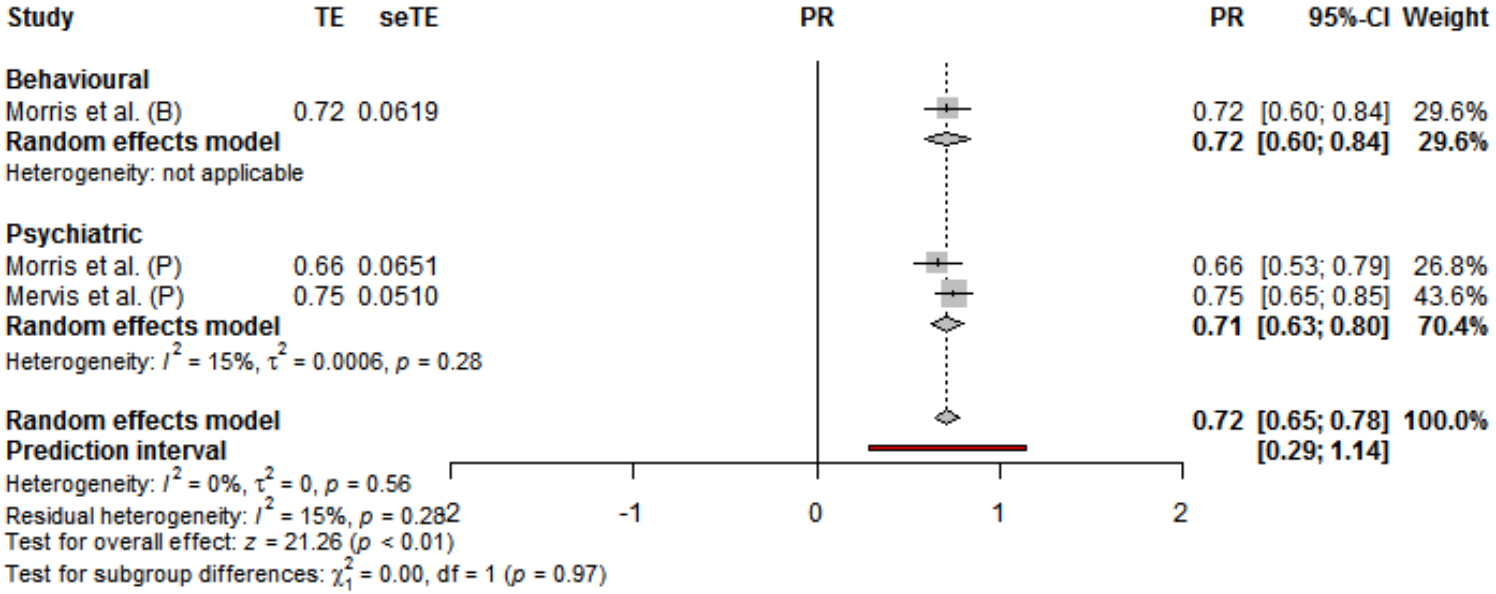
Appendices Figure 27. Forest plot for anxiety in 7q11.23 duplication syndrome using a quality-effects model.



Appendices Figure 28. Baujat chart used to identify sources of heterogeneity: 7q11.23 duplication syndrome.



Appendices Figure 29. “Leave one out” analysis for 7q11.23 duplication syndrome.

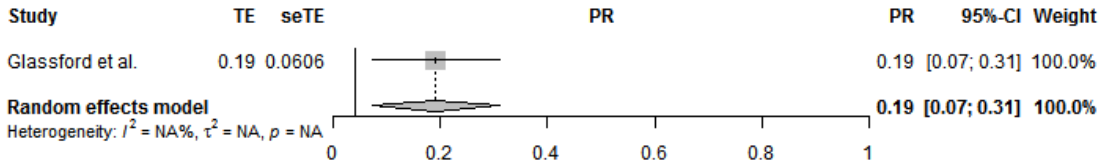


Appendices Figure 30. Between groups test for behavioural and psychiatric reports of anxiety in 7q11.23 duplication syndrome.

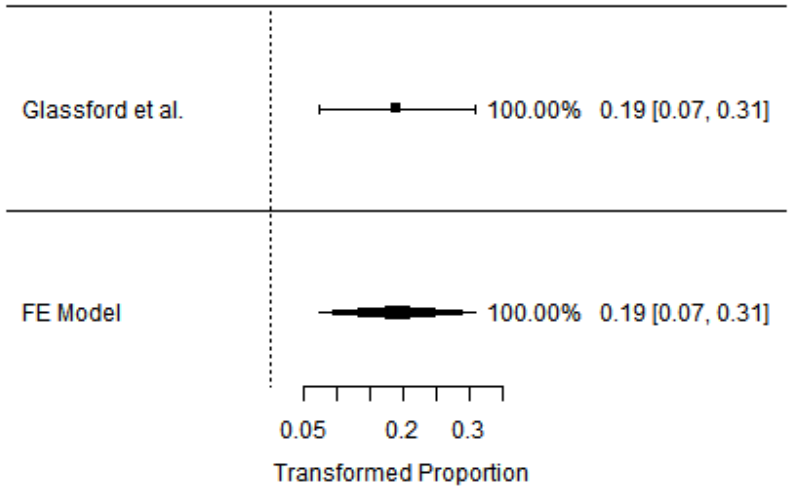
Appendices Table 12. Study characteristics, quality rating and reported prevalence rate of anxiety in 3q29 deletion syndrome

	Quality criteria								Outcome data	
Authors	Sample	Syndrome	Anxiety	N	Gender	Mean age (SD) Range	Syndrome diagnosis	Anxiety measure	% Anxiety (N)	Quality weighting
1. Glassford et al. 2018				44	29 m, 15 f	11.1 (NR), <1-76	Genetic testing confirmed for 25% (11) of sample	Parent report	19 (8)[39]	0.33

[39] Anxiety prevalence based on 42 participants



Appendices Figure 31. Forest plot for anxiety in 3q29 deletion syndrome using a random-effects model.



Appendices Figure 32. Forest plot for anxiety in 3q19 deletion syndrome using a quality-effects model.

Appendices Table 13. Study characteristics, quality rating and reported prevalence rate of anxiety in Tuberous Sclerosis Complex

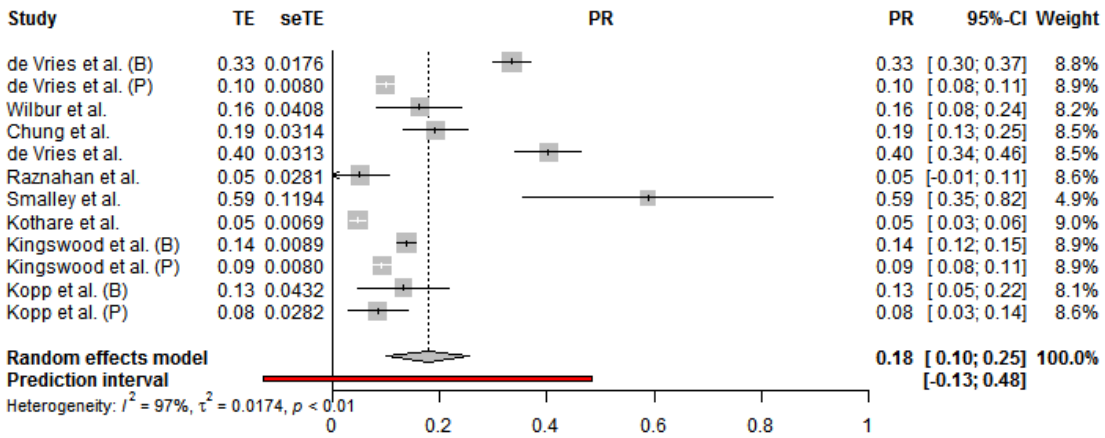
	Quality criteria									Outcome data	
Authors	Sample	Syndrome	Anxiety	N	Gender	Mean age (SD) Range	Syndrome diagnosis	Anxiety measure	% Anxiety (N)	Quality weighting
1. de Vries et al. 2018[40]				2216	1062 m, 1154 f	Mean & SD NR, Median: 13, <1-71	Molecular testing in 45% (1000) of sample	Not reported	33.3 (240)[41]	0.33
1b. de Vries et al. 2018				2216	1062 m, 1154 f	Mean & SD NR, Median: 13, <1-71	Molecular testing in 45% (1000) of sample	DSM-5/ICD-10 criteria	9.7 (133)[42]	0.44
2. Wilbur et al. 2016				81	41 m, 40 f	Mean & SD NR, Median: 10, 0.2-23.2	All met clinical diagnostic criteria, genetic testing in 7% (6) of sample	Chart review	16 (13)	0.33
3. Chung et al. 2011				157	35 m, 27 f[1]	15.4 (9.49), 3-48	Clinical criteria and/or genetic testing	DSM-IV-TR criteria	19.1 (30)	0.33
4. de Vries et al. 2007				265	106 m, 144 f, 15 not specified	Not reported	Not reported	Parent report	40 (99)[43]	0.22
5. Raznahan et al. 2006				60	30 m, 30 f	35.8 (13.8), range NR	Clinical examination	SADS-L/SAPPA and patient histories with consensus	5 (3)	0.67

[40] Paper reports anxiety prevalence on a behavioural (1) and psychiatric level (1b). Separate meta-analyses were conducted for behavioural and psychiatric prevalence
[41] Anxiety prevalence calculated based on 720 participants
[42] Based on participants formally diagnosed with a psychiatric comorbidity (*n*=62)
[43] Anxiety prevalence calculated based on 246 participants

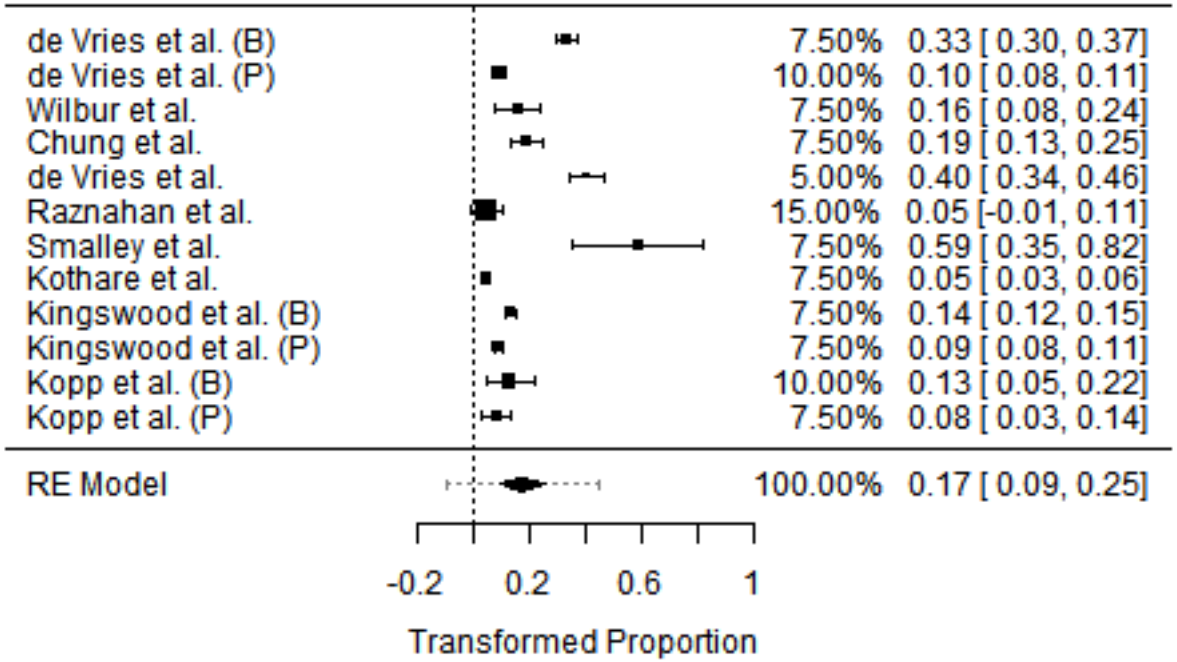
6. Smalley et al. 1994[44]	17	Not reported	Not reported	Based on physical criteria	SADS-LA/K-SADS-E	58.8 (10)	0.33
7. Kothare et al. 2014	916	445 m, 471 f	40 months (90 months), range NR	Clinical data review of genetic testing	Clinical data review	4.6 (42)	0.33
8. Kingswood et al. 2017[45]	2093	1009 m, 1084 f	Mean & SD NR, Median: 13, 0-71	Molecular testing in 43.1% (902) of sample	Not reported	13.7 (205)[46]	0.33
8b. Kingswood et al. 2017	2093	1009 m, 1084 f	Mean & SD NR, Median: 13, 0-71	Molecular testing in 43.1% (902) of sample	Not reported	9.1 (118)[47]	0.33
9. Kopp et al. 2008[48]	99	45 m, 54 f	7.7 (4.17), 6 months-17 years	Report of genetic testing in 95% (94) participants	BASC-2	13.1 (8)[49]	0.44
9b. Kopp et al. 2008	99	45 m, 54 f	7.7 (4.17), 6 months-17 years	Report of genetic testing in 95% (94) participants	Parent report/chart review	8.3 (8)[50]	0.33

SAPPA=Schedule for the Assessment of Psychiatric Problems Associated with Autism (and Other Developmental Disorders), SADS-LA=Schedule of Affective Disorders and Schizophrenia Lifetime Anxiety version, BASC-2=Behavior Assessment System for Children, 2nd Edition

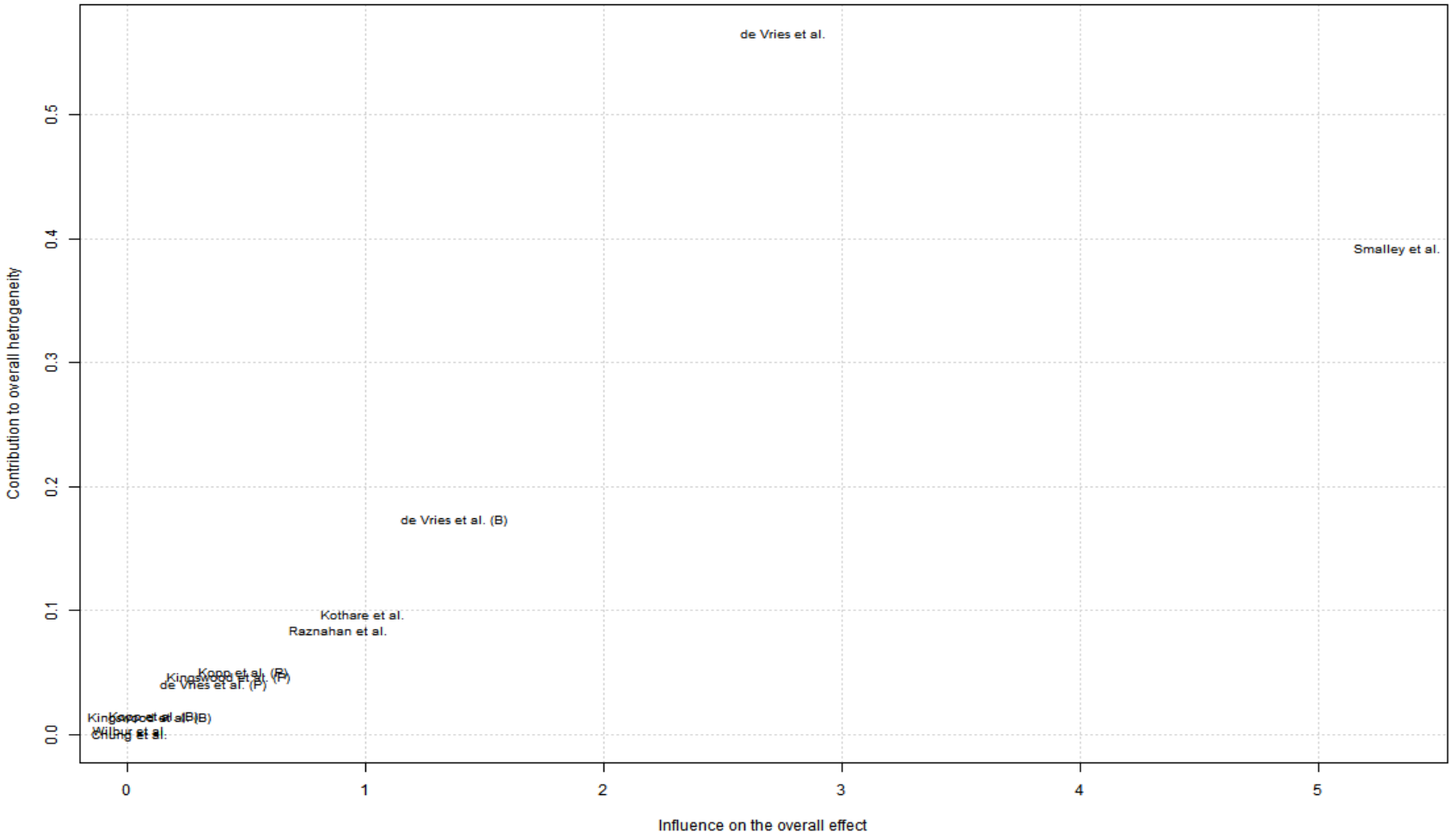
[44] Paper identified as heterogeneous with the rest of the literature and having a disproportionate influence on the overall effect (see Baujat chart and forest plot below). Paper re-reviewed and potential bias identified that may have an impact on reported anxiety prevalence. Paper reports on a large, single kindred. Paper removed from final meta-analysis.
[45] Paper reports anxiety prevalence on a behavioural (8) and psychiatric level (8b). Separate meta-analyses were conducted for behavioural and psychiatric prevalence
[46] Anxiety prevalence calculated based on 1498 participants
[47] Anxiety prevalence calculated based on 1294 participants
[48] Paper reports anxiety prevalence on a behavioural (9) and psychiatric level (9b). Separate meta-analyses were conducted for behavioural and psychiatric prevalence
[49] Anxiety prevalence calculated based on 61 participants
[50] Anxiety prevalence calculated based on 96 participants



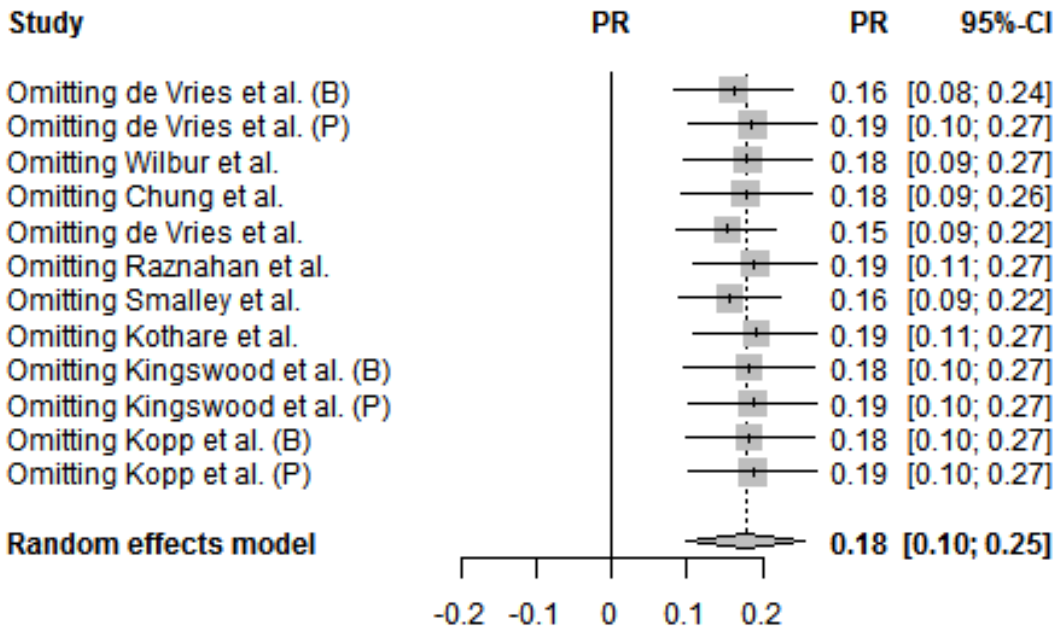
Appendices Figure 33. Forest plot for anxiety in Tuberous Sclerosis Complex using a random-effects model.



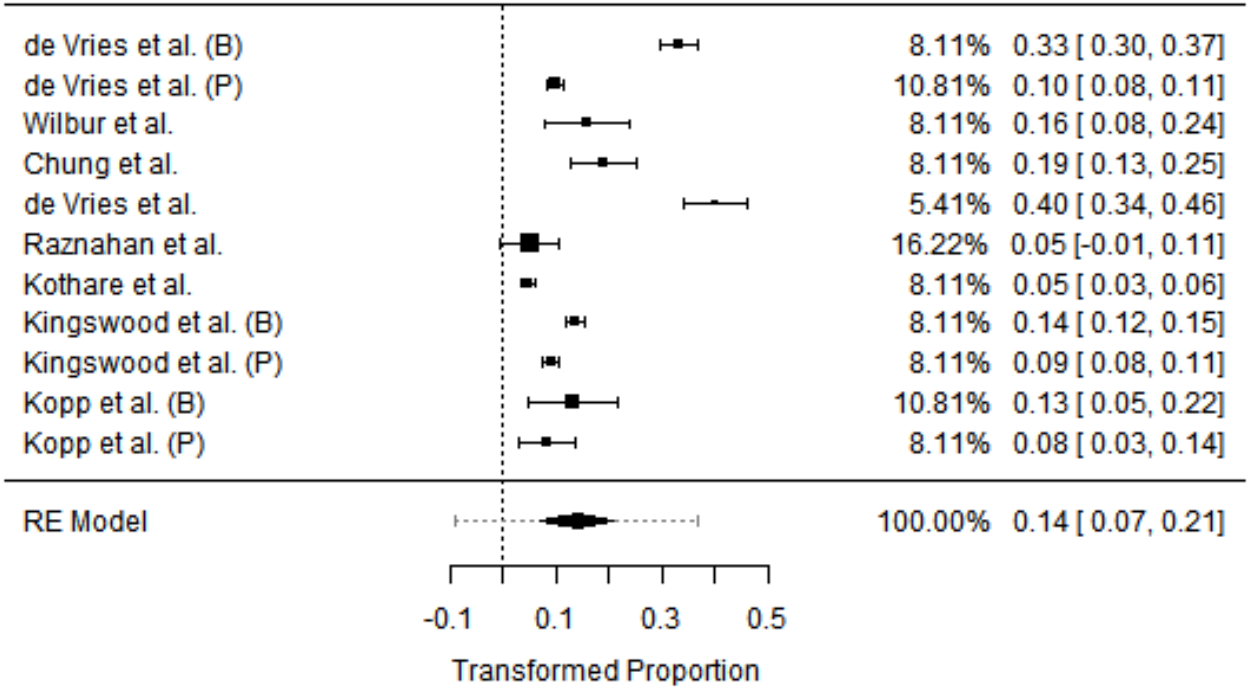
Appendices Figure 34. Forest plot for anxiety in Tuberous Sclerosis Complex using a quality-effects model.



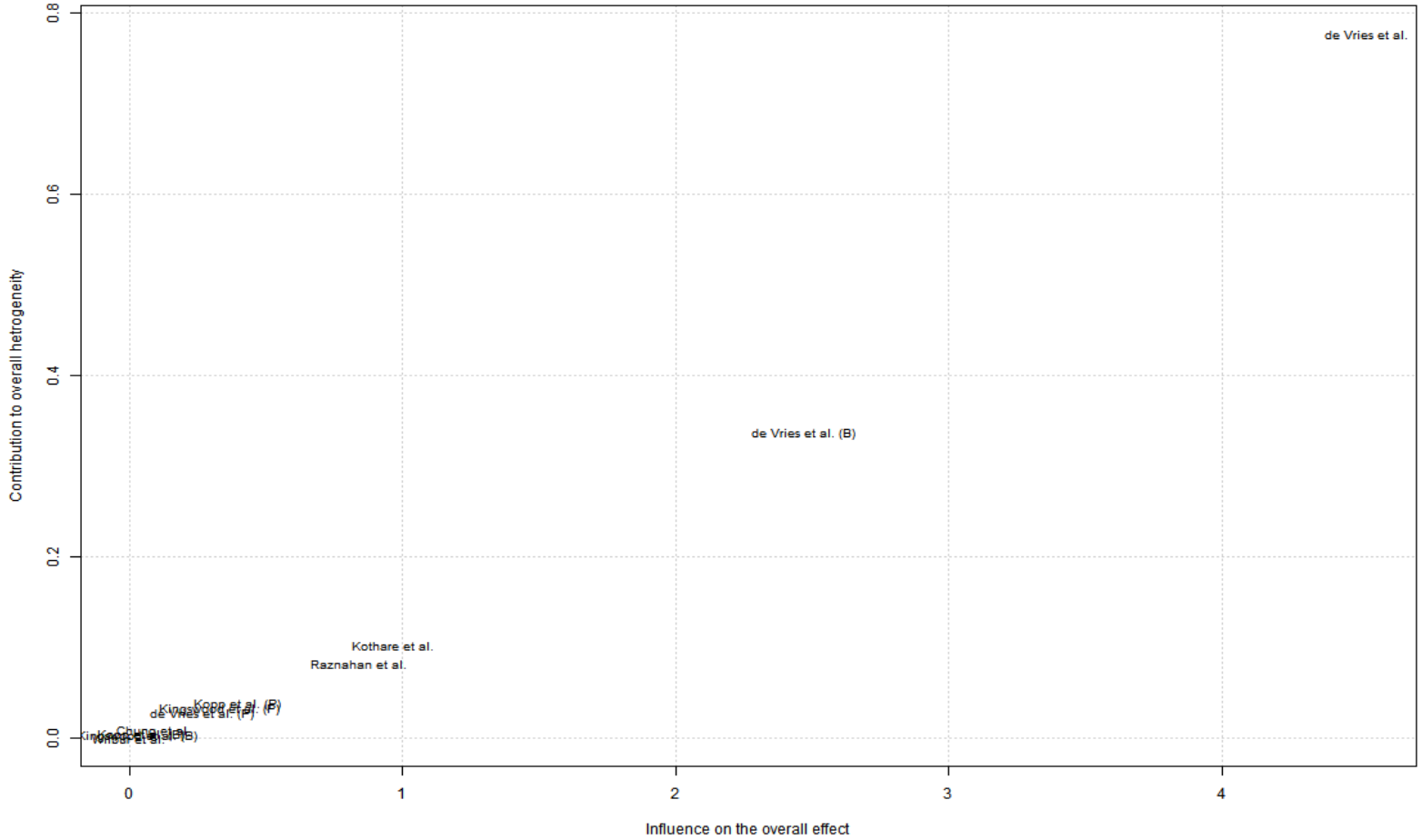
Appendices Figure 35. Baujat chart used to identify sources of heterogeneity: Tuberous Sclerosis Complex.



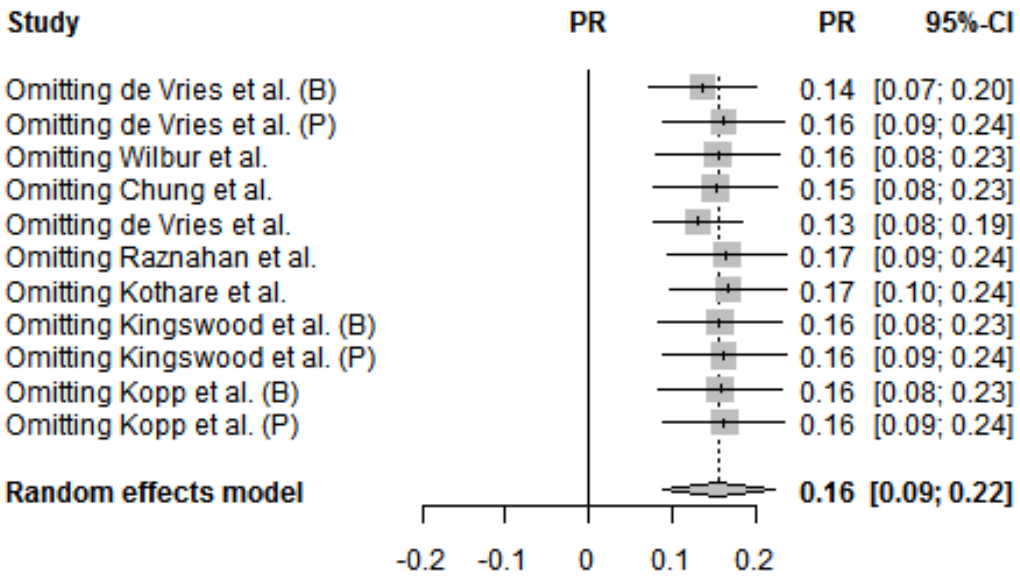
Appendices Figure 36. “Leave one out” analysis for Tuberous Sclerosis Complex.



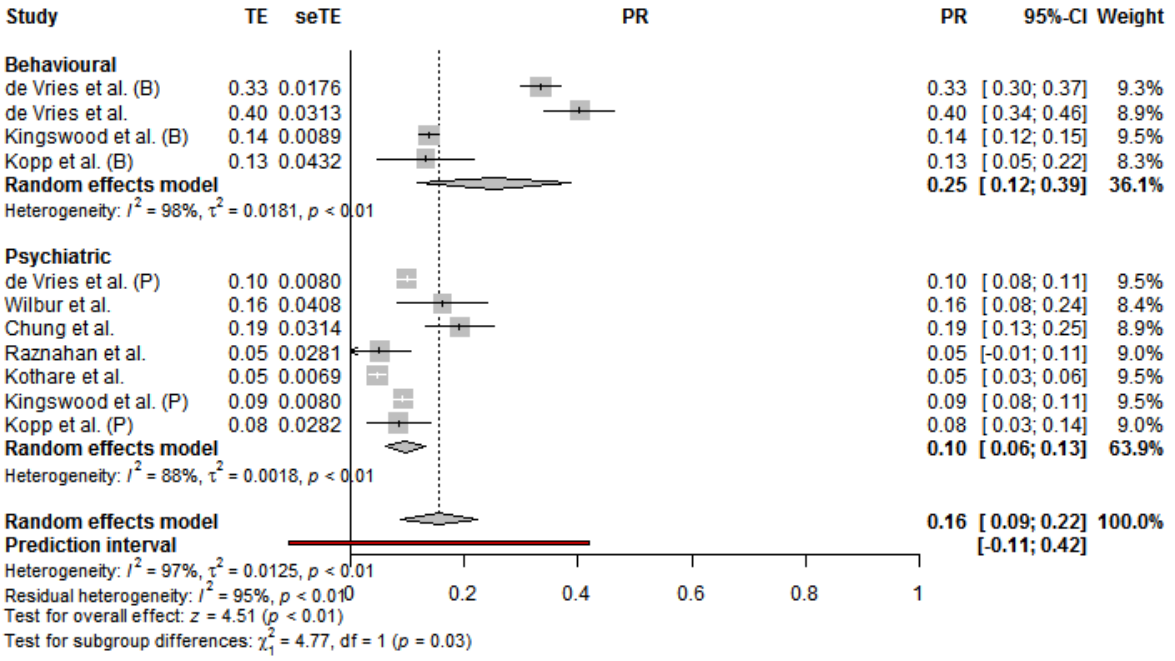
Appendices Figure 37. Forest plot for anxiety in Tuberous Sclerosis Complex using a quality-effects model (final analysis with removal of Smalley).



Appendices Figure 38. Baujat chart used to identify sources of heterogeneity: Tuberous Sclerosis Complex (final analysis with removal of Smalley).



Appendices Figure 39. “Leave one out” analysis for Tuberous Sclerosis Complex (final analysis with removal of Smalley).



Appendices Figure 40. Between groups test for behavioural and psychiatric reports of anxiety in Tuberous sclerosis complex (final analysis with removal of Smalley).

Appendices Table 14. Subgroup analysis of quality ratings and subsequent prevalence of anxiety between subgroups.

Syndrome		Anxiety prevalence for quality rating of 'poor'[51]	Anxiety prevalence for quality rating of 'good'	Number of papers[52]	χ^2	*p*
22q11.2 deletion syndrome	Sample identification	35%	41%	34 (19)	0.68	0.4081
	Syndrome confirmation	44%	38%	34 (30)	0.49	0.4830
	Anxiety assessment	13%	42%	34 (30)	15.15	<0.0001
Fragile X syndrome	Sample identification	51%	49%	19 (13)	0.05	0.8269
	Syndrome confirmation	37%	50%	19 (18)	1.12	0.2893
	Anxiety assessment	50%	48%	19 (6)	0.02	0.8989
Down syndrome	Sample identification	16%	7%	11 (9)	3.74	0.0532
	Syndrome confirmation	12%	4%	11 (4)	3.67	0.0554
	Anxiety assessment	9%	3%	11 (1)	5.13	0.0235

[51] Quality ratings were collapsed into two categories, where scores of 0 and one were combined for a score of 0 and categorised as 'poor' and scores of two and three were combined for a score of one and categorised as 'good'
[52] Total number of papers in subgroup analysis (number of papers given quality rating of 'good')

Appendices Table 15. Subgroup analysis of outcome type and subsequent prevalence of anxiety between subgroups.

	Anxiety prevalence based on behavioural report	Anxiety prevalence based on psychiatric report	Number of papers[53]	χ^2	*p*
22q11 deletion syndrome	5%	42%	34 (31)	122.72	<0.0001
Fragile X syndrome	39%	55%	19 (12)	2.26	0.1328
Down syndrome	25%	7%	11 (10)	10.59	0.0011

[53] Total number of papers included in the subgroup analysis (number of papers reporting psychiatric prevalence)

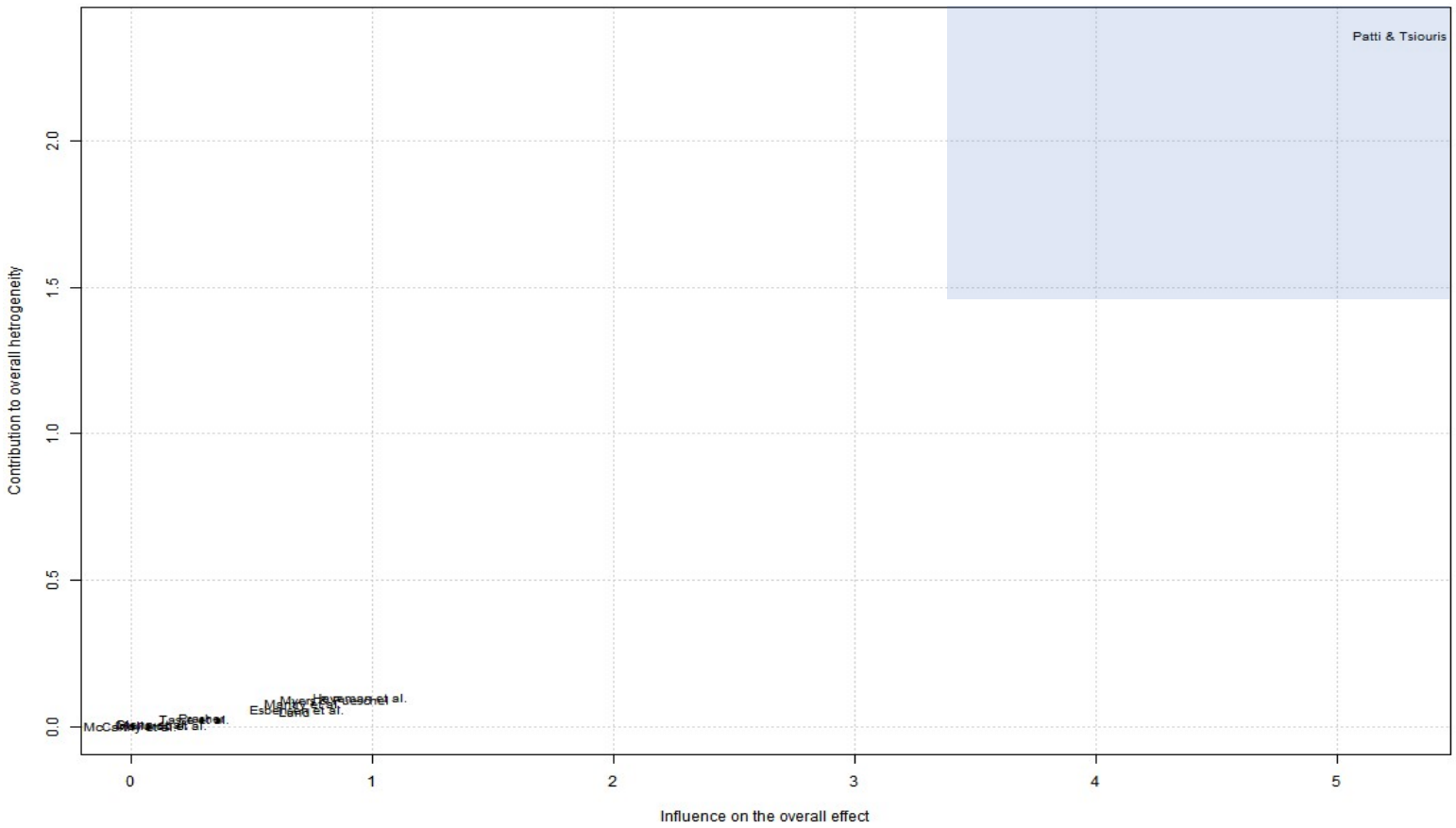
Appendices Table 16. Meta-regression analysis exploring year of publication in relation to prevalence of anxiety.

	Year of publication					
	Estimate	S.E.	Z	*p*	Lower 95% CI	Upper 95% CI
22q11.2 deletion syndrome	0.0042	0.0058	0.7342	0.4628	-0.0071	0.0155
Fragile X syndrome	0.0047	0.0059	0.7978	0.4250	-0.0068	0.0162
Down syndrome	0.0029	0.0021	1.3654	0.1721	-0.0013	0.0070

Appendices Table 17. Meta-regression analysis exploring total number of participants assessed for anxiety in relation to the prevalence of anxiety

	Number of participants					
	Estimate	S.E.	Z	*p*	Lower 95% CI	Upper 95% CI
22q11.2 deletion syndrome	0.0003	0.0006	0.4637	0.6429	-0.0010	0.0016
Fragile X syndrome	0.0002	0.0001	1.7617	0.0781	-0.0000	0.0005
Down syndrome	-0.0004	0.0001	-3.5133	0.0004	-0.0006	-0.0002

Appendix 4 Chapter two Baujat chart



Appendices figure 41. Baujat chart for meta-analysis of anxiety prevalence in Down syndrome highlighting the area of high heterogeneity and high influence. On the y-axis, each study's contribution to the overall heterogeneity is plotted. On the x-axis is the influence on the overall effect, which is the square of the difference between the overall effect with and without a particular study effect. The most discrepant and influential studies are plotted in the top right-hand corner of the chart (the shaded area).

Appendix 5 Chapter two specific anxiety prevalence analysis

Appendices Table 18. Pooled prevalence estimates for specific anxiety profiles across genetic syndromes

	Specific anxiety symptom/disorder	**Number of papers (reference number)[1]**	**Number of papers reporting psychiatric prevalence n (%)**	**Part-icipants (n)**	**Mean quality weight-ing**	**Hetero-geneity I^2**	**Random-effects pooled prevalence (95% CI)**	**Quality-effects pooled prevalence**
22q11.2 deletion syndrome	SP	**18** (26,30,31,32,33,35,37,38, 41,42,43,45,46,47,48,54,55,59)	18 (100)	1412	0.64	86.4%	28% (21-35)	30% (24-37)
	SoP	**15** (26,30,31,32,33,35,38,42, 43,45,47,48,54,58,59)	15 (100)	1252	0.65	49.8%	9% (7-11)	11% (8-13)
	GAD	**17** (26,30,32,33,35,37,38,40, 41,42,45,46,47,48,55,57,59)	17 (100)	1448	0.66	62.4-%	13% (10-16)	14% (11-17)
	SAD	**14** (26,30,32,33,35,38,39,42, 46,47,48,54,55,58)	14 (100)	762	0.69	31.9%	6% (4-8)	9% (6-11)
	OCD	**21** (30,31,32,33,35,36,37,38, 39,41,42,43,45,46,47,48,50, 54,55,58,59)	21 (100)	1541	0.67	60.3%	9% (7-12)	11% (9-14)

Appendix 5 Chapter two specific anxiety prevalence analysis

Appendices Table 18. Pooled prevalence estimates for specific anxiety profiles across genetic syndromes

	Specific anxiety symptom/disorder	**Number of papers (reference number)[1]**	**Number of papers reporting psychiatric prevalence n (%)**	**Participants (n)**	**Mean quality weighting**	**Heterogeneity I^2**	**Random-effects pooled prevalence (95% CI)**	**Quality-effects pooled prevalence**
	PD	**4** (30,33,35,47)	4 (100)	449	0.67	0.0%	1% (0-2)	1% (0-2)
	PD with Ago	**1** (42)	1 (100)	79	0.67	N/A	3% (-1-6)	3% (-1-6)
	PD without Ago	**1** (42)	1 (100)	79	0.67	N/A	1% (-1-4)	1% (-1-4)
	Ago	**3** (30,33,42)	3 (100)	226	0.71	0.0%	2% (0-3)	2% (0-4)
	PTSD	**6** (29,33,35,38,47,48)	6 (100)	483	0.63	57.2%	2% (1-3)	8% (4-11)
	SM	**1** (42)	1 (100)	80	0.67	N/A	1% (-1-4)	1% (-1-4)
Fragile X syndrome[2]	SP	**2** (13,18)	1 (50)	44	0.50	0.0%	52% (38-67)	53% (38-67)
	SoP	**7** (4,13,18,19,20,23,24)	4 (57)	123	0.59	64.7%	28% (16-41)	33% (20-47)
	GAD	**5** (4,12,13,20,23)	3 (60)	172	0.56	67.4%	14% (5-22)	13% (4-22)
	SAD	**5** (4,13,16,18,20)	3 (60)	125	0.56	0.0%	13% (7-19)	15% (7-22)
	PD	**1** (19)	1 (100)	13	0.78	N/A	8% (-·07-22)	8% (-·07-22)
	PD with Ago	**2** (4,19)	1 (50)	32	0.56	88.2%	27% (-12-65)	20% (-22-61)
	OCD	**4** (4,12,16,18)	3 (75)	187	0.53	89.4%	16% (2-30)	15% (1-29)
	PTSD	**1** (13)	0 (0)	22	0.44	N/A	32% (12-51)	32% (12-51)

Appendix 5 Chapter two specific anxiety prevalence analysis

Appendices Table 18. Pooled prevalence estimates for specific anxiety profiles across genetic syndromes

	Specific anxiety symptom/disorder	**Number of papers (reference number)[1]**	**Number of papers reporting psychiatric prevalence n (%)**	**Participants (n)**	**Mean quality weighting**	**Heterogeneity I^2**	**Random-effects pooled prevalence (95% CI)**	**Quality-effects pooled prevalence**
	Physical injury fears	**1** (4)	0 (0)	19	0.33	N/A	37% (15-59)	37% (15-59)
	SM	**1** (25)	0 (0)	118	0.33	N/A	18% (11-25)	18% (11-25)
Down syndrome	SP	**4** (65,66,69,70)	4 (100)	933	0.53	84.0%	4% (0-9)	5% (0-10)
	GAD	**1** (70)	1 (100)	201	0.56	N/A	1% (0-3)	1% (-0-3)
	OCD[3]	**4** (65,66,69,70)	4 (100)	933	0.53	61.5%	2% (0-4)	2% (0-4)
	SM	**2** (63,66)	1 (50)	155	0.28	0.0%	6% (2-10)	6% (2-10)

[1]Reference numbers align with numbers of included papers listed in Supplementary material 6.

[2] 1 papers report of specific phobia, social anxiety, separation anxiety, panic disorder, agoraphobia, PTSD and selective mutism were not included due to inexact percentage rates reported in the paper. Clarification was not obtained after contact with the author.

[3] 1 paper reports "Obsessive-compulsive behaviour" while the remaining 3 papers report "obsessive-compulsive disorder". There was no significant difference between the reported prevalence of obsessive-compulsive behaviour versus obsessive-compulsive disorder (1% and 3% respectively; p=0.2683) and so presented above is the combined rate for behavioural and psychiatric rates of anxiety.

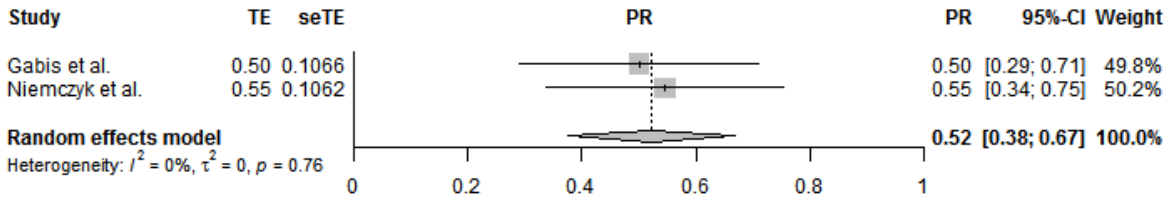
[4] 1 paper reports "obsessive-compulsive behaviours" while the other paper reports "obsessive-compulsive disorder". There was no significant difference between the reported prevalence of obsessive-compulsive behaviours and obsessive-compulsive disorder (6% and 2% respectively; p=0.1517) and so presented above is the combined rate for behavioural and psychiatric rates of anxiety.

[5] 1 paper reports parent report of "obsessive-compulsive behaviour" and diagnosis of obsessive-compulsive disorder while 1 paper reports diagnoses of obsessive-compulsive disorder. There was no significant difference between the behavioural and psychiatric ratings (9% and 3% respectively; p=0.1165) and so presented above is the combined rate for behavioural and psychiatric rates of anxiety.

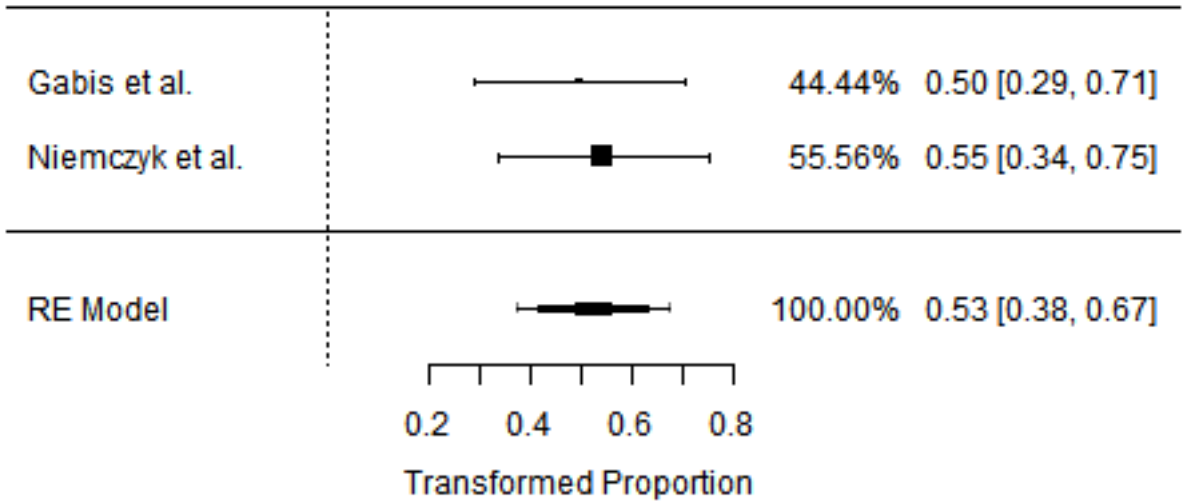
	Specific anxiety disorder	Number of papers (reference number)	Number of papers reporting psychiatric prevalence n (%)	Participants (n)	Mean quality weighting	Heterogeneity I^2	Random-effects pooled prevalence (95% CI)	Quality-effects pooled prevalence
Tuberous Sclerosis Complex	SP	**1** (94)	1 (100)	60	0.67	N/A	2% (-2-5)	2% (-2-5)
	PD	**1** (94)	1 (100)	60	0.67	N/A	2% (-2-5)	2% (-2-5)
	OCD[4]	**2** (91,94)	2 (100)	141	0.50	51.3%	3% (-1-8)	3% (-1-8)
CHARGE syndrome	OCD	**4** (82,83,84,85)	3 (75)	269	0.19	97.2%	35% (4-65)	38% (7-70)
7q11.23 duplication syndrome	SP	**1** (87)	1 (100)	72	0.44	N/A	50% (38-62)	50% (38-62)
	SoP	**2** (86,87)	2 (100)	125	0.50	0.0%	51% (42-60)	51% (42-60)
	GAD	**1** (87)	1 (100)	72	0.44	N/A	8% (2-15)	8% (2-15)
	SAD	**3** (86,87,88)	3 (100)	135	0.56	32.2%	16% (10-22)	20% (12-28)
	OCD[5]	**2** (86,87)	2 (100)	161	0.44	22.4%	4% (1-6)	4% (1-7)
	SM	**1** (87)	1 (100)	62	0.44	N/A	29% (18-40)	29% (18-40)
3q29 deletion syndrome	Panic attacks	**1** (89)	1 (100)	42	0.33	N/A	10% (1-18)	10% (1-18)

SP: specific phobia, SoP: social anxiety disorder/phobia, GAD: generalised anxiety disorder, OCD: obsessive-compulsive disorder, SAD: separation anxiety disorder, PD: panic disorder, PD with/without Ago: panic disorder with/without agoraphobia, PTSD: post-traumatic stress disorder, SM: selective mutism

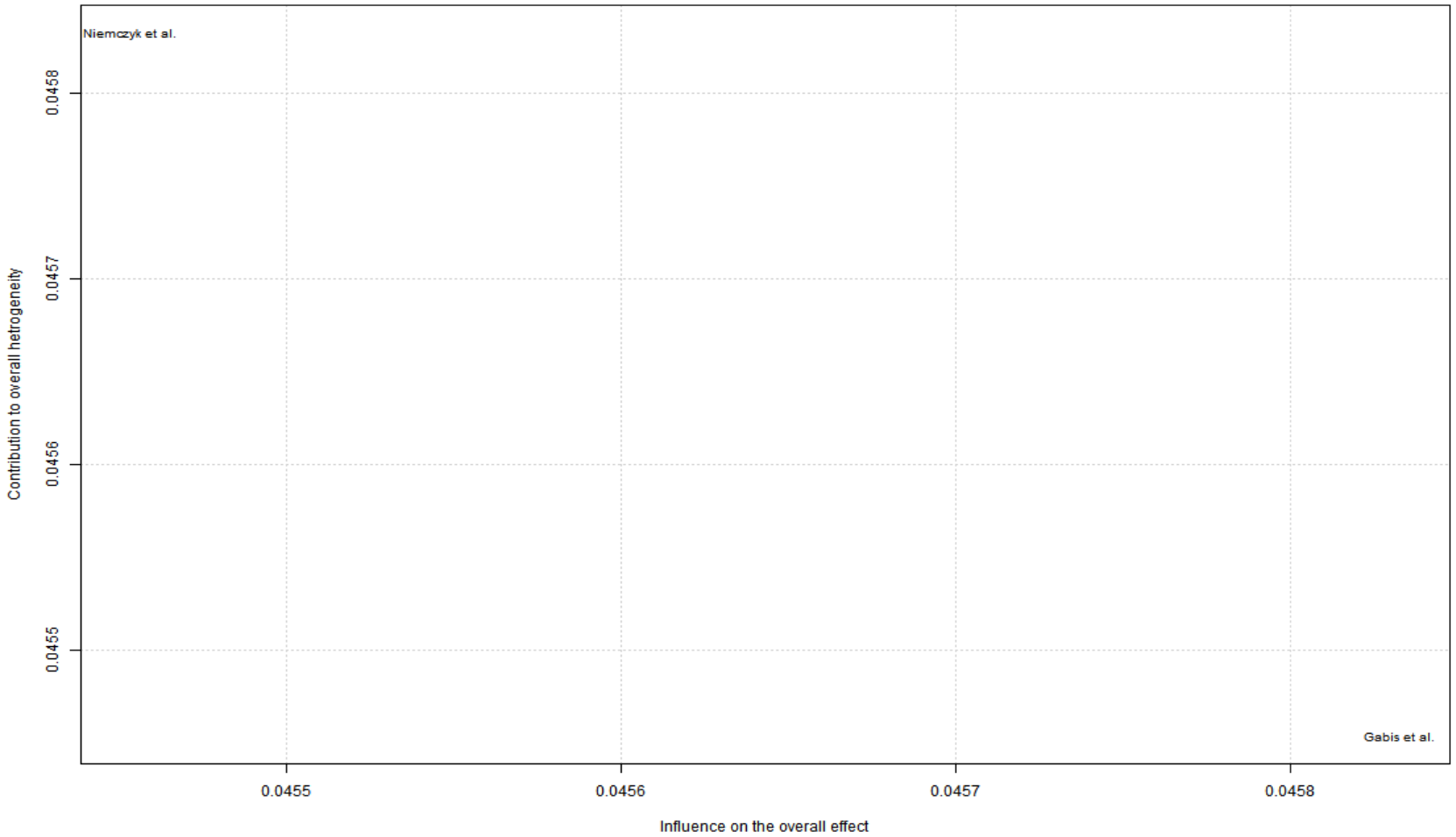
Specific anxiety profile analyses: Fragile X syndrome (Specific phobia)



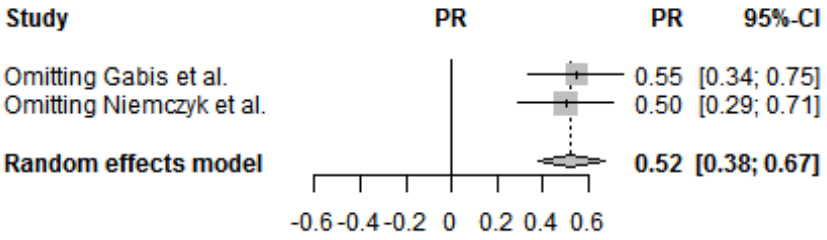
Appendices Figure 42. Forest plot for specific phobia in Fragile X syndrome using a random-effects model.



Appendices Figure 43. Forest plot for specific phobia in Fragile X syndrome using a quality-effects model.

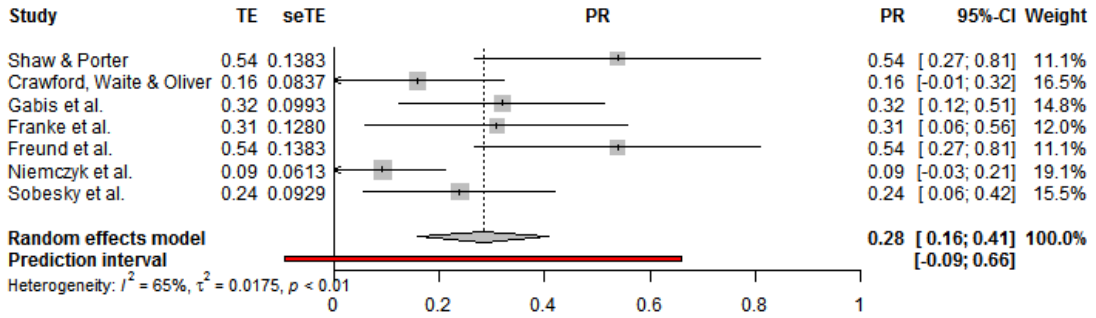


Appendices Figure 44. Baujat chart used to identify sources of heterogeneity: Specific phobia in Fragile X syndrome.

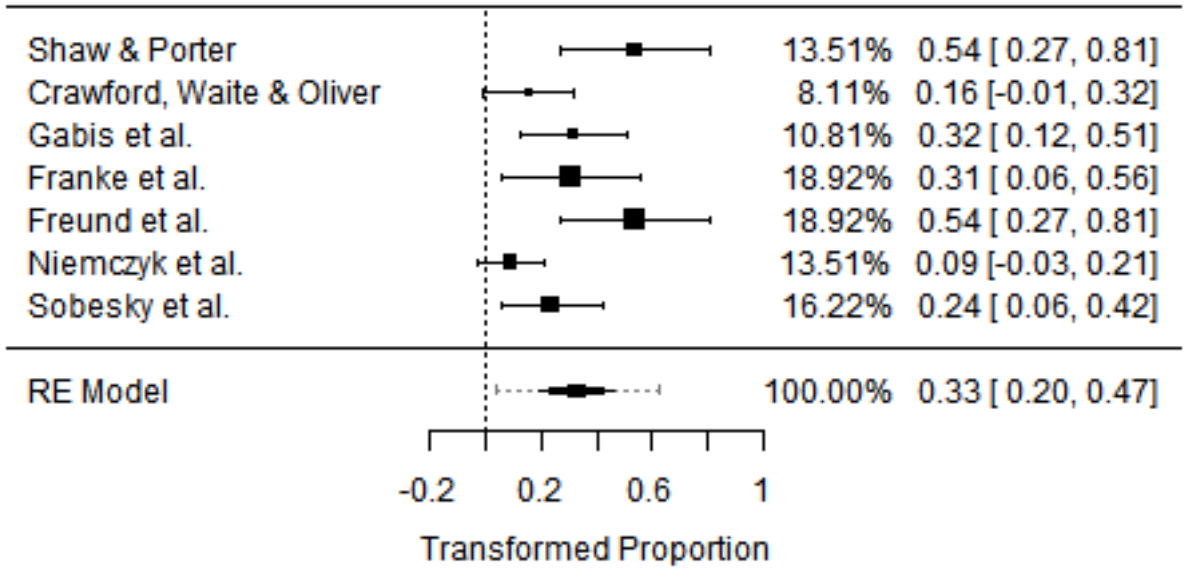


Appendices Figure 45. “Leave one out” analysis for specific phobia in Fragile X syndrome.

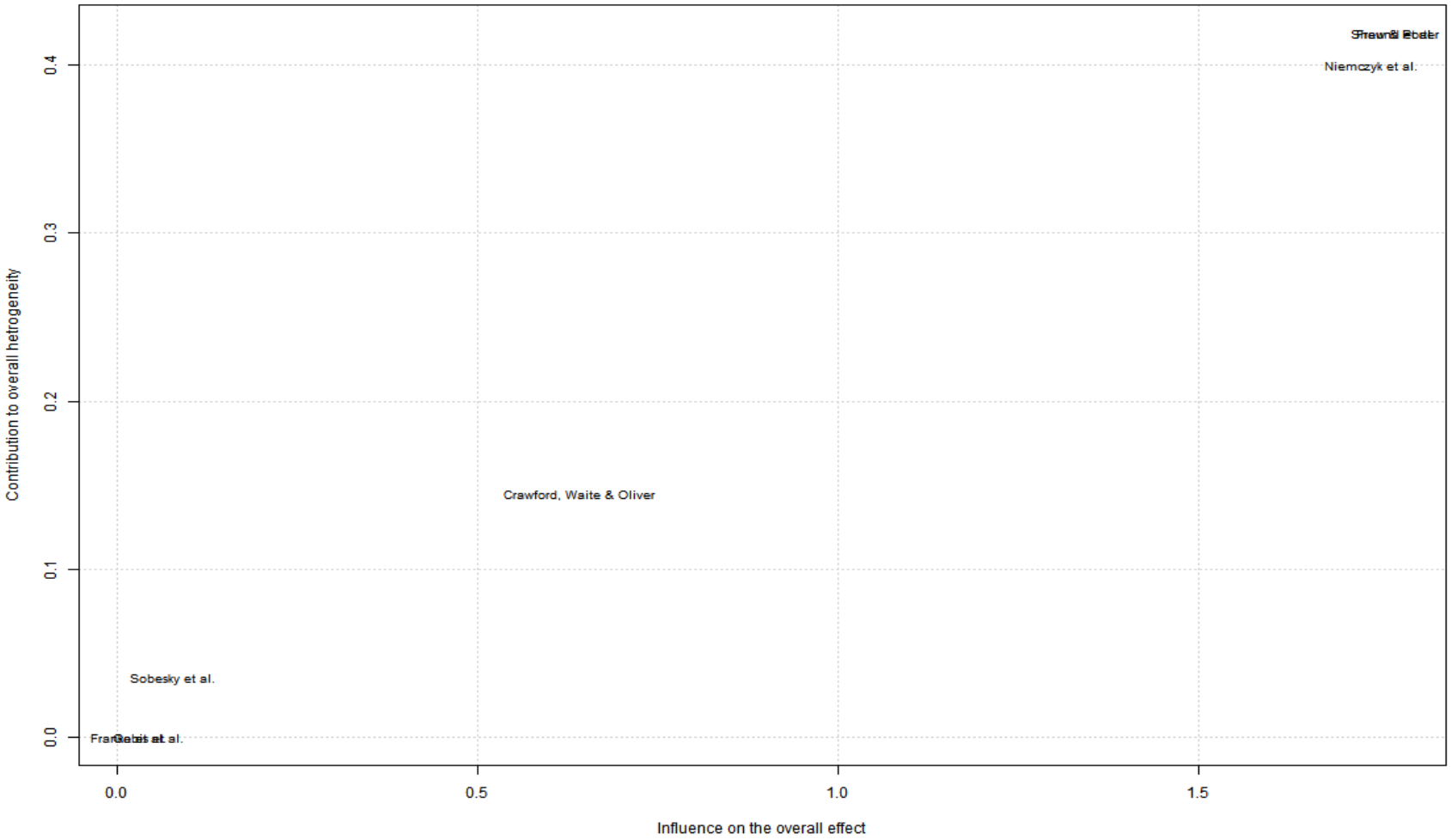
Specific anxiety profile analyses: Fragile X syndrome (Social anxiety)



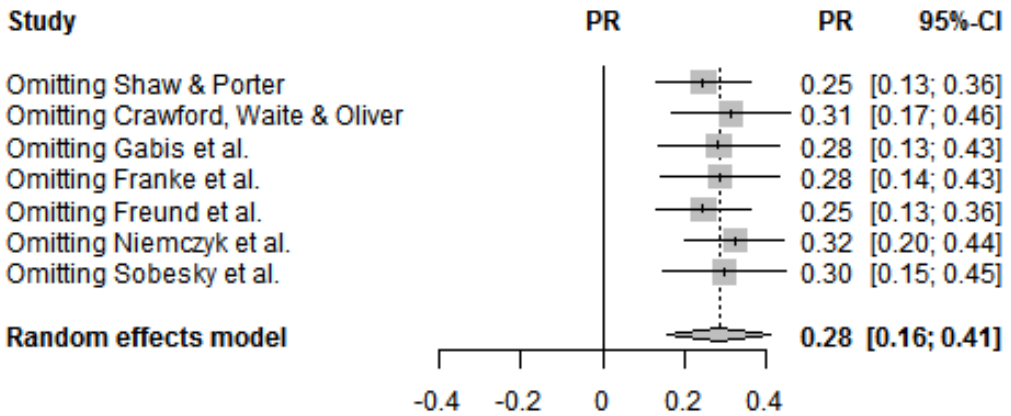
Appendices Figure 46. Forest plot for social anxiety in Fragile X syndrome using a random-effects model.



Appendices Figure 47. Forest plot for social anxiety in Fragile X syndrome using a quality-effects model.

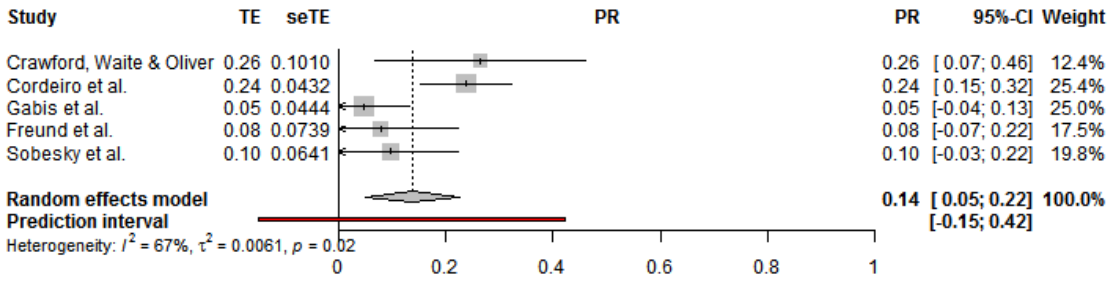


Appendices Figure 48. Baujat chart used to identify sources of heterogeneity: Social anxiety in Fragile X syndrome.

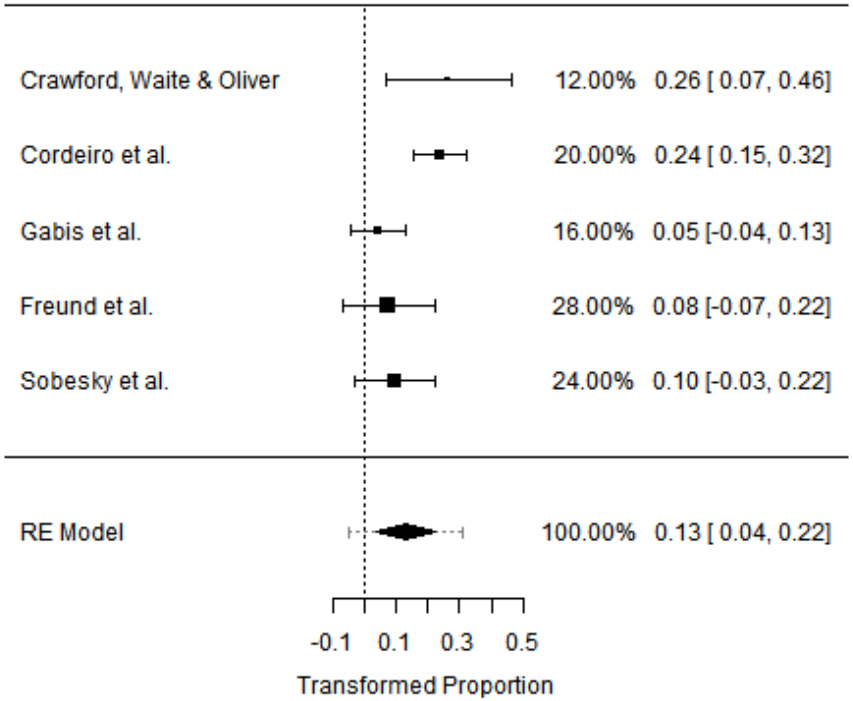


Appendices Figure 49. “Leave one out” analysis for Social anxiety in Fragile X syndrome.

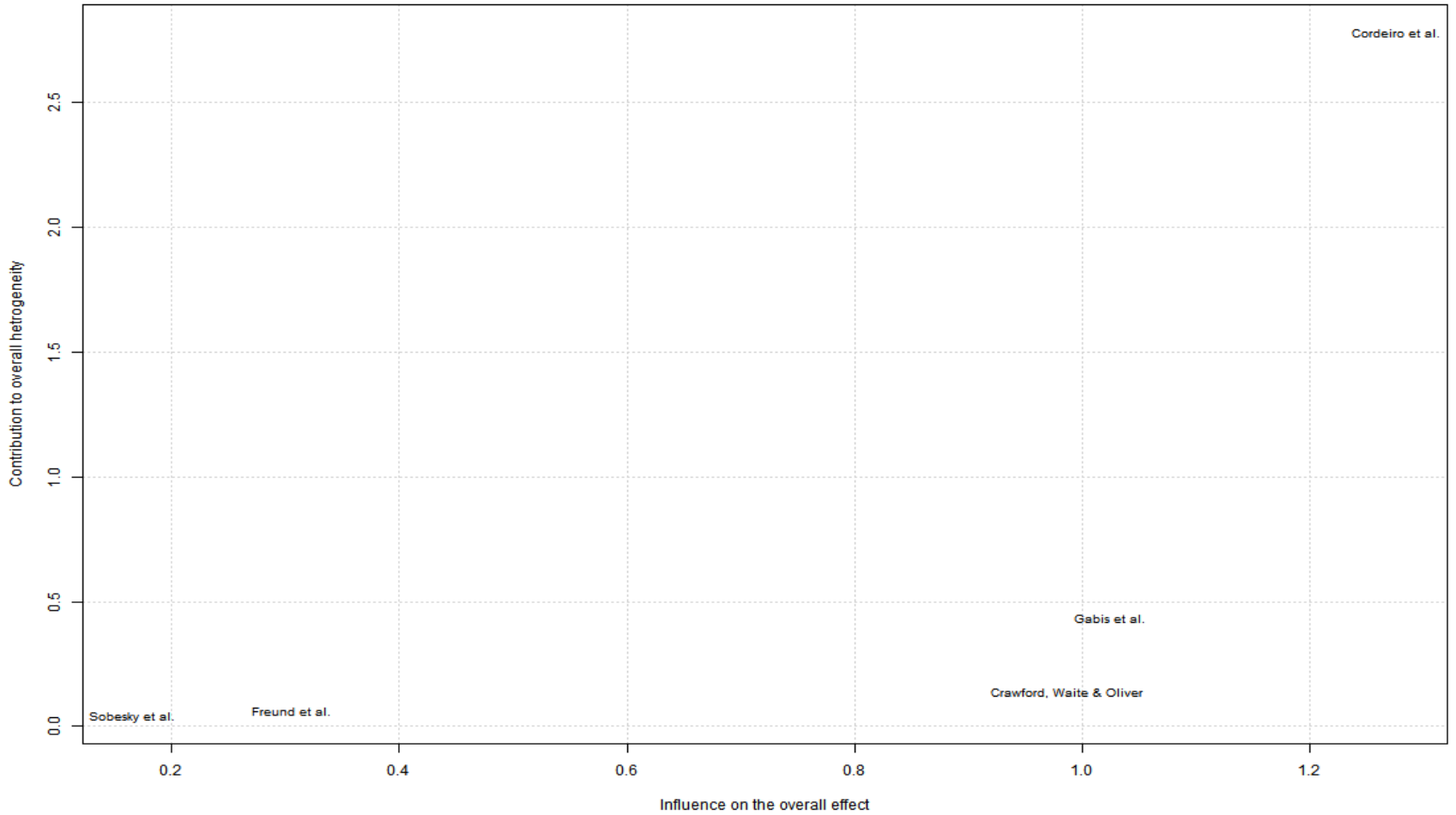
Specific anxiety profile analyses: Fragile X syndrome (Generalised anxiety)



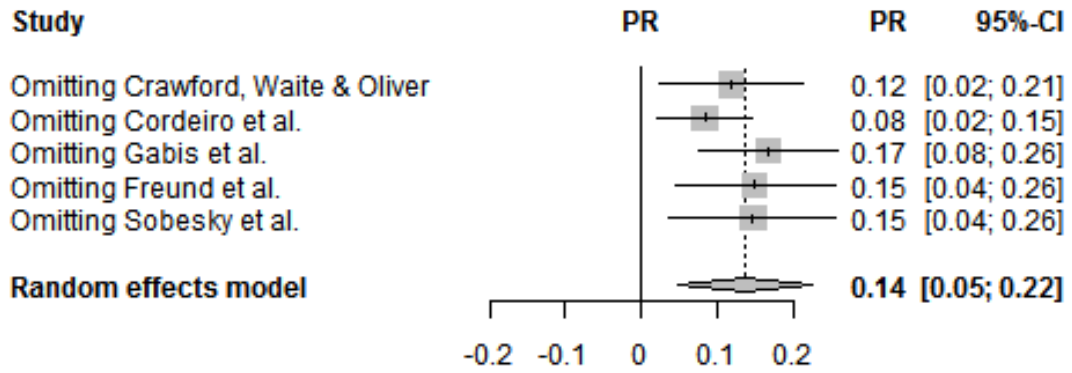
Appendices Figure 50. Forest plot for generalised anxiety in Fragile X syndrome using a random-effects model.



Appendices Figure 51. Forest plot for generalised anxiety in Fragile X syndrome using a quality-effects model.

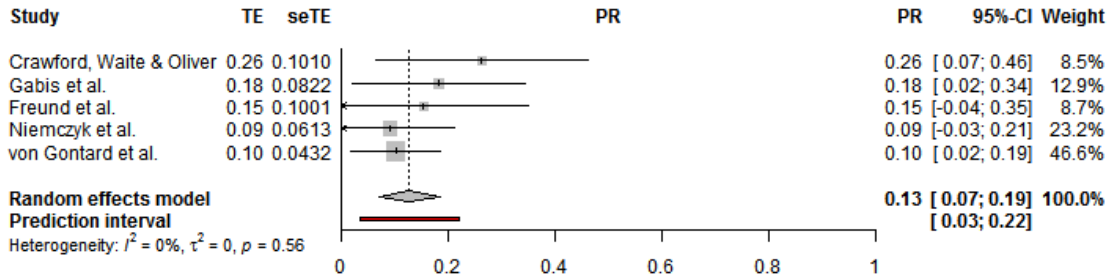


Appendices Figure 52. Baujat chart used to identify sources of heterogeneity: Generalised anxiety in Fragile X syndrome.

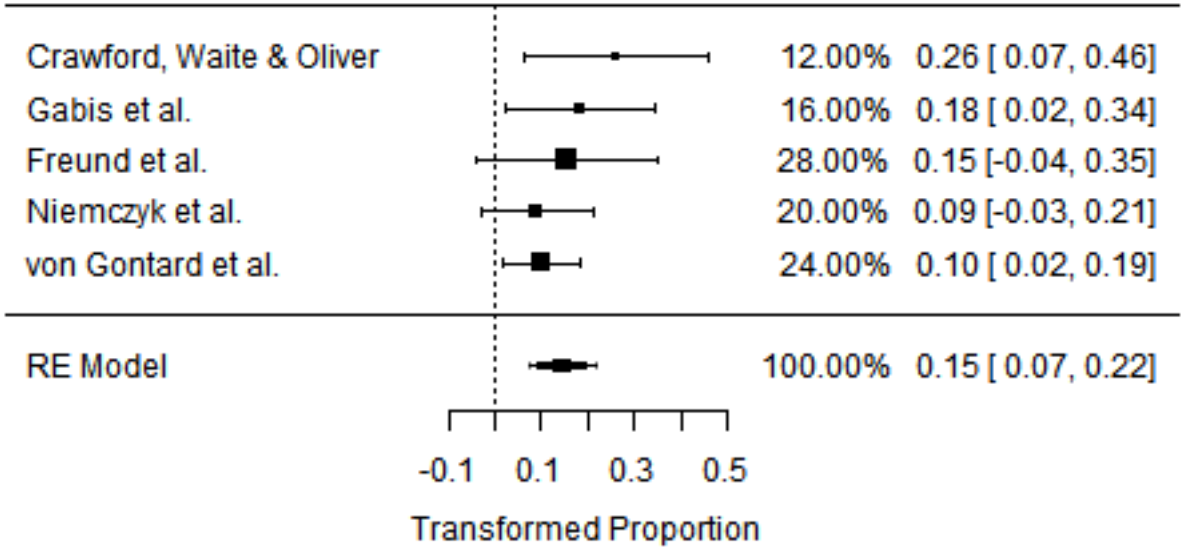


Appendices Figure 53. “Leave one out” analysis for generalised anxiety in Fragile X syndrome.

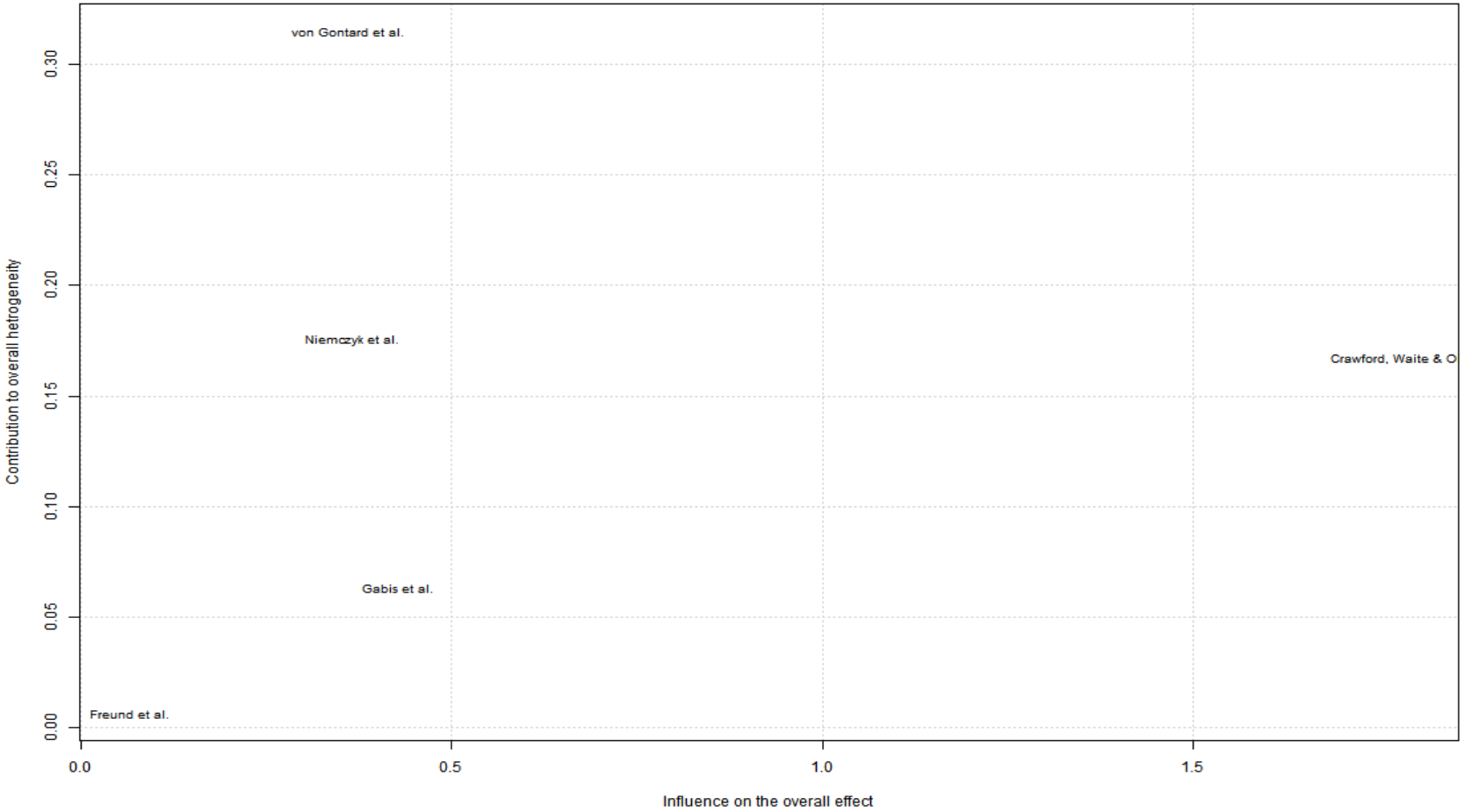
Specific anxiety profile analyses: Fragile X syndrome (Separation anxiety)



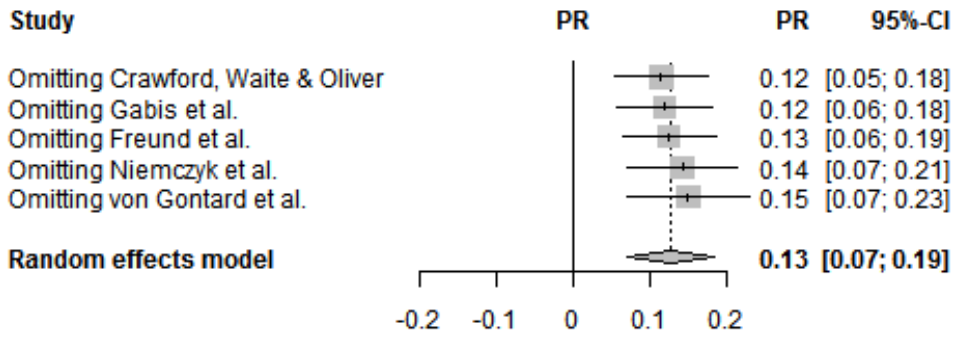
Appendices Figure 54. Forest plot for separation anxiety in Fragile X syndrome using a random-effects model.



Appendices Figure 55. Forest plot for separation anxiety in Fragile X syndrome using a quality-effects model.

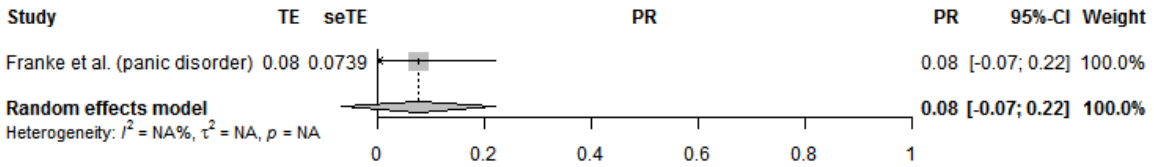


Appendices Figure 56. Baujat chart used to identify sources of heterogeneity: Separation anxiety in Fragile X syndrome.

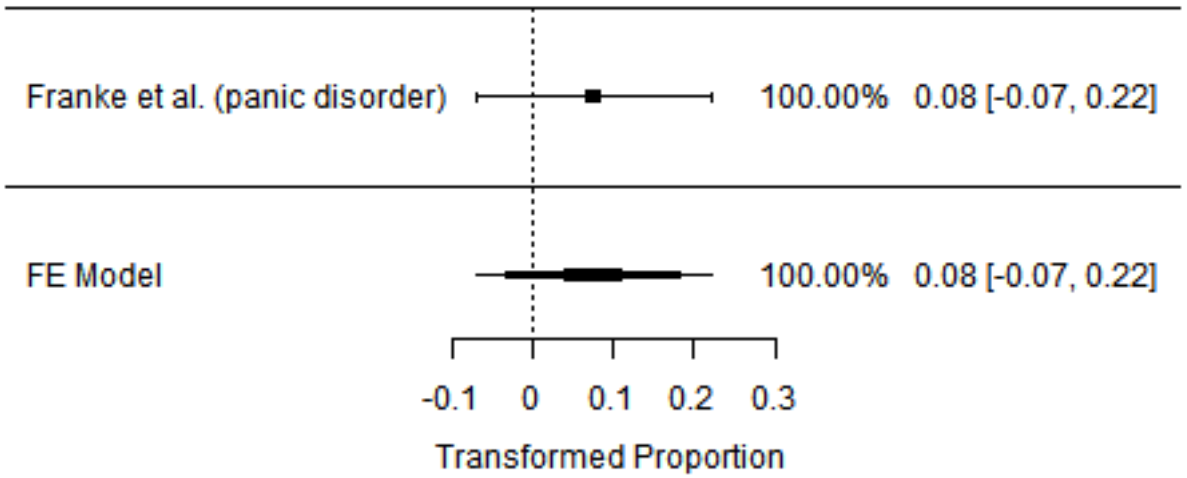


Appendices Figure 57. “Leave one out” analysis for separation anxiety in Fragile X syndrome.

Specific anxiety profile analyses: Fragile X syndrome (Panic)

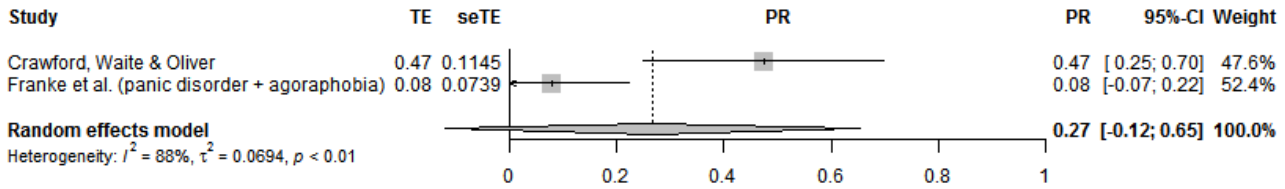


Appendices Figure 58. Forest plot for panic in Fragile X syndrome using a random-effects model.

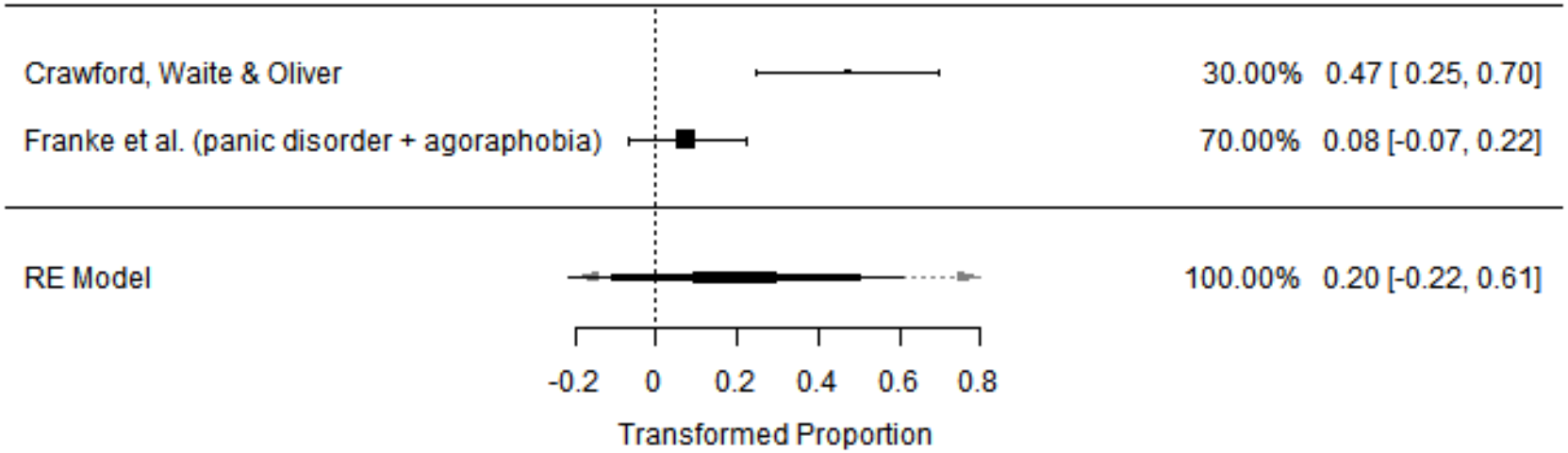


Appendices Figure 59. Forest plot for panic in Fragile X syndrome using a quality-effects model.

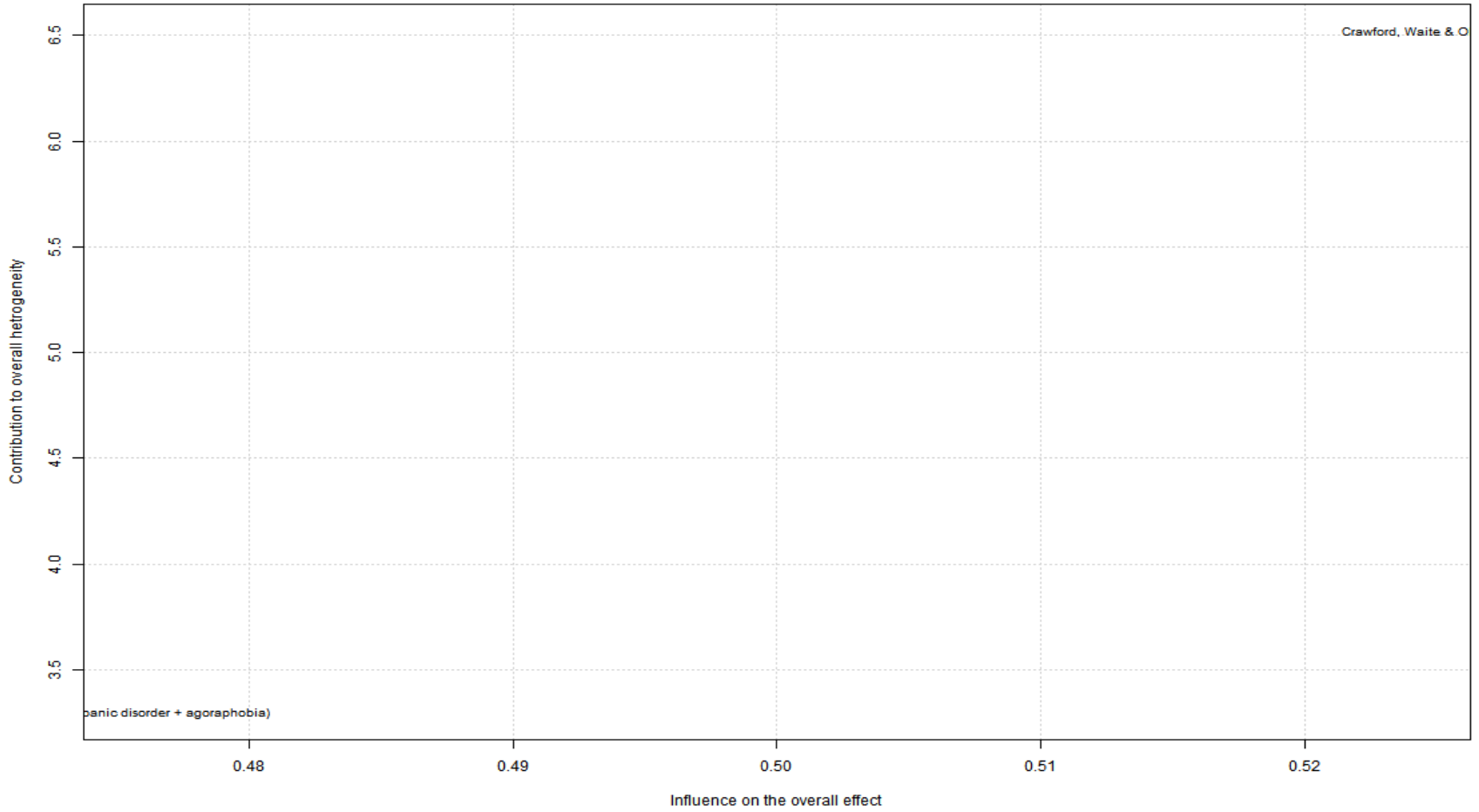
Specific anxiety profile analyses: Fragile X syndrome (Panic and agoraphobia)



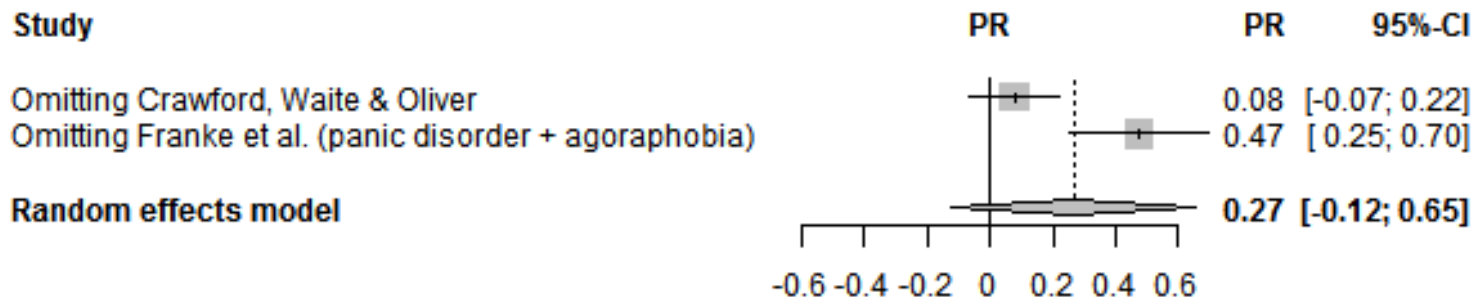
Appendices Figure 60. Forest plot for panic and agoraphobia in Fragile X syndrome using a random-effects model.



Appendices Figure 61. Forest plot for panic and agoraphobia in Fragile X syndrome using a quality-effects model.

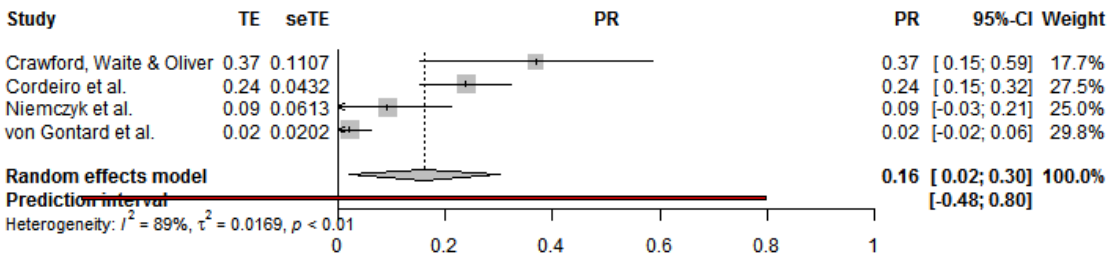


Appendices Figure 62. Baujat chart used to identify sources of heterogeneity: Panic and agoraphobia in Fragile X syndrome.

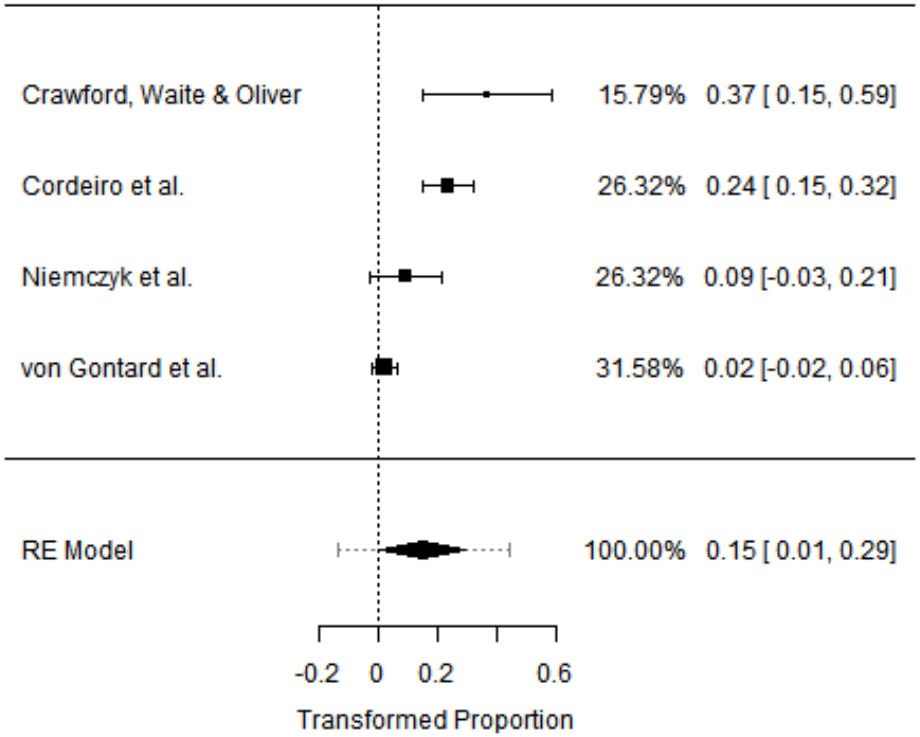


Appendices Figure 63. “Leave one out” analysis for panic and agoraphobia in Fragile X syndrome.

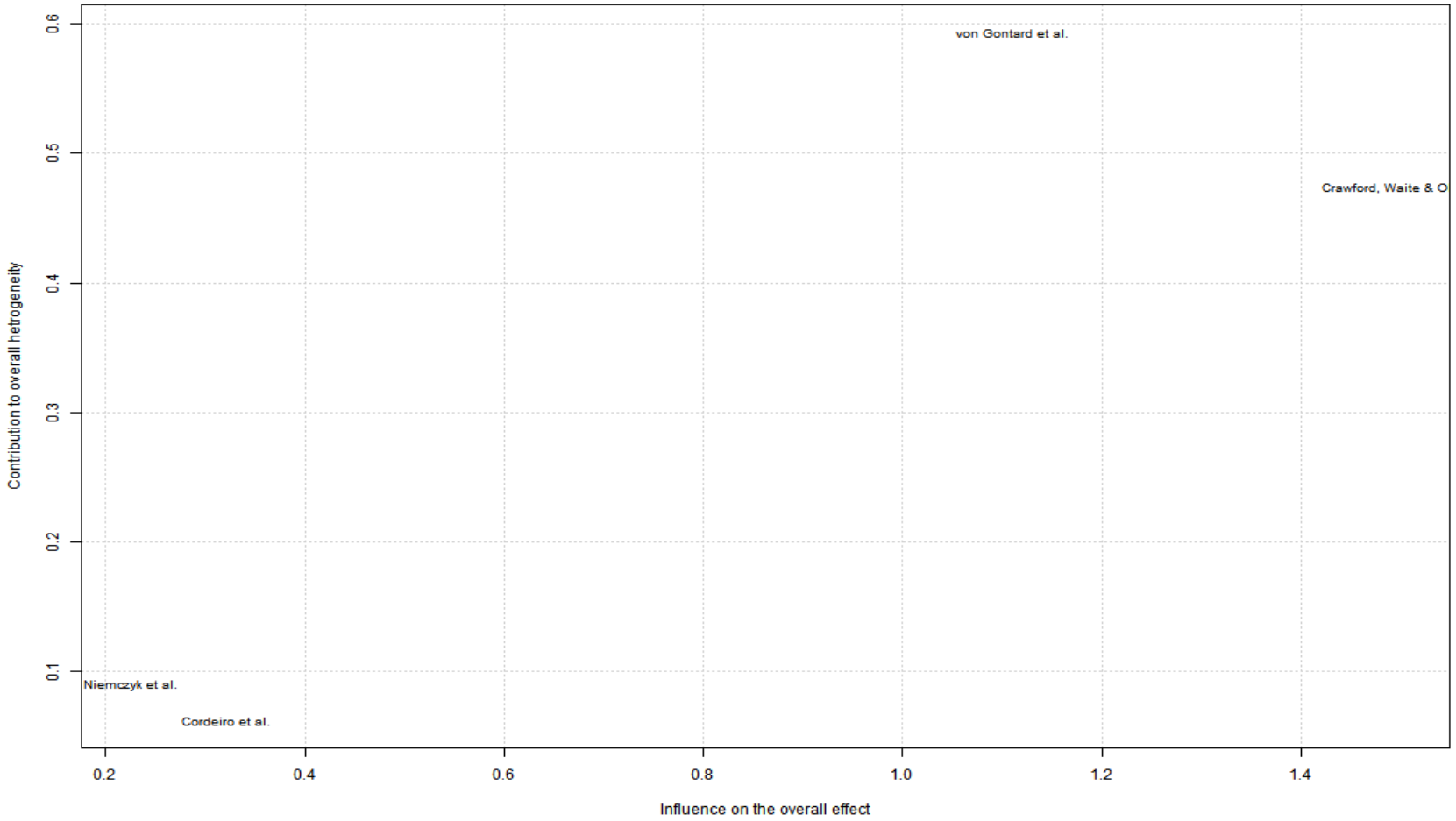
Specific anxiety profile analyses: Fragile X syndrome (Obsessive-compulsive symptomatology/diagnosis)



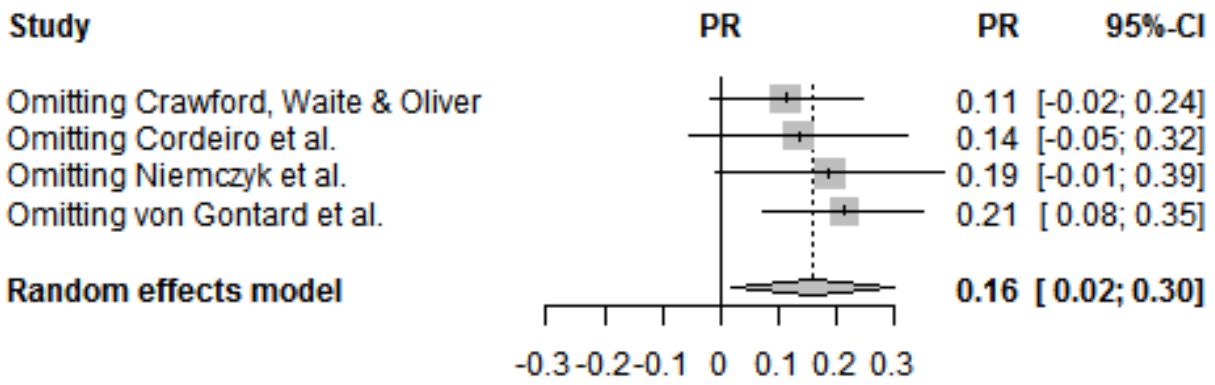
Appendices Figure 64. Forest plot for obsessive-compulsive symptomatology/diagnosis in Fragile X syndrome using a random-effects model.



Appendices Figure 65. Forest plot for obsessive-compulsive symptomatology/diagnosis in Fragile X syndrome using a quality-effects model.

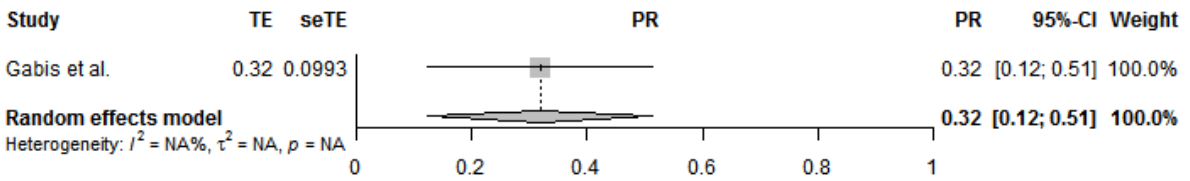


Appendices Figure 66. Baujat chart used to identify sources of heterogeneity: obsessive-compulsive symptomatology/diagnosis in Fragile X syndrome.

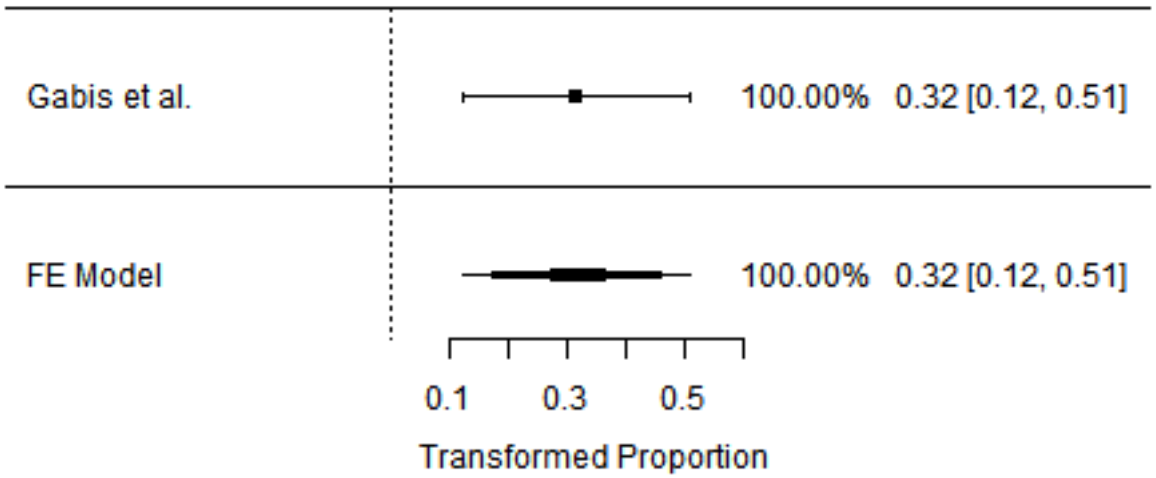


Appendices Figure 67. “Leave one out” analysis for obsessive-compulsive symptomatology/diagnosis in Fragile X syndrome.

Specific anxiety profile analyses: Fragile X syndrome (Post-traumatic-stress symptomatology/diagnosis)

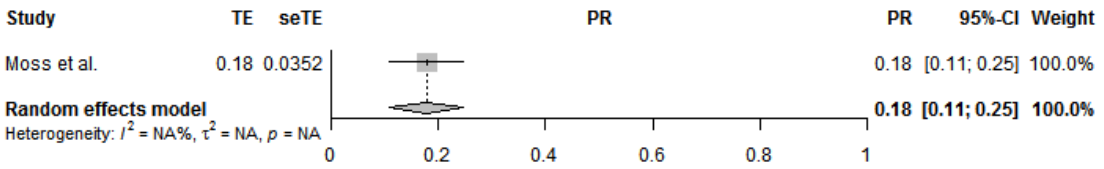


Appendices Figure 68. Forest plot for post-traumatic-stress symptomatology/diagnosis in Fragile X syndrome using a random-effects model.

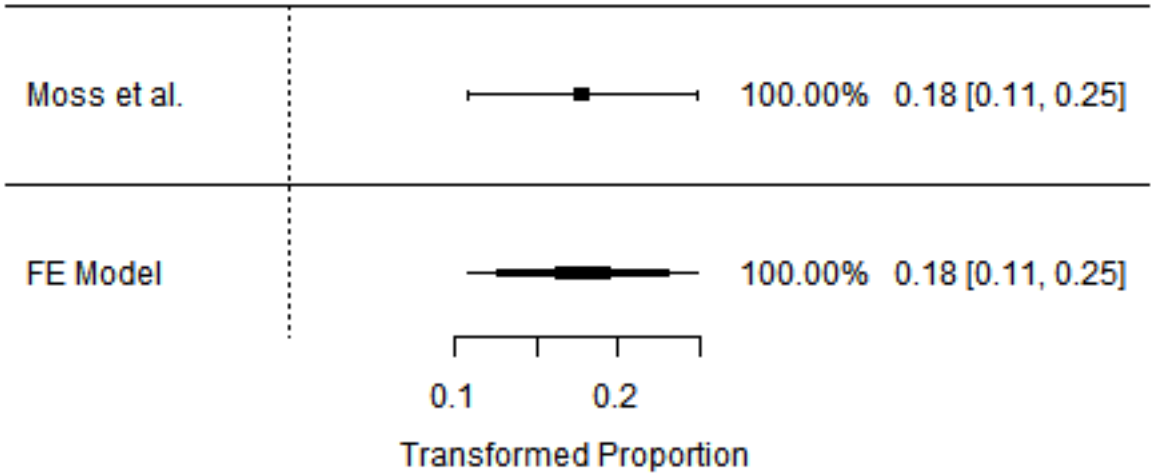


Appendices Figure 69. Forest plot for post-traumatic-stress symptomatology/diagnosis in Fragile X syndrome using a quality-effects model.

Specific anxiety profile analyses: Fragile X syndrome (Selective mutism)

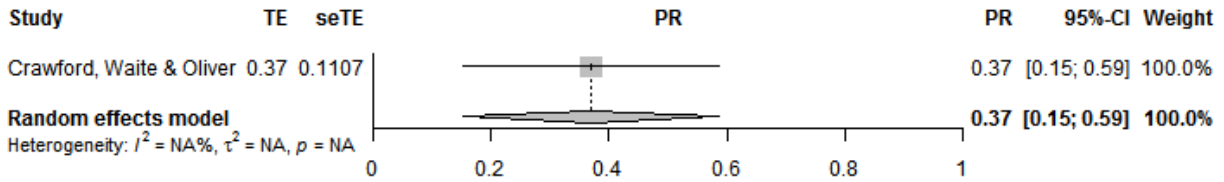


Appendices Figure 70. Forest plot for selective mutism in Fragile X syndrome using a random-effects model.

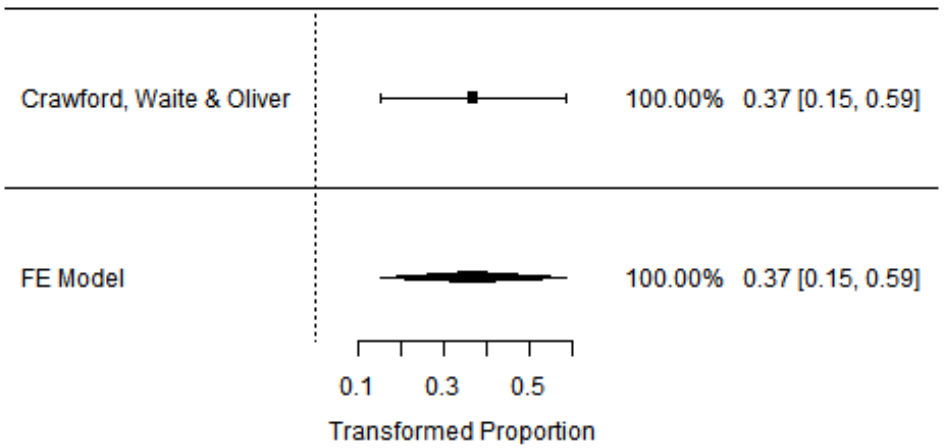


Appendices Figure 71. Forest plot for selective mutism in Fragile X syndrome using a quality-effects model.

Specific anxiety profile analyses: Fragile X syndrome (Physical injury fears)

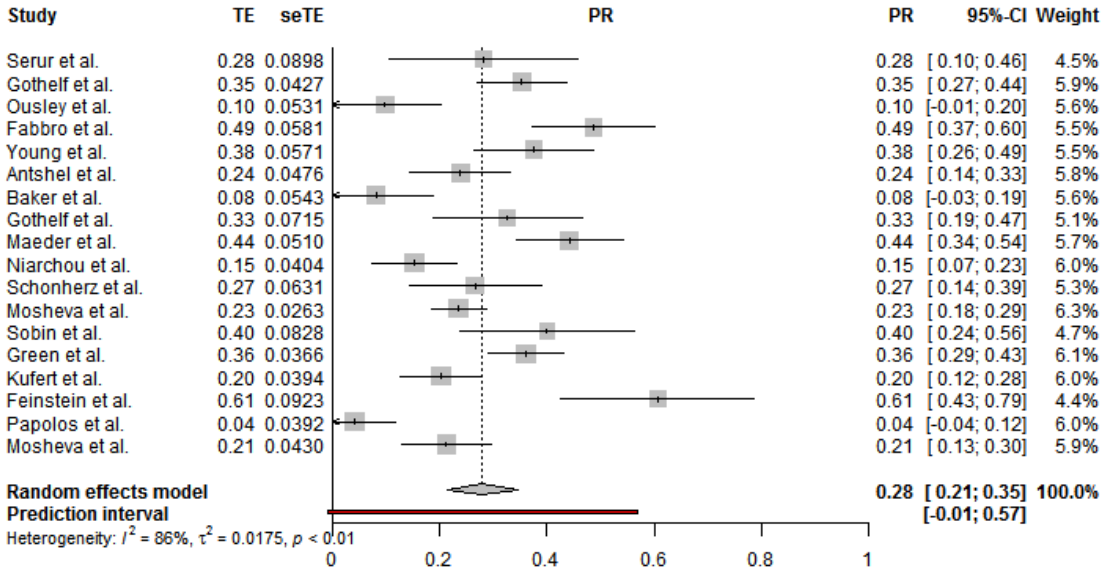


Appendices Figure 72. Forest plot for physical injury fears in Fragile X syndrome using a random-effects model.

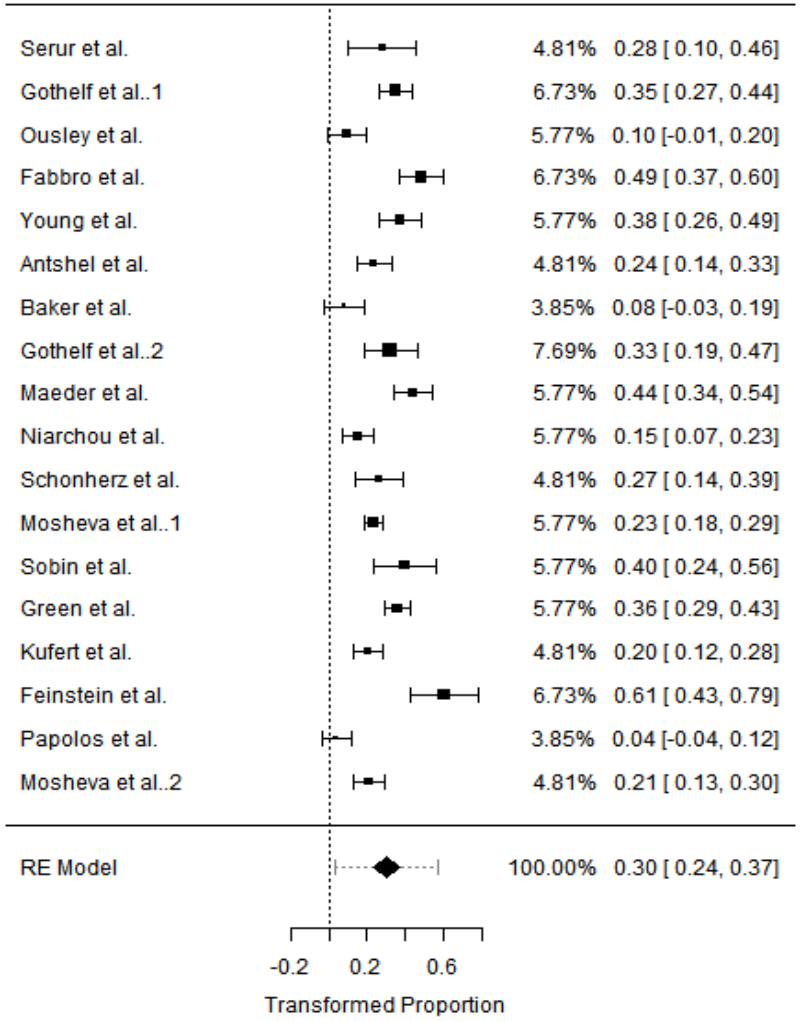


Appendices Figure 73. Forest plot for physical injury fears in Fragile X syndrome using a quality-effects model.

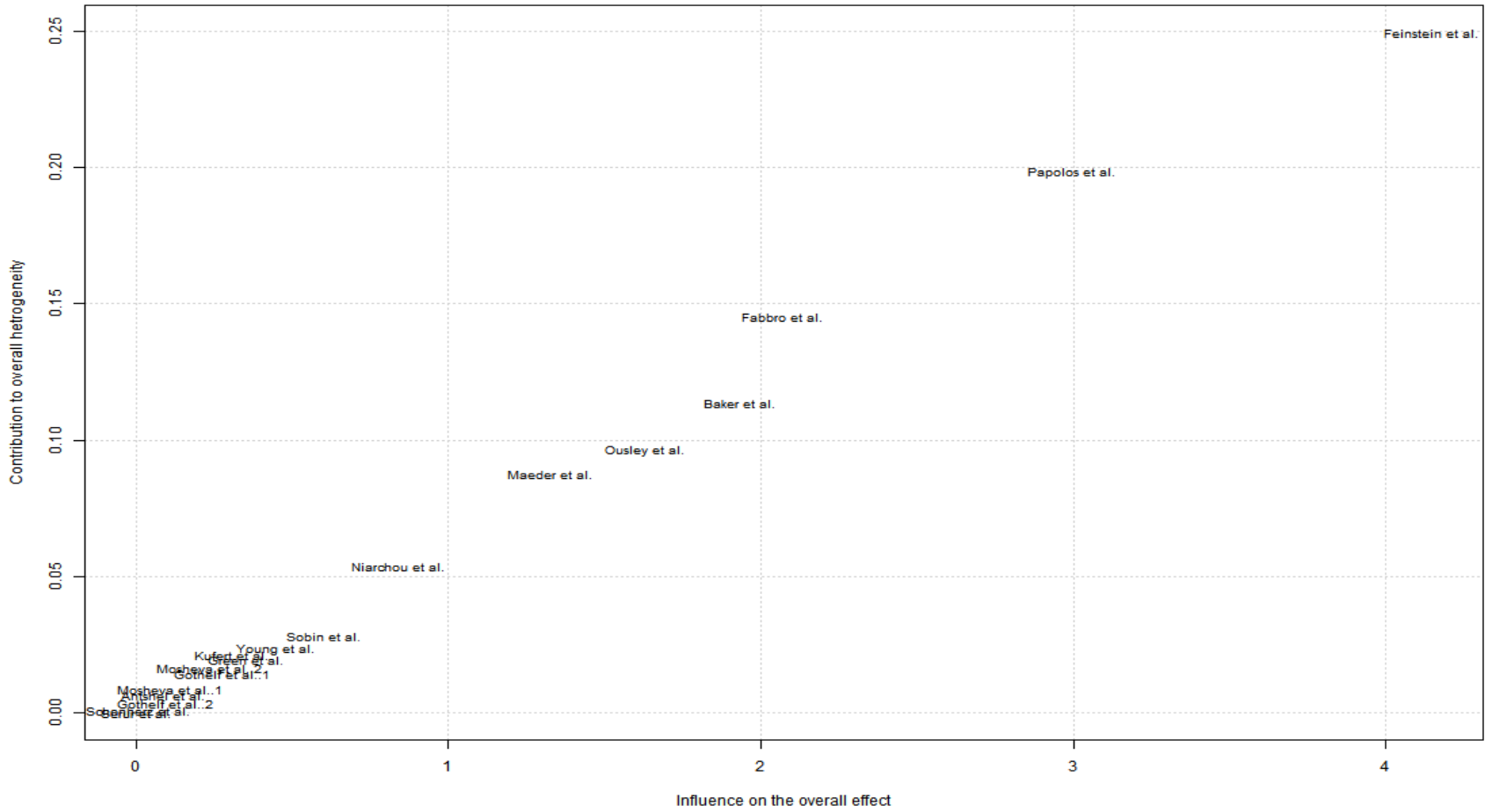
Specific anxiety profile analyses: 22q11.2 deletion syndrome (Specific phobia)



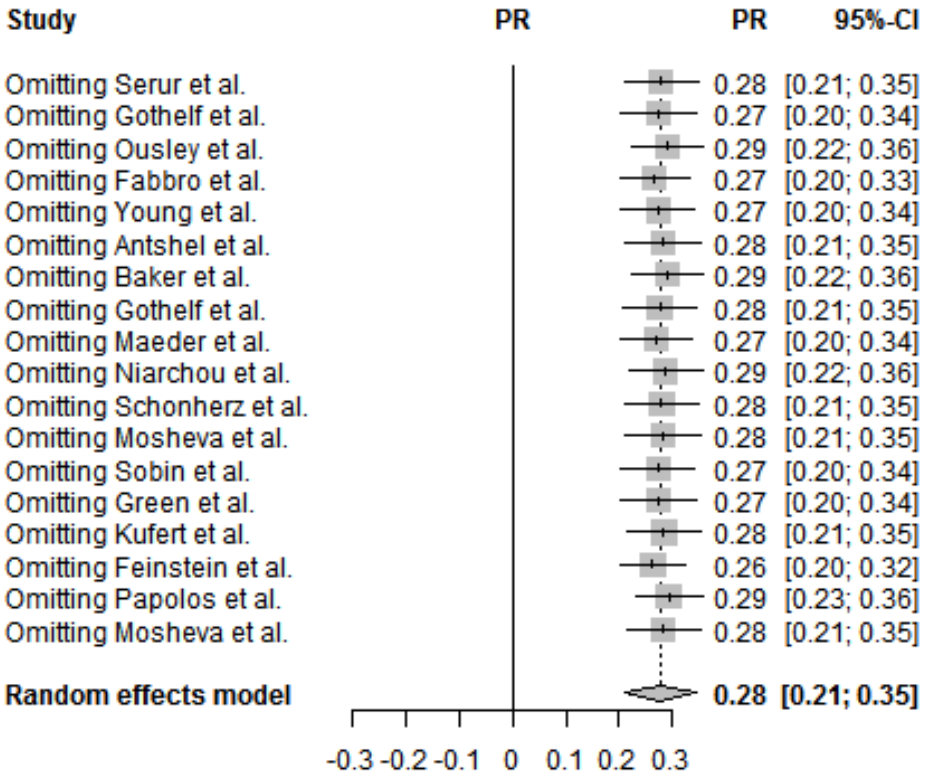
Appendices Figure 74. Forest plot for specific phobia in 22q11.2 deletion syndrome using a random-effects model.



Appendices Figure 75. Forest plot for specific phobia in 22q11.2 deletion syndrome using a quality-effects model.

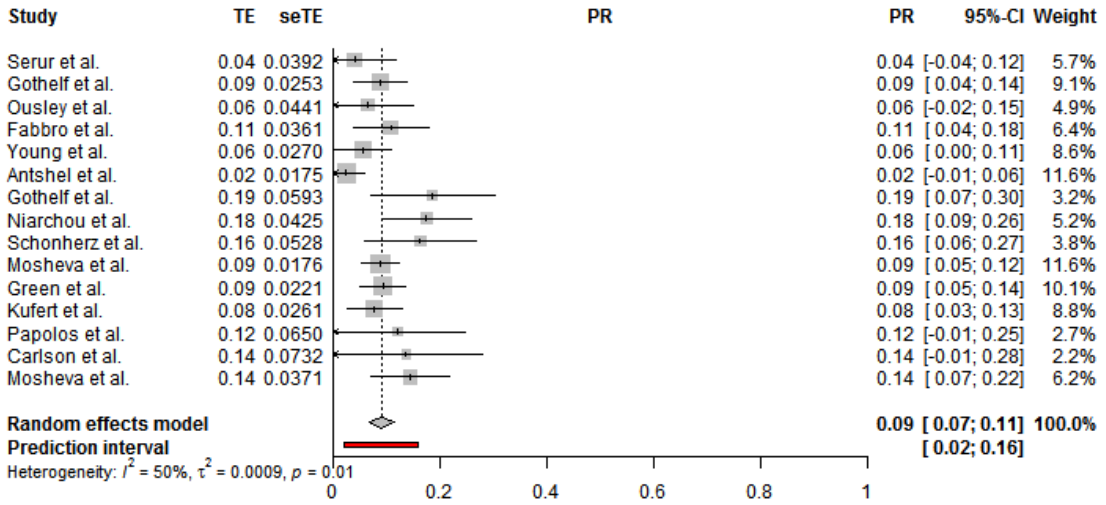


Appendices Figure 76. Baujat chart used to identify sources of heterogeneity: specific phobia in 22q11.2 deletion syndrome.

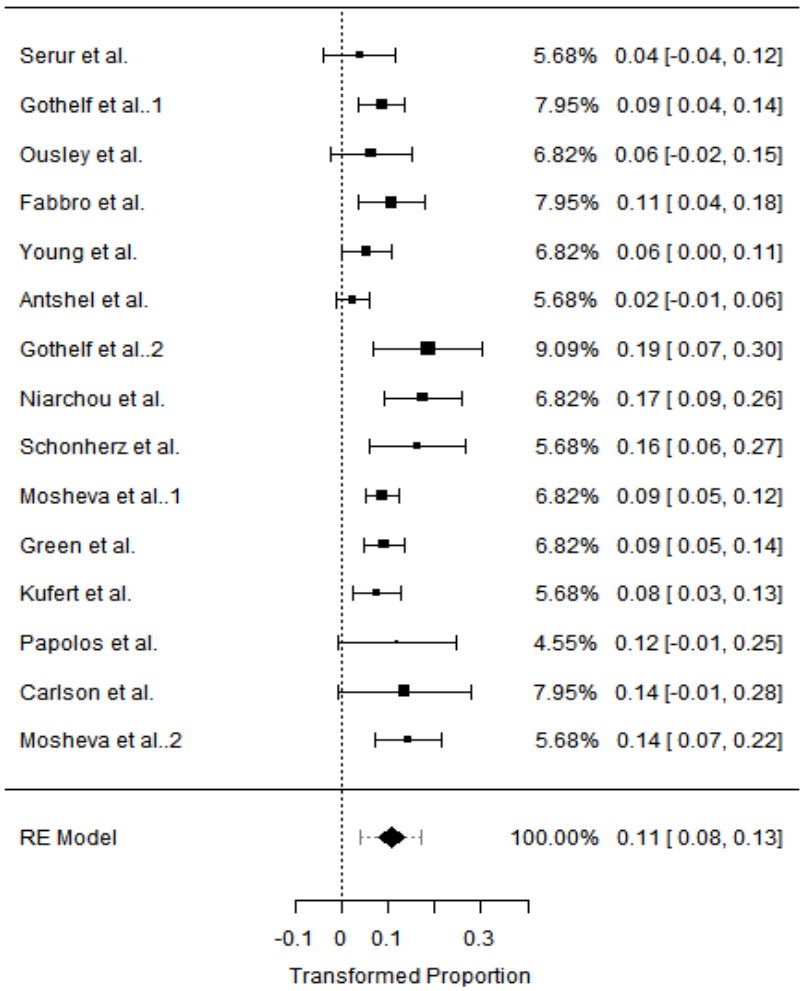


Appendices Figure 77. “Leave one out” analysis for specific phobia in 22q11.2 deletion syndrome.

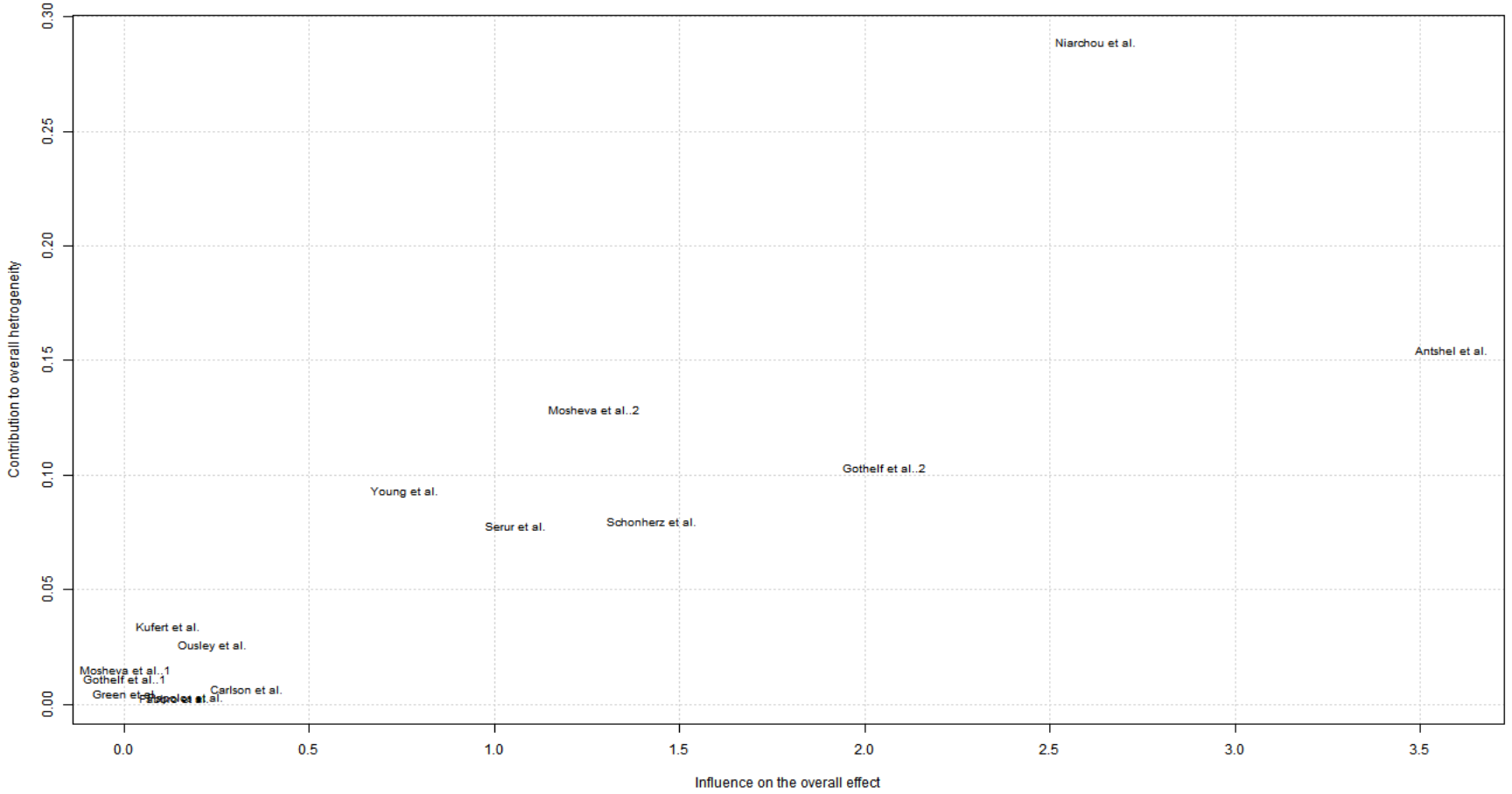
Specific anxiety profile analyses: 22q11.2 deletion syndrome (Social anxiety)



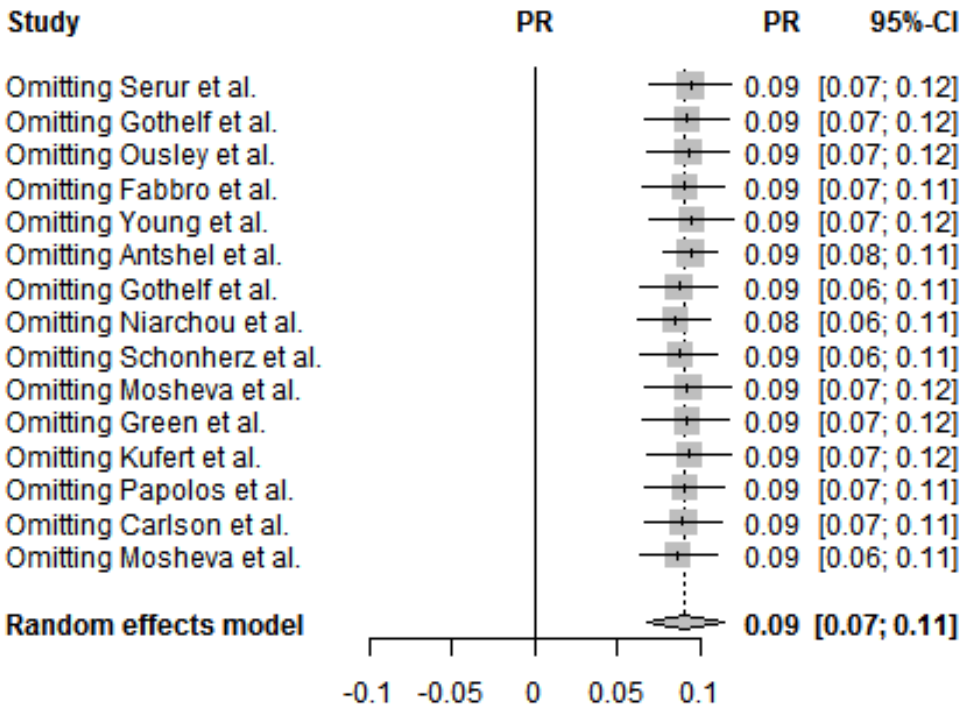
Appendices Figure 78. Forest plot for social anxiety in 22q11.2 deletion syndrome using a random-effects model.



Appendices Figure 79. Forest plot for social anxiety in 22q11.2 deletion syndrome using a quality-effects model.

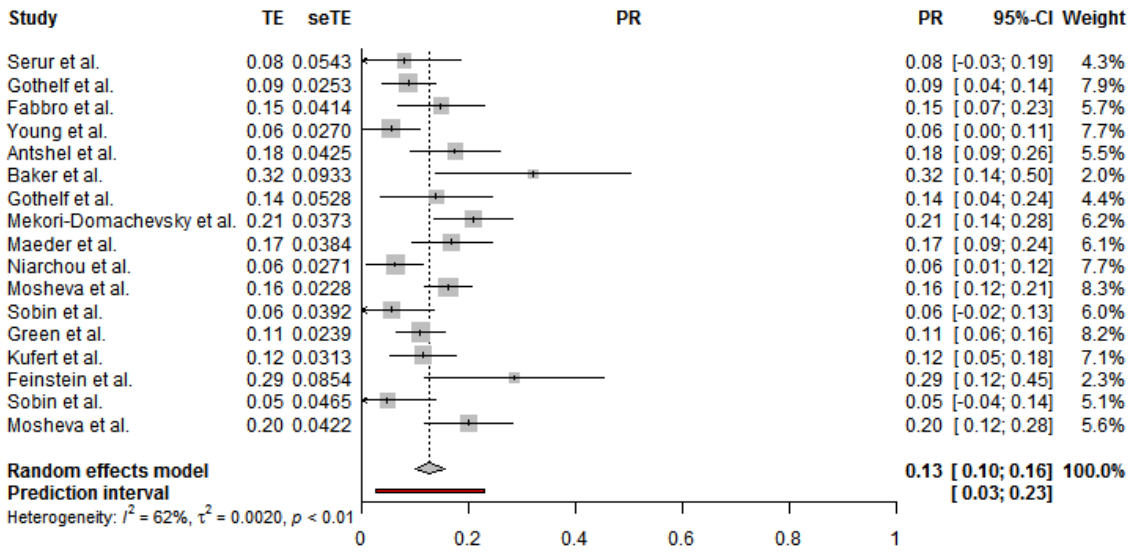


Appendices Figure 80. Baujat chart used to identify sources of heterogeneity: social anxiety in 22q11.2 deletion syndrome.

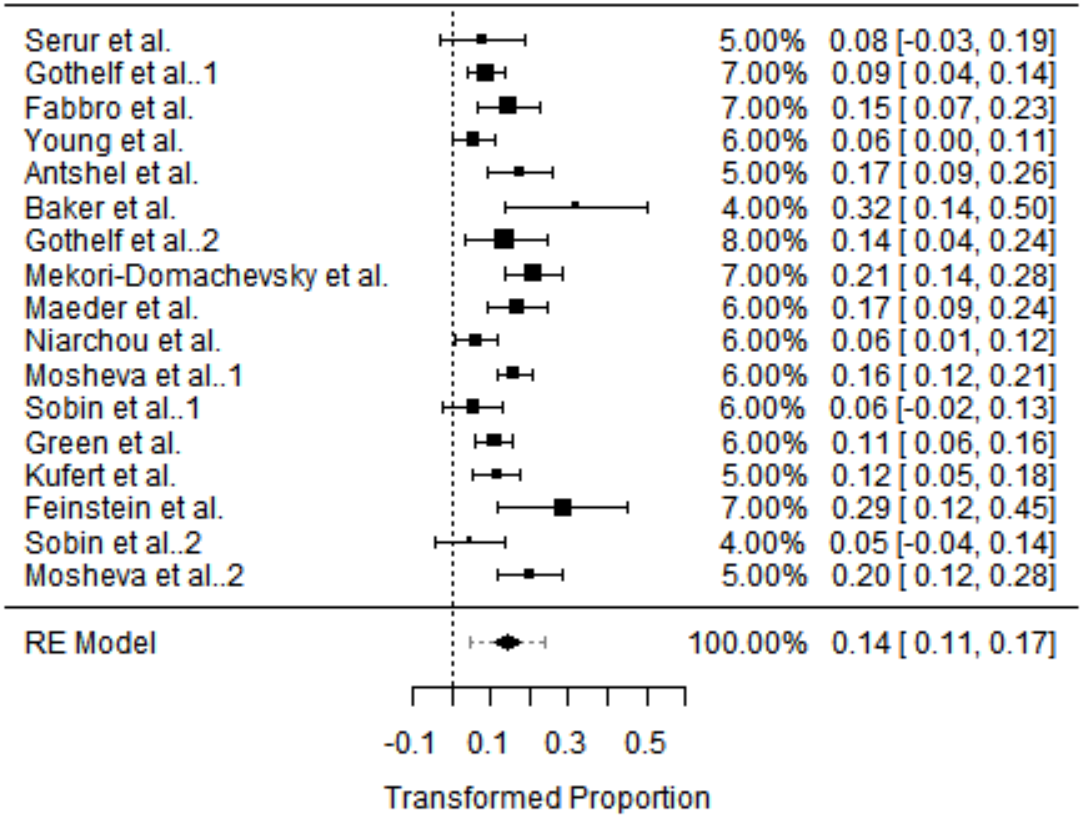


Appendices Figure 81. “Leave one out” analysis for social anxiety in 22q11.2 deletion syndrome.

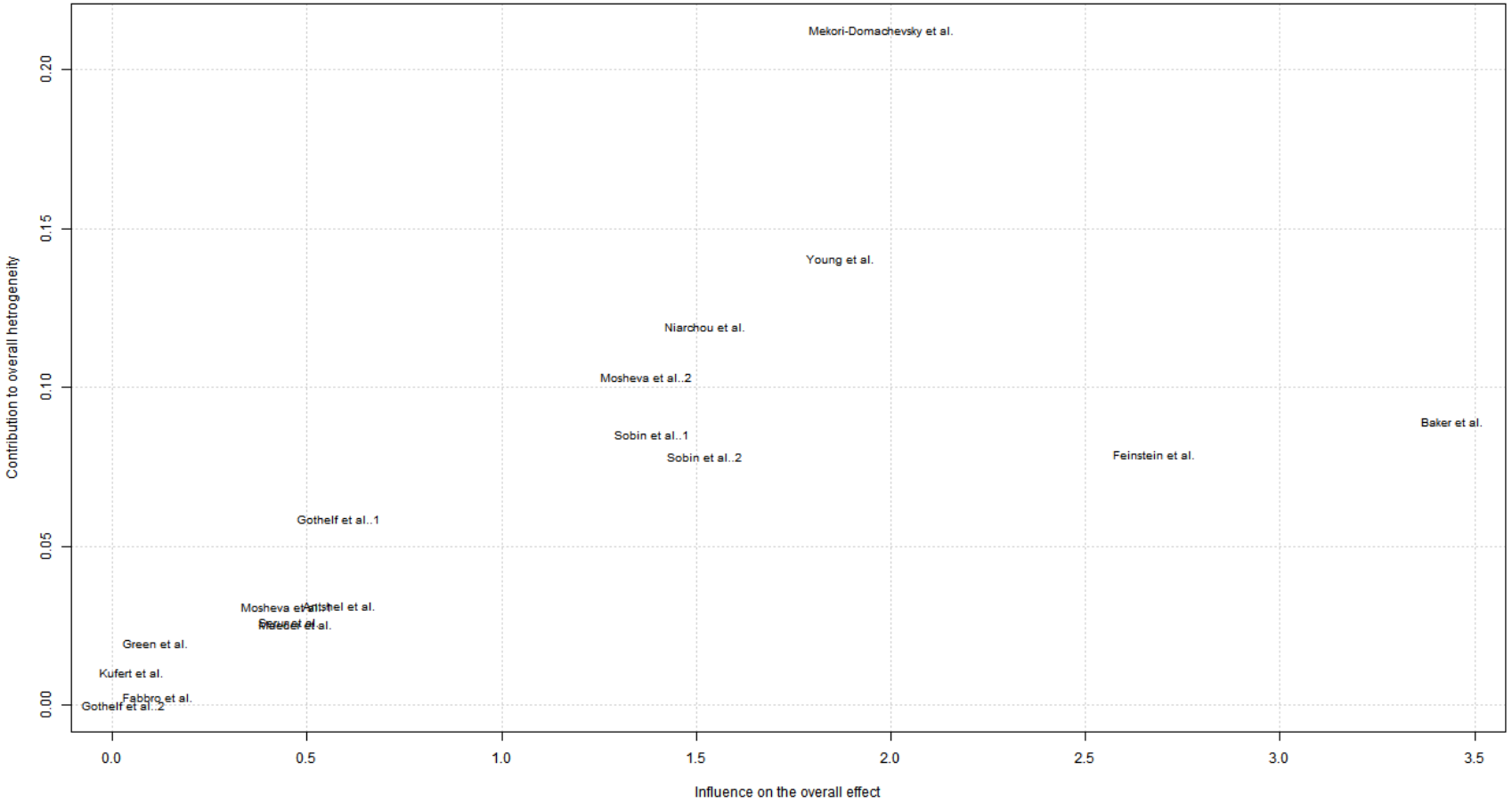
Specific anxiety profile analyses: 22q11.2 deletion syndrome (Generalised anxiety)



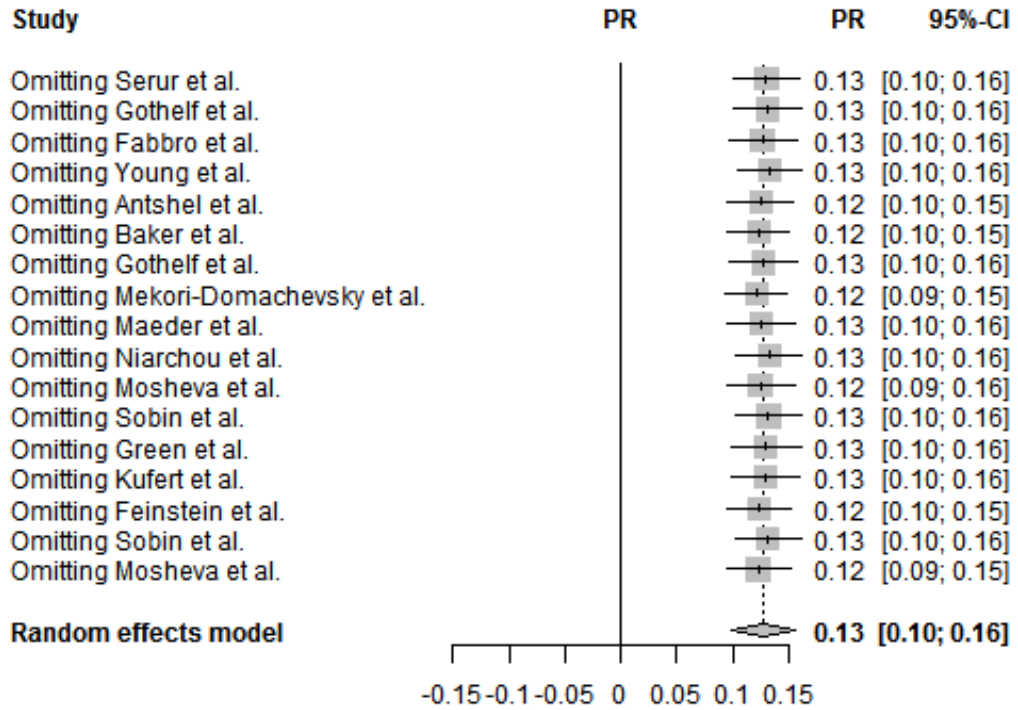
Appendices Figure 82. Forest plot for generalised anxiety in 22q11.2 deletion syndrome using a random-effects model.



Appendices Figure 83. Forest plot for generalised anxiety in 22q11.2 deletion syndrome using a quality-effects model.

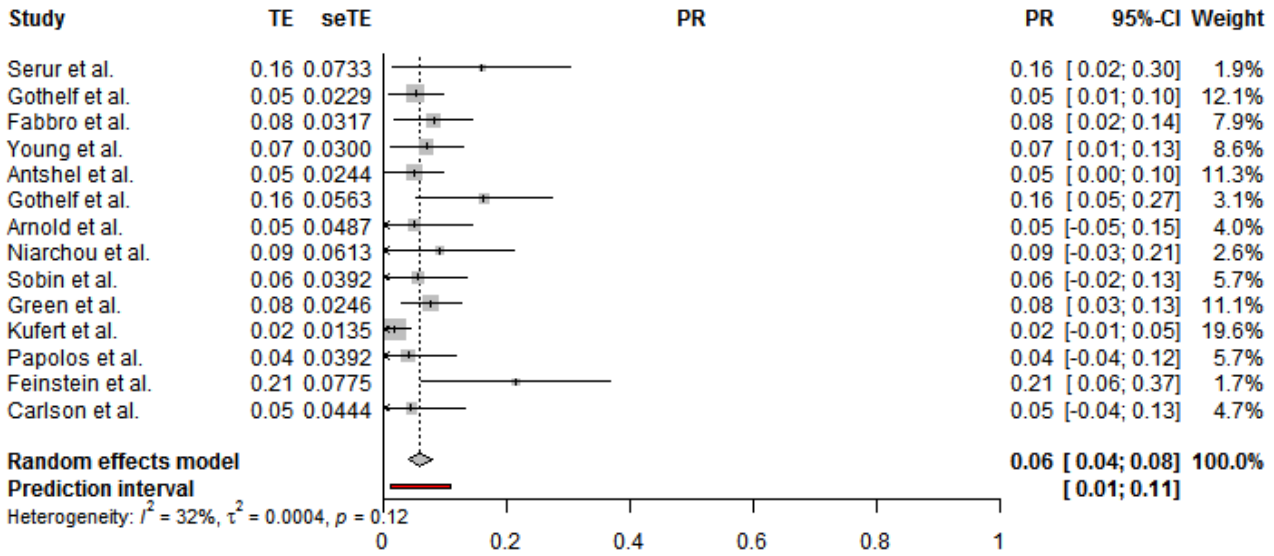


Appendices Figure 84. Baujat chart used to identify sources of heterogeneity: generalised anxiety in 22q11.2 deletion syndrome

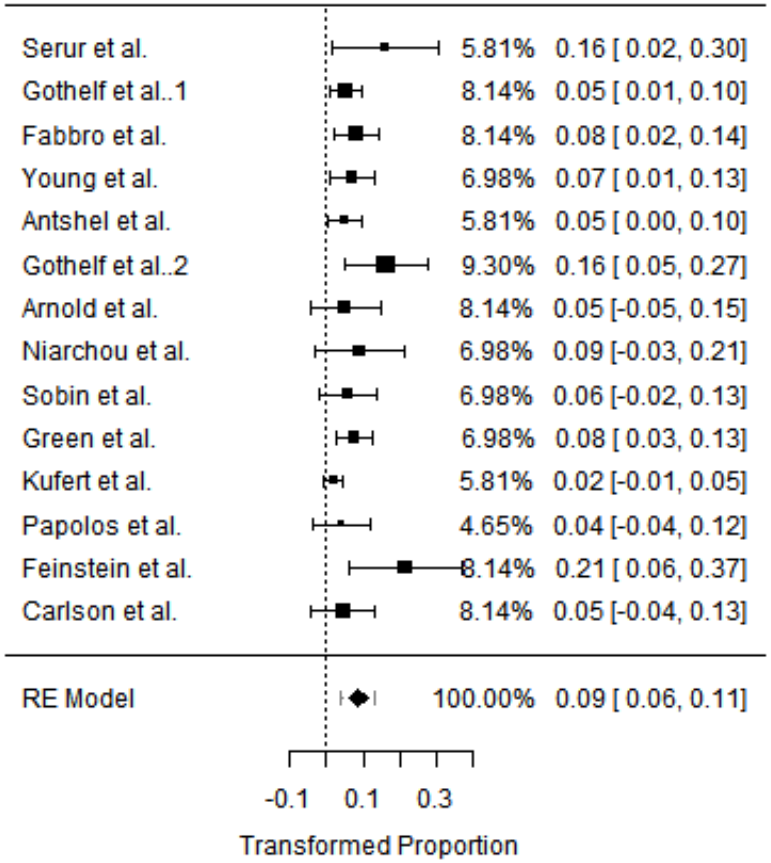


Appendices Figure 85. “Leave one out” analysis for generalised anxiety in 22q11.2 deletion syndrome.

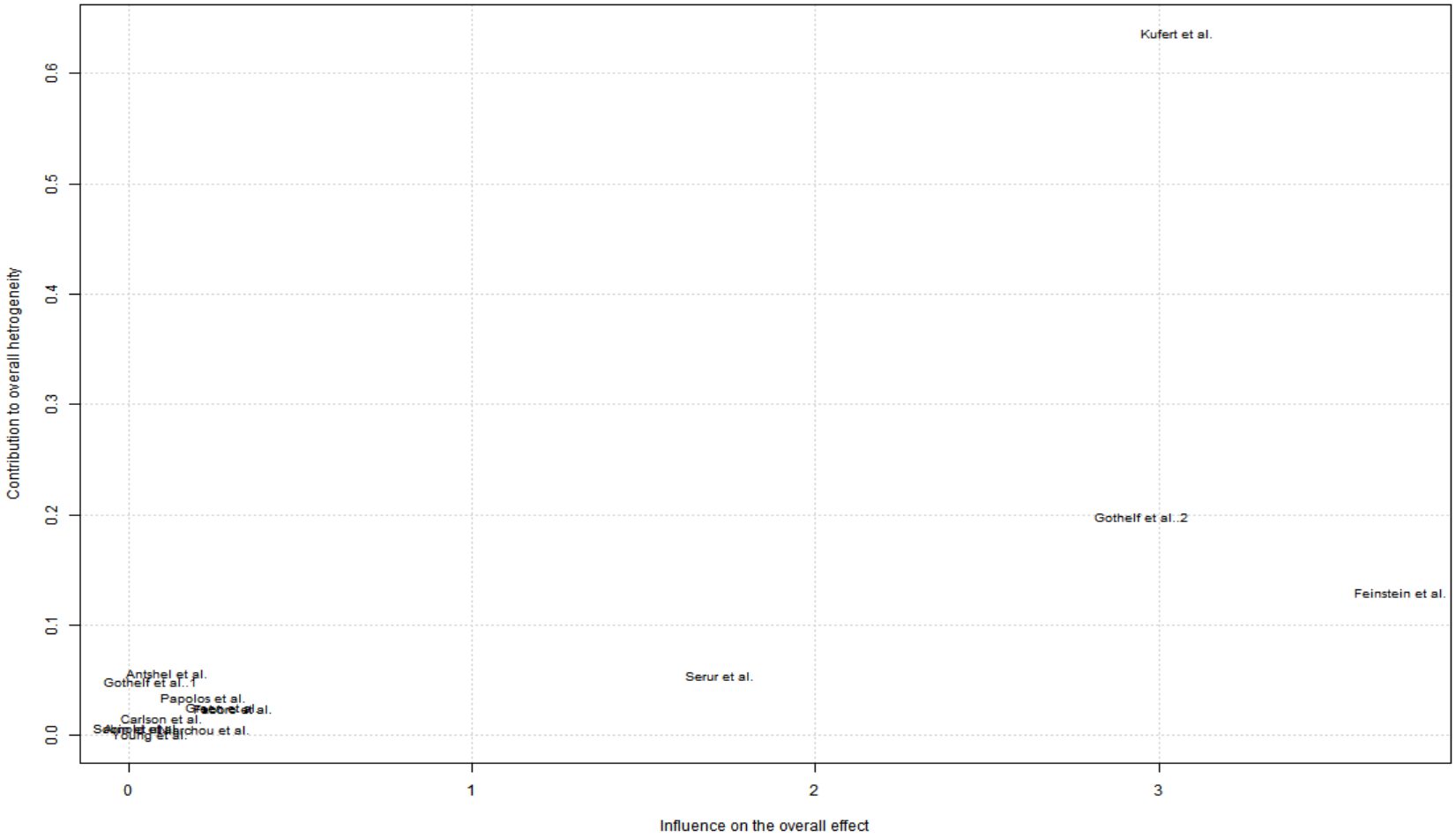
Specific anxiety profile analyses: 22q11.2 deletion syndrome (Separation anxiety)



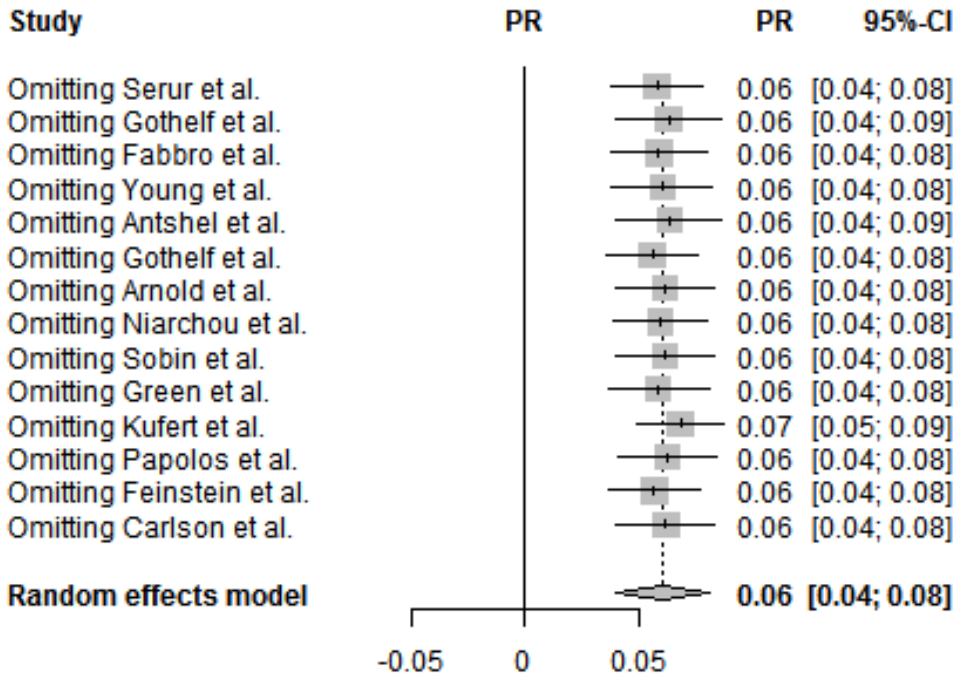
Appendices Figure 86. Forest plot for separation anxiety in 22q11.2 deletion syndrome using a random-effects model.



Appendices Figure 87. Forest plot for separation anxiety in 22q11.2 deletion syndrome using a quality-effects model.

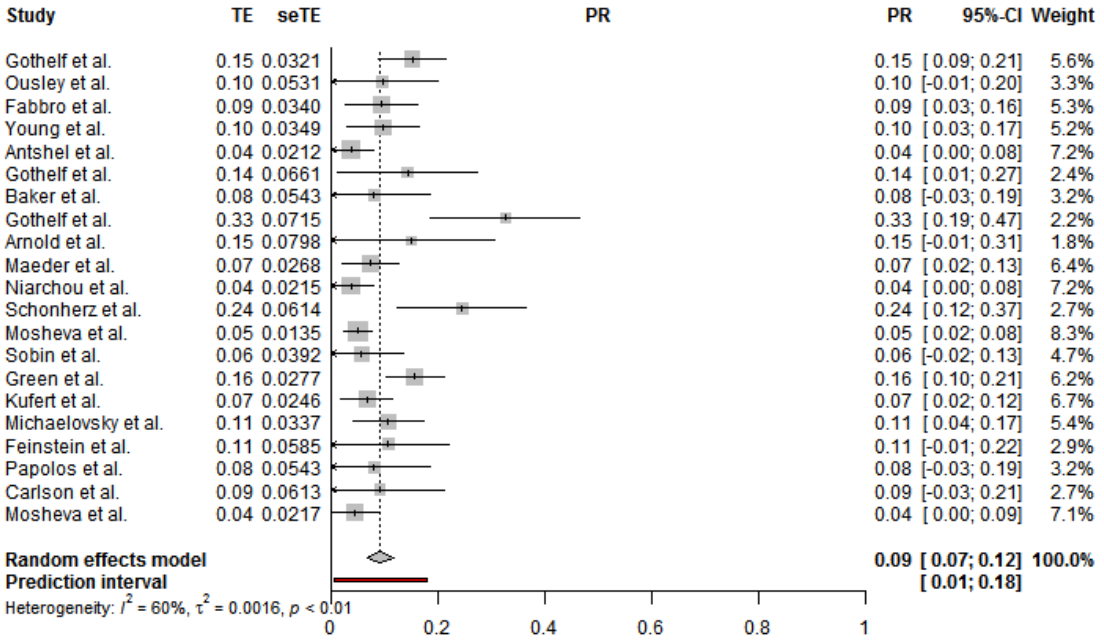


Appendices Figure 88. Baujat chart used to identify sources of heterogeneity: separation anxiety in 22q11.2 deletion syndrome.

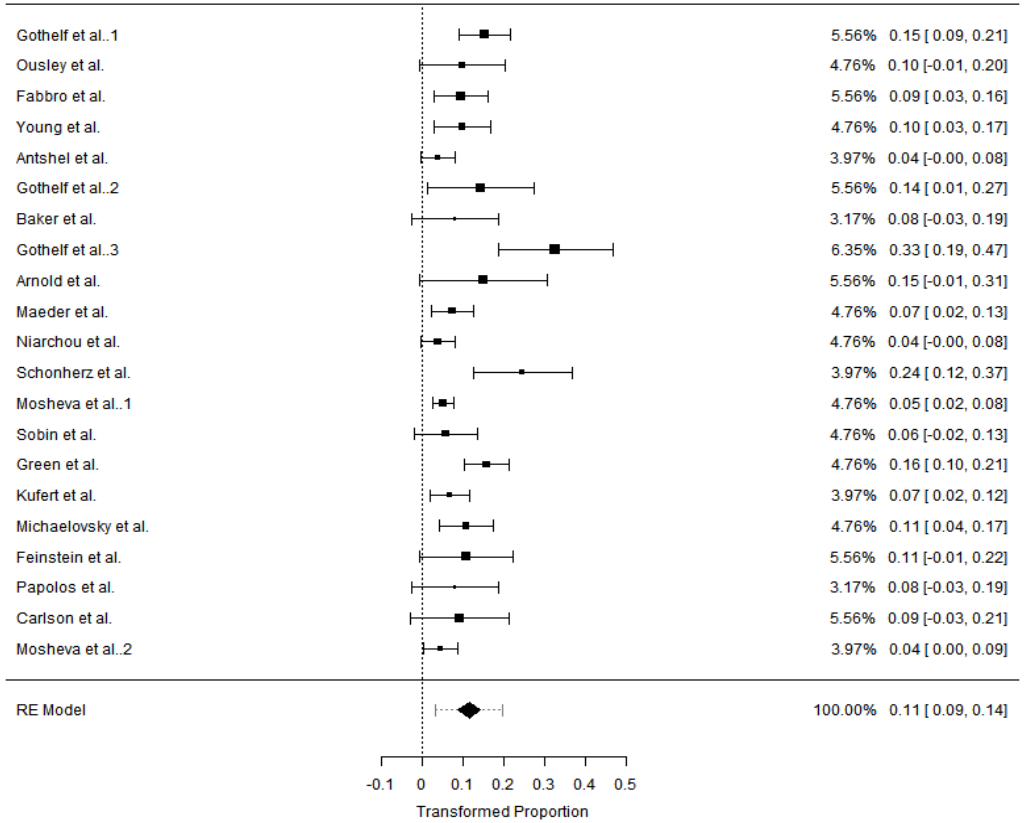


Appendices Figure 89. “Leave one out” analysis for separation anxiety in 22q11.2 deletion syndrome.

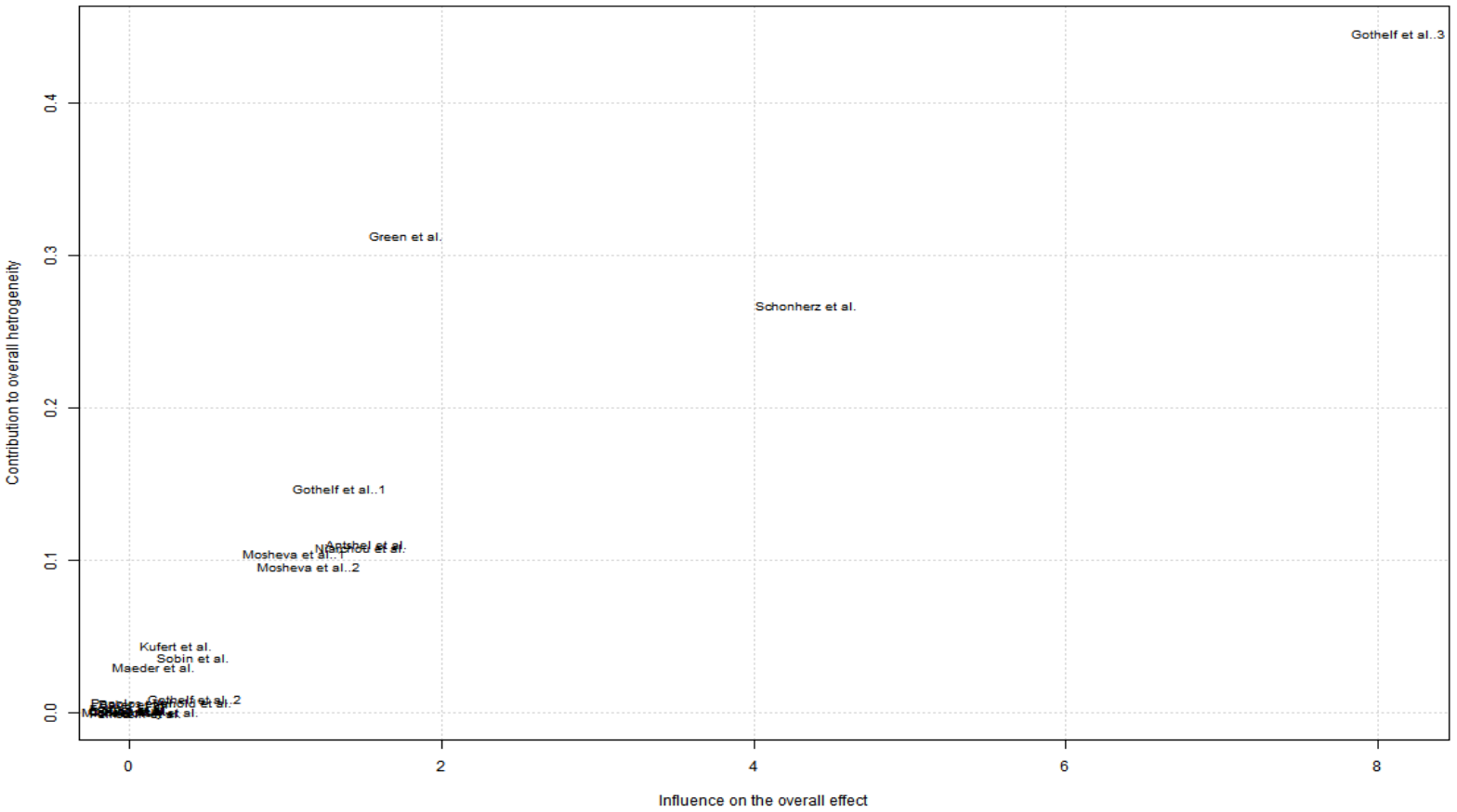
Specific anxiety profile analyses: 22q11.2 deletion syndrome (Obsessive compulsive symptomatology/diagnosis)



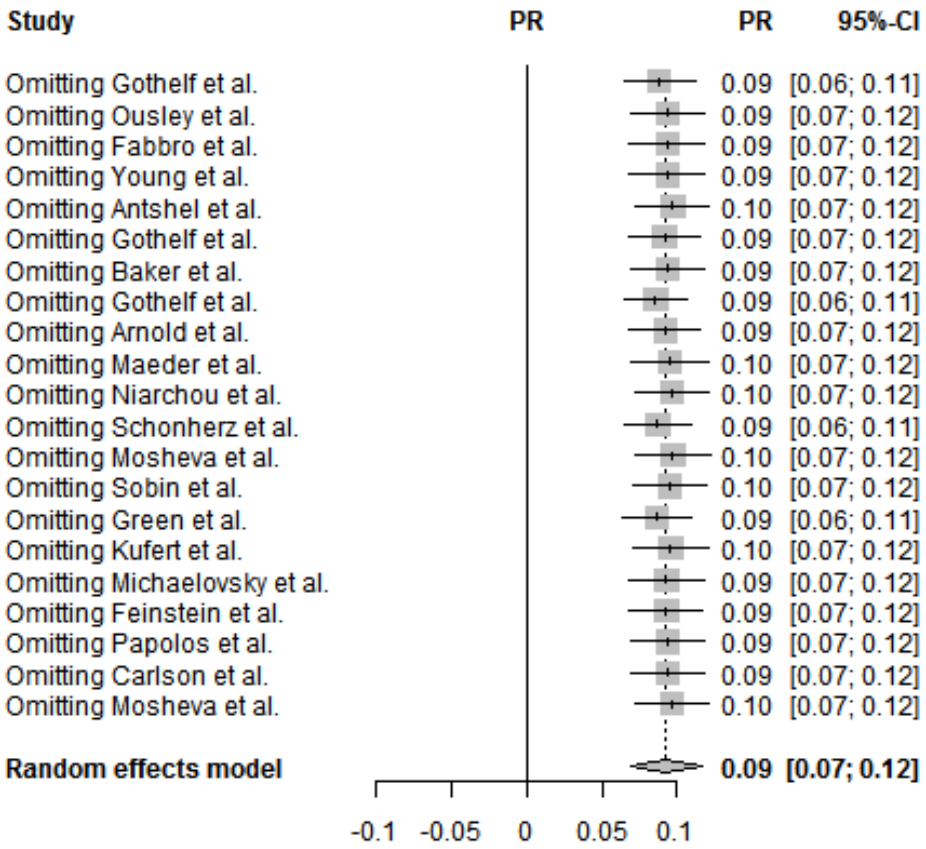
Appendices Figure 90. Forest plot for obsessive compulsive symptomatology/diagnosis in 22q11.2 deletion syndrome using a random-effects model.



Appendices Figure 91. Forest plot for obsessive compulsive symptomatology/diagnosis in 22q11.2 deletion syndrome using a quality-effects model

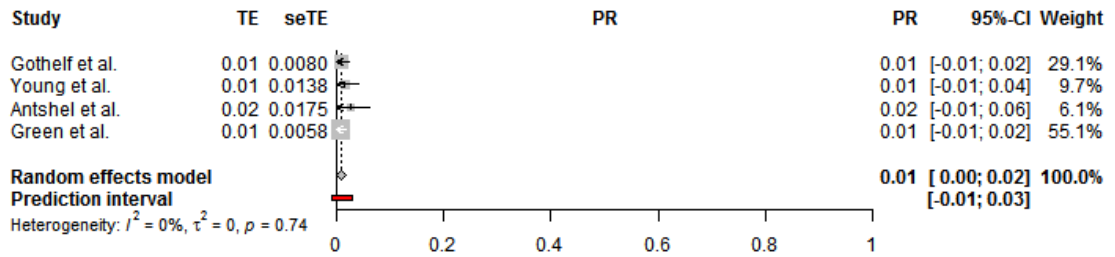


Appendices Figure 92. Baujat chart used to identify sources of heterogeneity: obsessive compulsive symptomatology/diagnosis in 22q11.2 deletion syndrome.

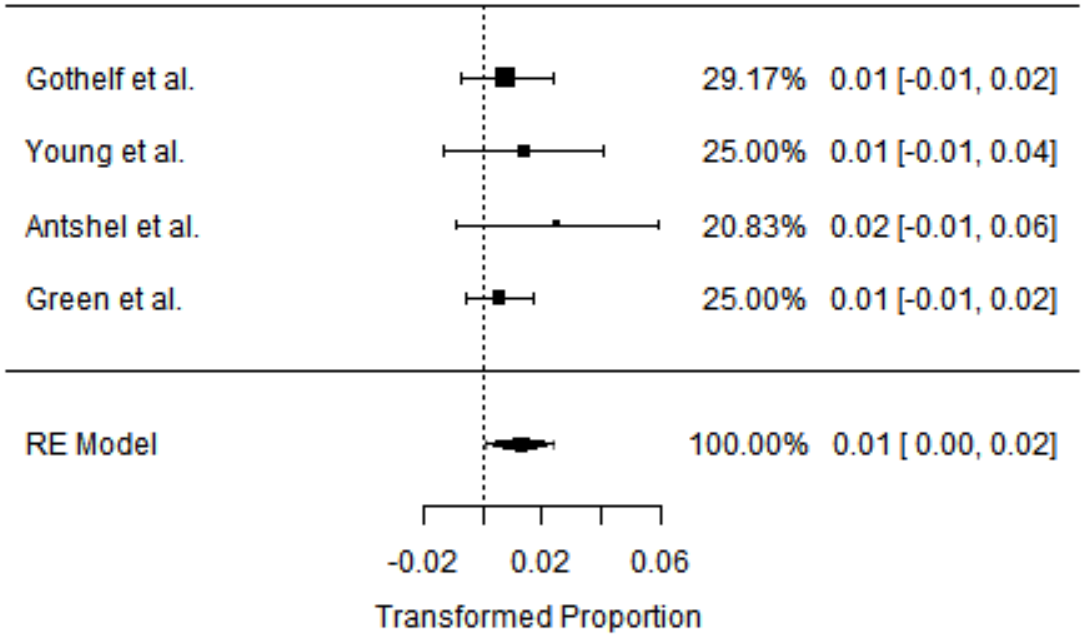


Appendices Figure 93. “Leave one out” analysis for obsessive compulsive symptomatology/diagnosis in 22q11.2 deletion syndrome.

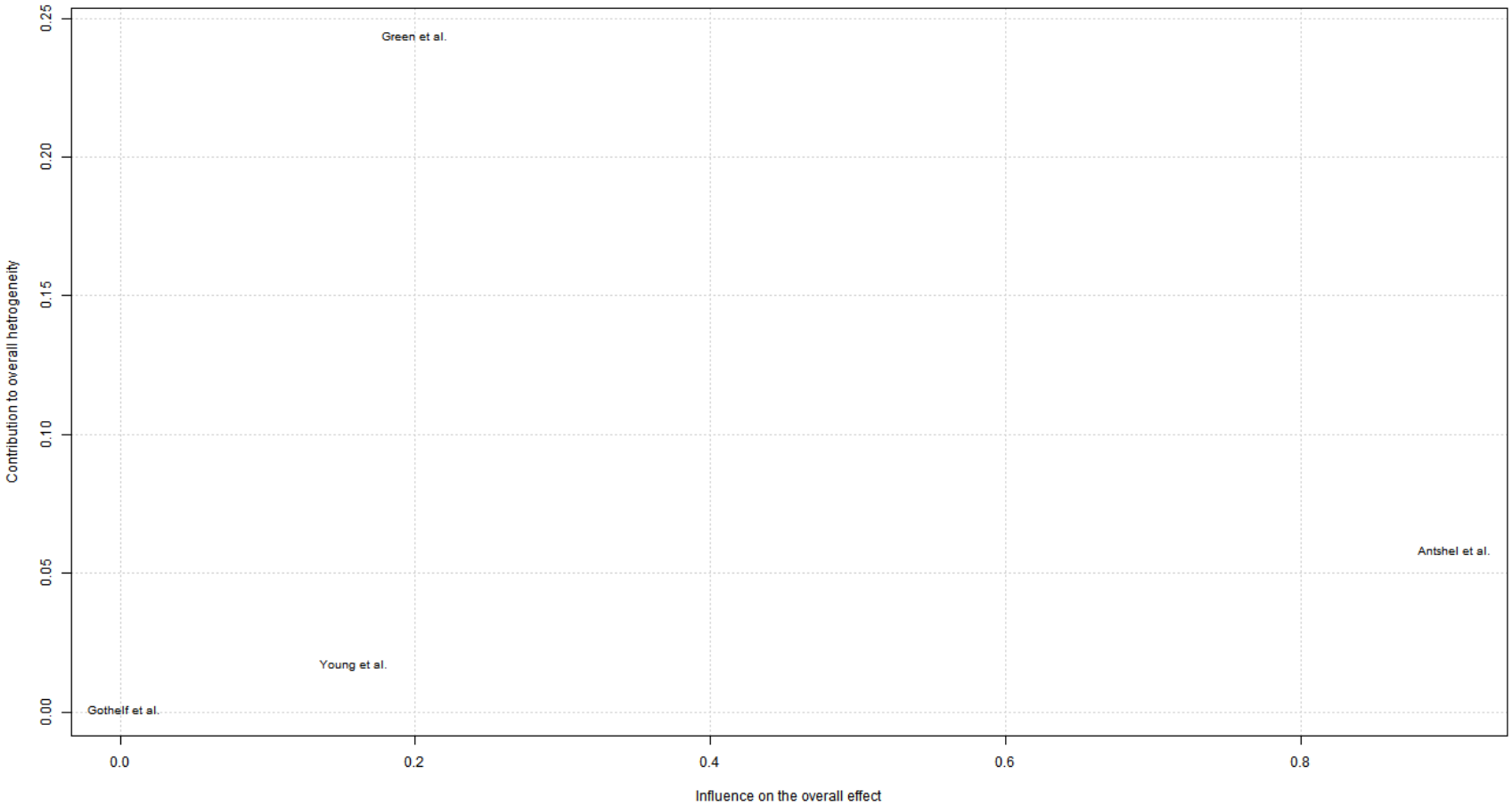
Specific anxiety profile analyses: 22q11.2 deletion syndrome (Panic)



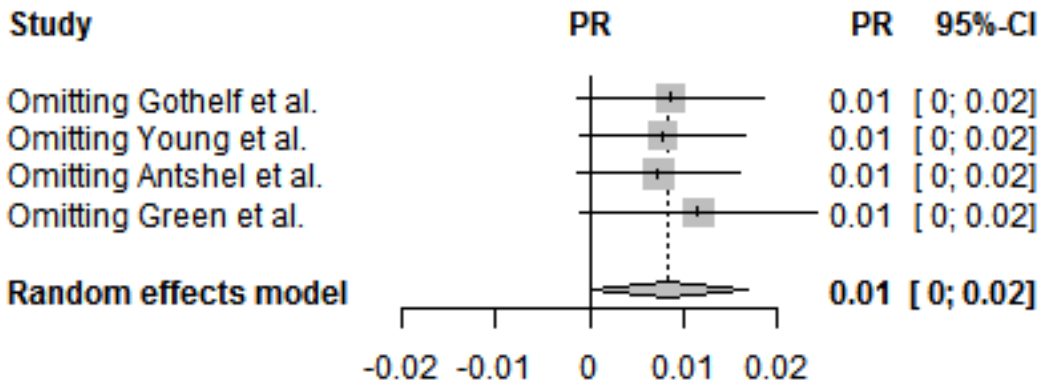
Appendices Figure 94. Forest plot for panic in 22q11.2 deletion syndrome using a random-effects model.



Appendices Figure 95. Forest plot for panic in 22q11.2 deletion syndrome using a quality-effects model.

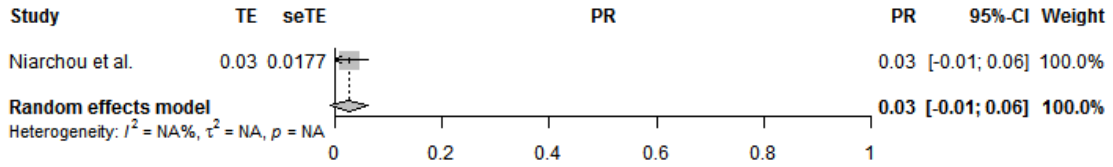


Appendices Figure 96. Baujat chart used to identify sources of heterogeneity: panic in 22q11.2 deletion syndrome.

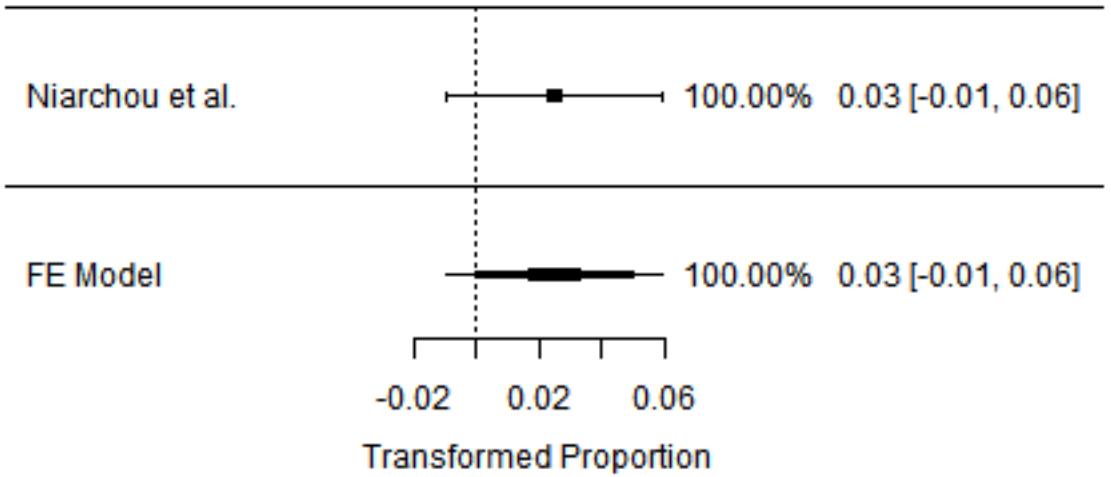


Appendices Figure 97. “Leave one out” analysis for panic in 22q11.2 deletion syndrome.

Specific anxiety profile analyses: 22q11.2 deletion syndrome (Panic and agoraphobia)

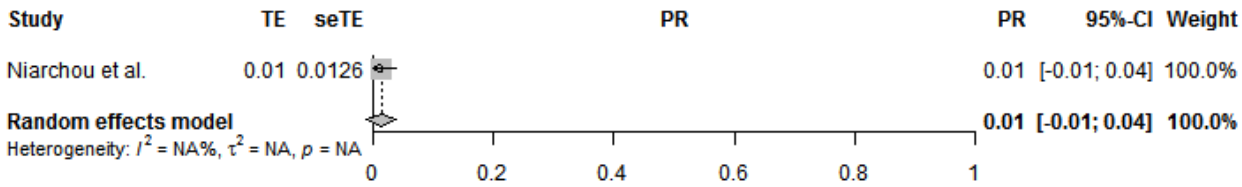


Appendices Figure 98. Forest plot for panic and agoraphobia in 22q11.2 deletion syndrome using a random-effects model.

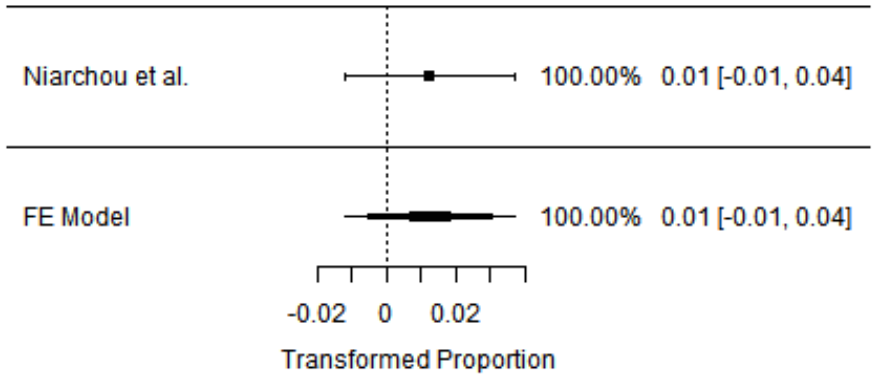


Appendices Figure 99. Forest plot for panic and agoraphobia in 22q11.2 deletion syndrome using a quality-effects model.

Specific anxiety profile analyses: 22q11.2 deletion syndrome (Panic without agoraphobia)

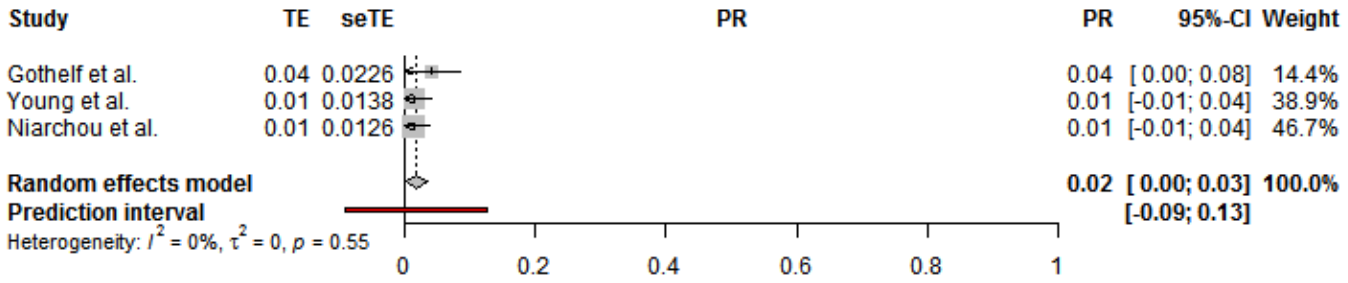


Appendices Figure 100. Forest plot for panic without agoraphobia in 22q11.2 deletion syndrome using a random-effects model.

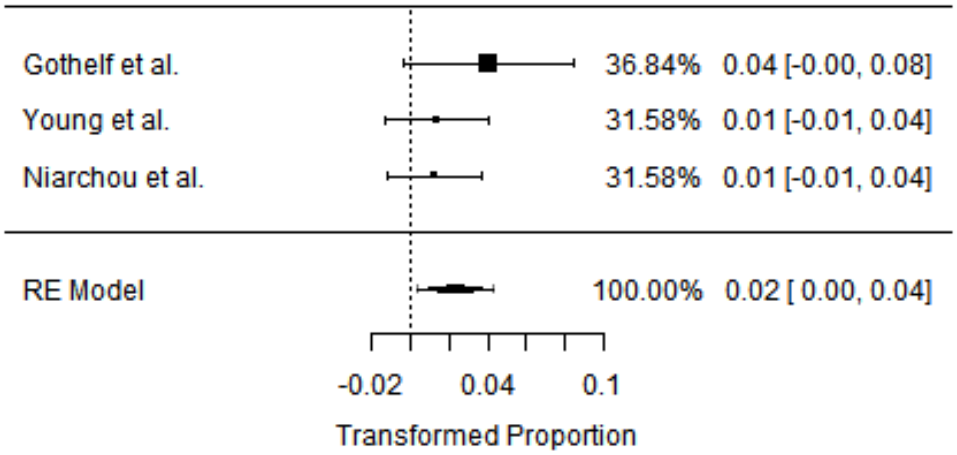


Appendices Figure 101. Forest plot for panic without agoraphobia in 22q11.2 deletion syndrome using a quality-effects model.

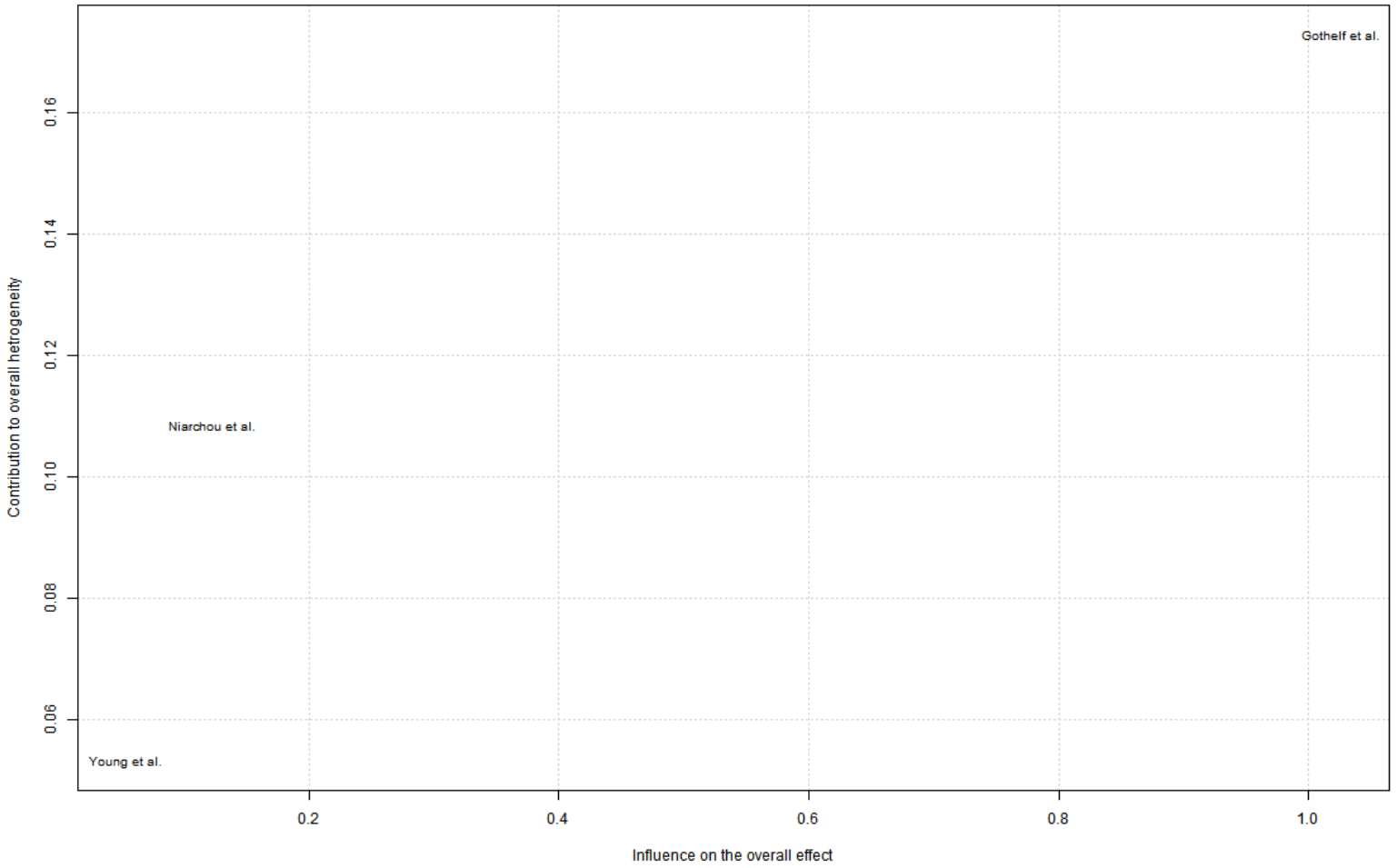
Specific anxiety profile analyses: 22q11.2 deletion syndrome (Agoraphobia)



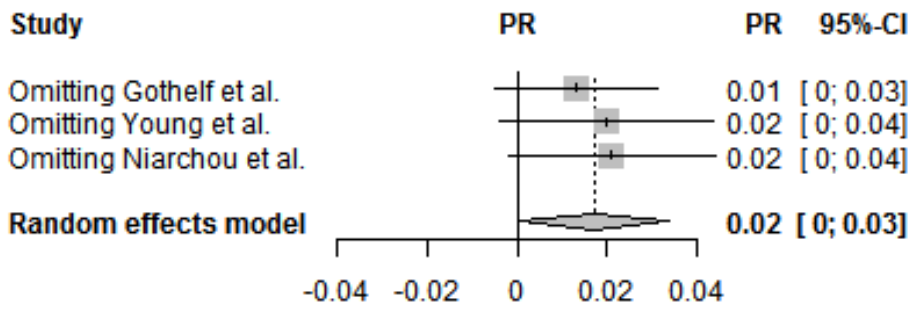
Appendices Figure 102. Forest plot for agoraphobia in 22q11.2 deletion syndrome using a random-effects model.



Appendices Figure 103. Forest plot for agoraphobia in 22q11.2 deletion syndrome using a quality-effects model.

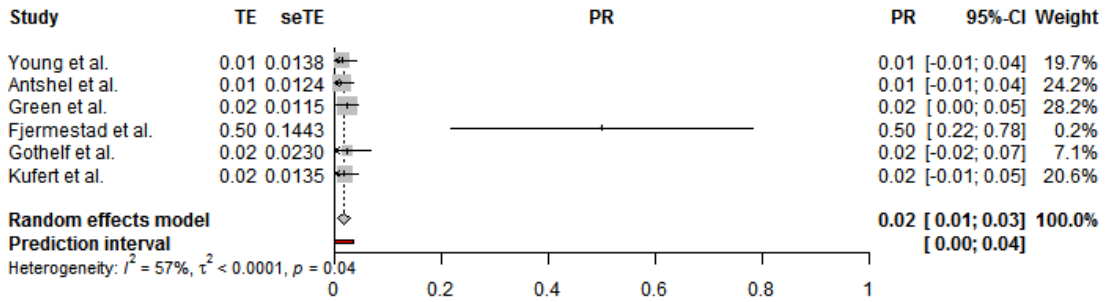


Appendices Figure 104. Baujat chart used to identify sources of heterogeneity: agoraphobia in 22q11.2 deletion syndrome.

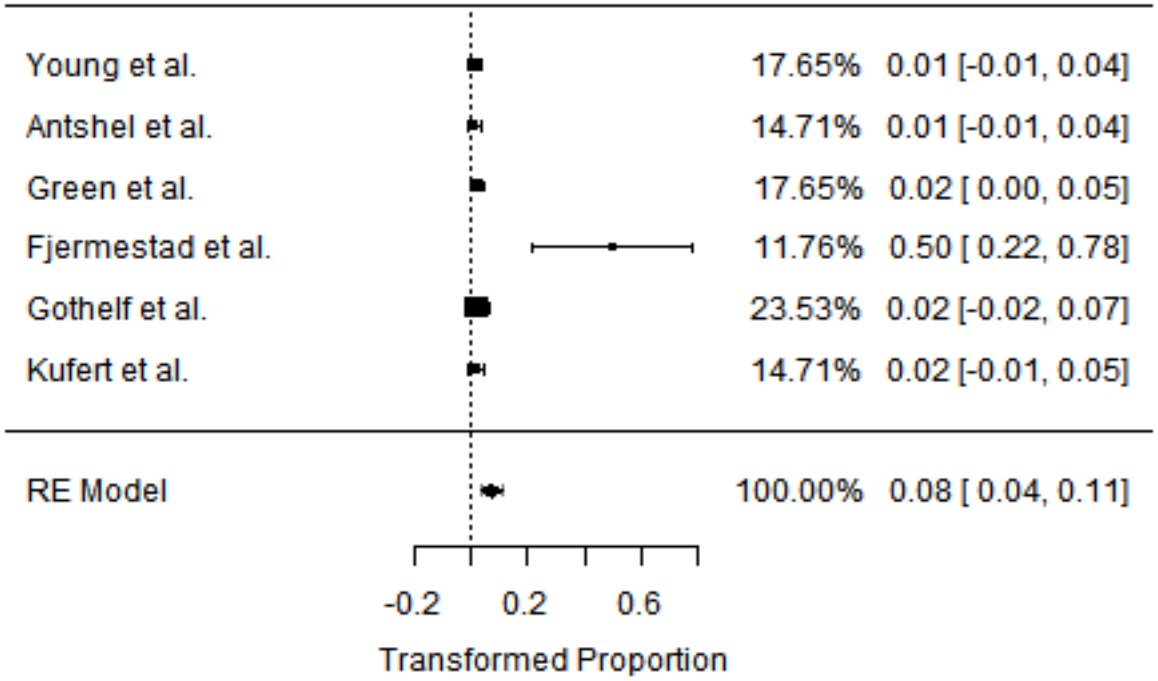


Appendices Figure 105. “Leave one out” analysis for agoraphobia in 22q11.2 deletion syndrome.

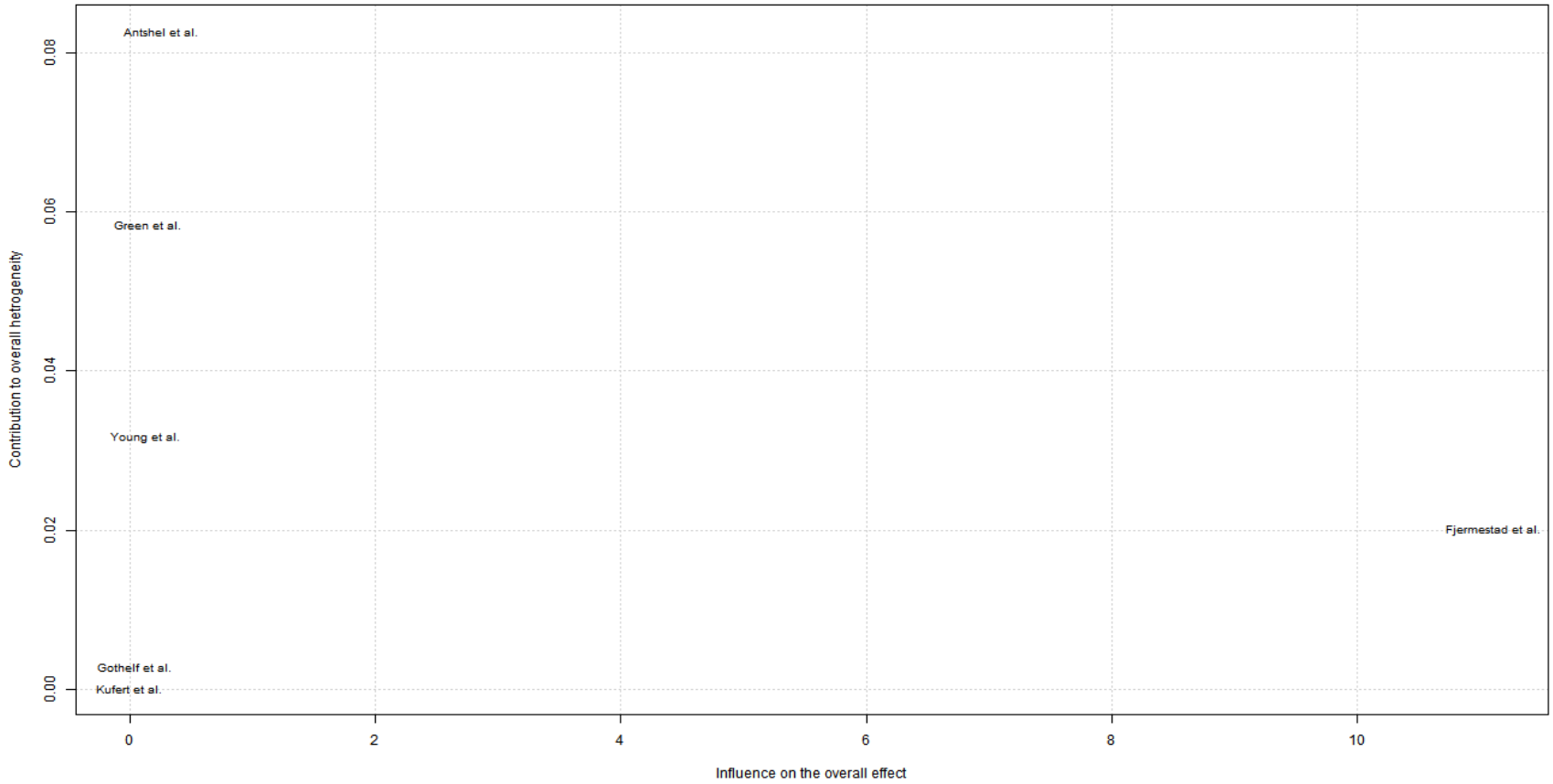
Specific anxiety profile analyses: 22q11.2 deletion syndrome (Post-traumatic stress symptomatology/diagnosis)



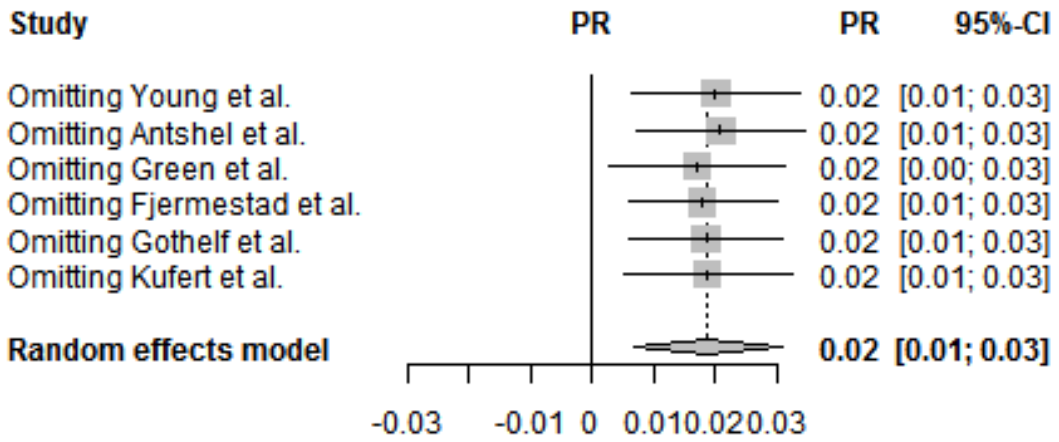
Appendices Figure 106. Forest plot for post-traumatic stress symptomatology/diagnosis in 22q11.2 deletion syndrome using a random-effects model.



Appendices Figure 107. Forest plot for post-traumatic stress symptomatology/diagnosis in 22q11.2 deletion syndrome using a quality-effects model.

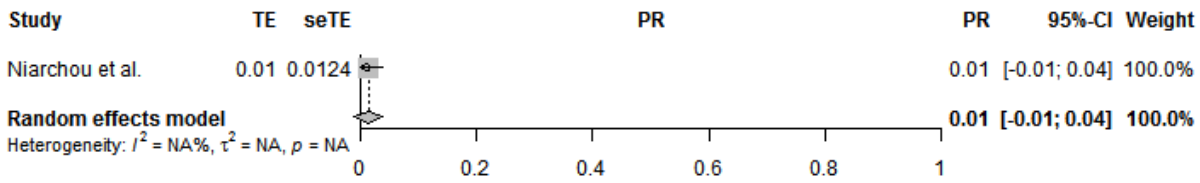


Appendices Figure 108. Baujat chart used to identify sources of heterogeneity: post-traumatic stress symptomatology/diagnosis in 22q11.2 deletion syndrome.

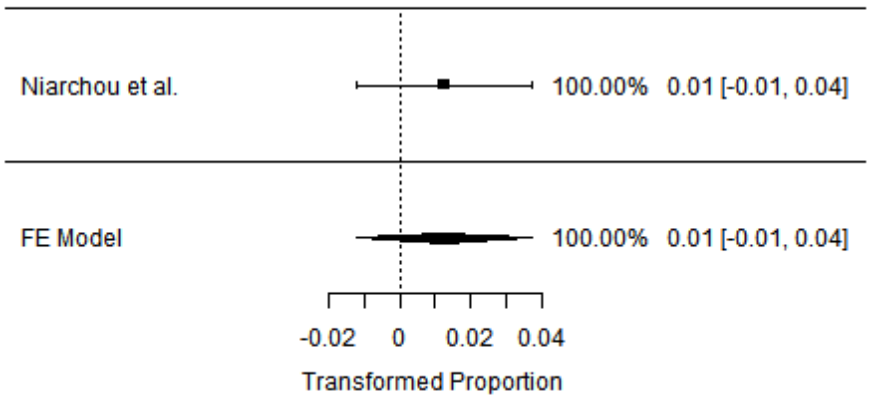


Appendices Figure 109. “Leave one out” analysis for post-traumatic stress symptomatology/diagnosis in 22q11.2 deletion syndrome.

Specific anxiety profile analyses: 22q11.2 deletion syndrome (Selective mutism)

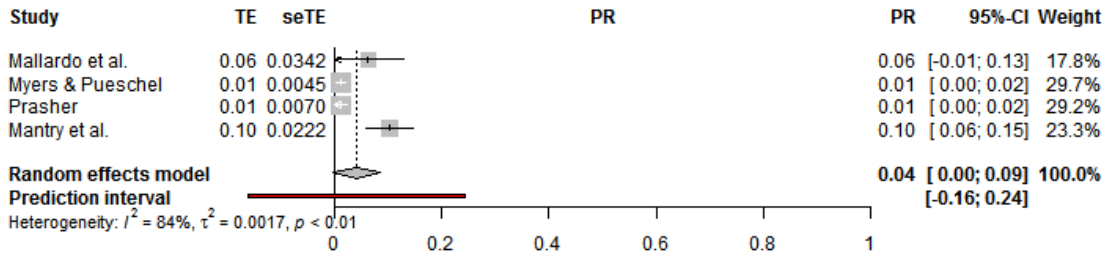


Appendices Figure 110. Forest plot for selective mutism in 22q11.2 deletion syndrome using a random-effects model.

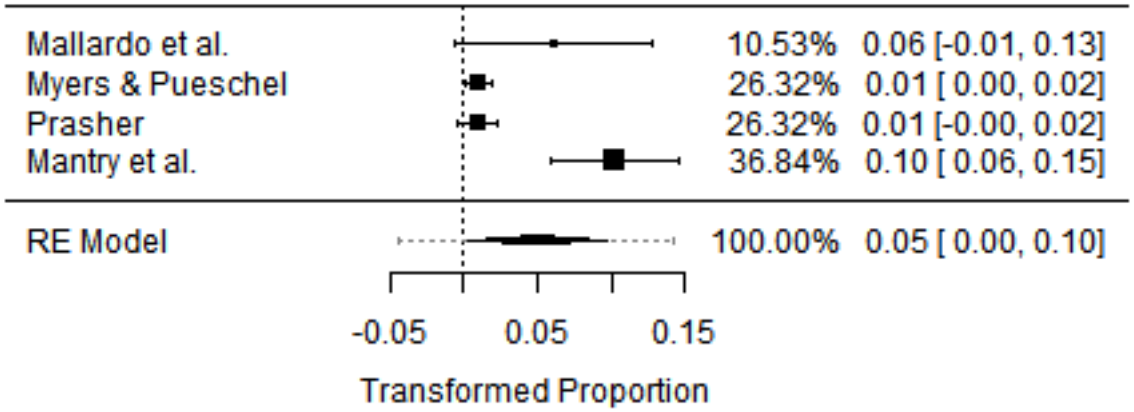


Appendices Figure 111. Forest plot for selective mutism in 22q11.2 deletion syndrome using a quality-effects model.

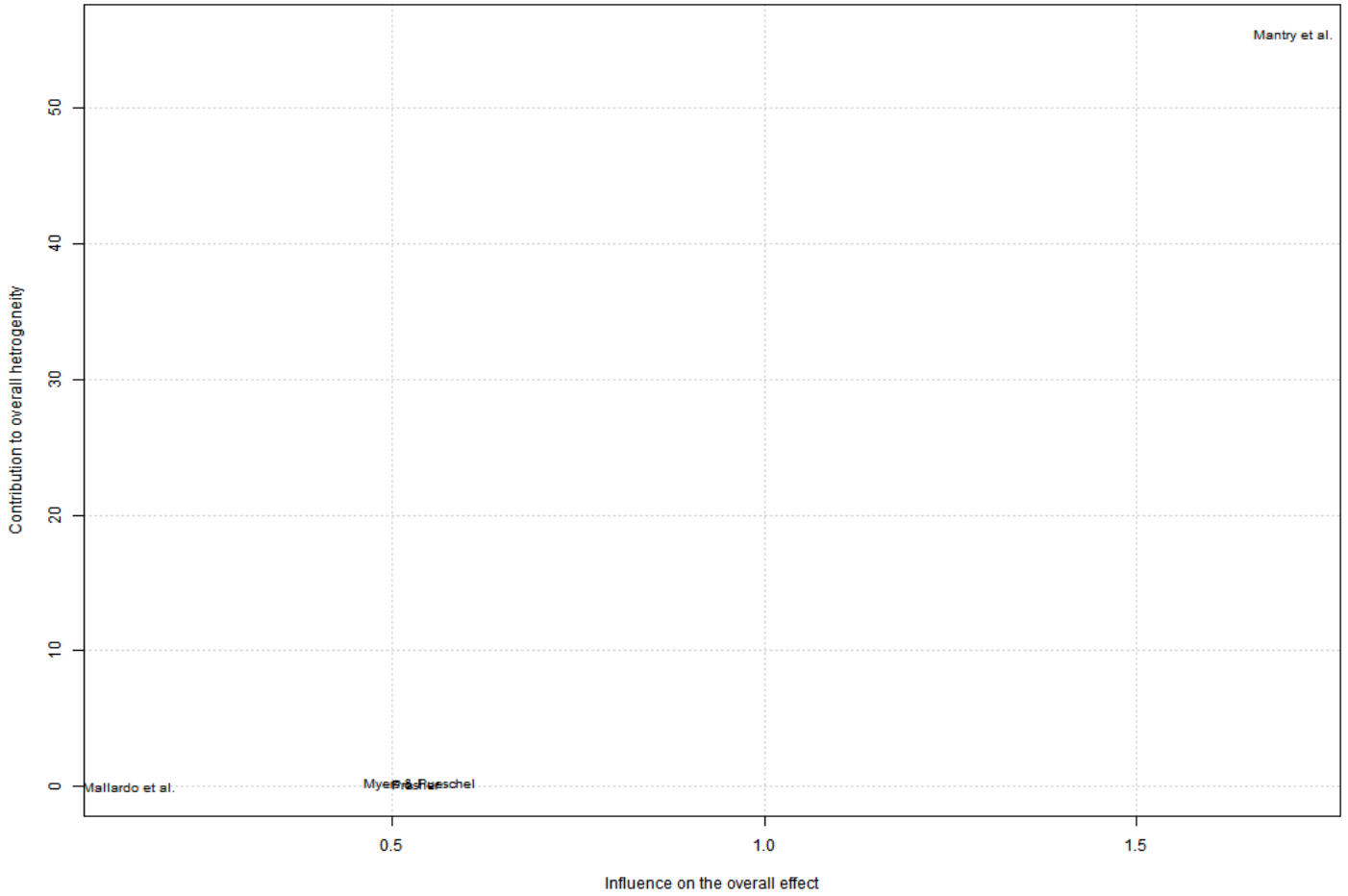
Specific anxiety profile analyses: Down syndrome (Specific phobia)



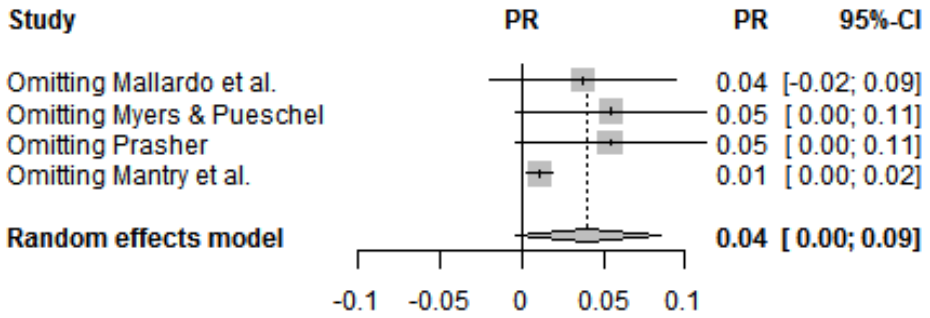
Appendices Figure 112. Forest plot for specific phobia in Down syndrome using a random-effects model.



Appendices Figure 113. Forest plot for specific phobia in Down syndrome using a quality-effects model.

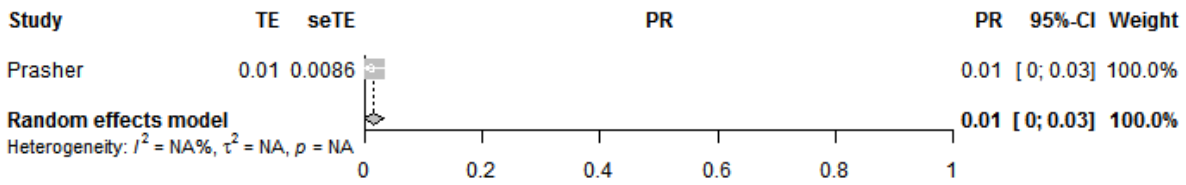


Appendices Figure 114. Baujat chart used to identify sources of heterogeneity: Specific phobia in Down syndrome.

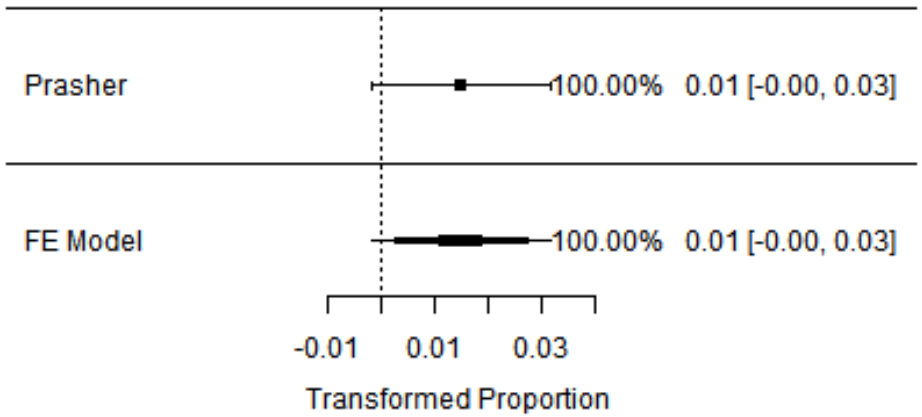


Appendices Figure 115. “Leave one out” analysis for specific phobia in Down syndrome.

Specific anxiety profile analyses: Down syndrome (Generalised anxiety)

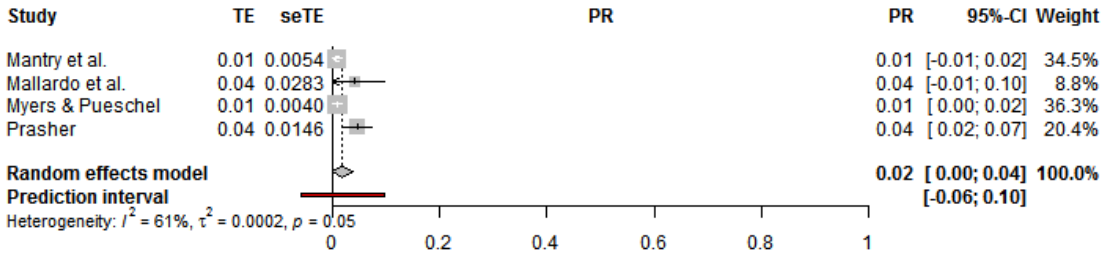


Appendices Figure 116. Forest plot for generalised anxiety in Down syndrome using a random-effects model.

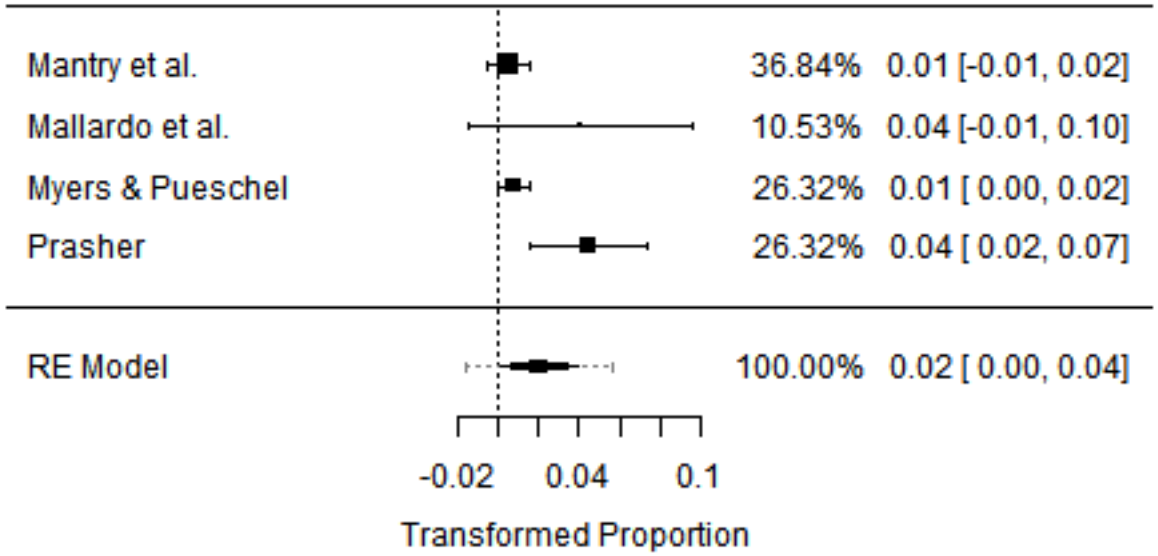


Appendices Figure 117. Forest plot for generalised anxiety in Down syndrome using a quality-effects model.

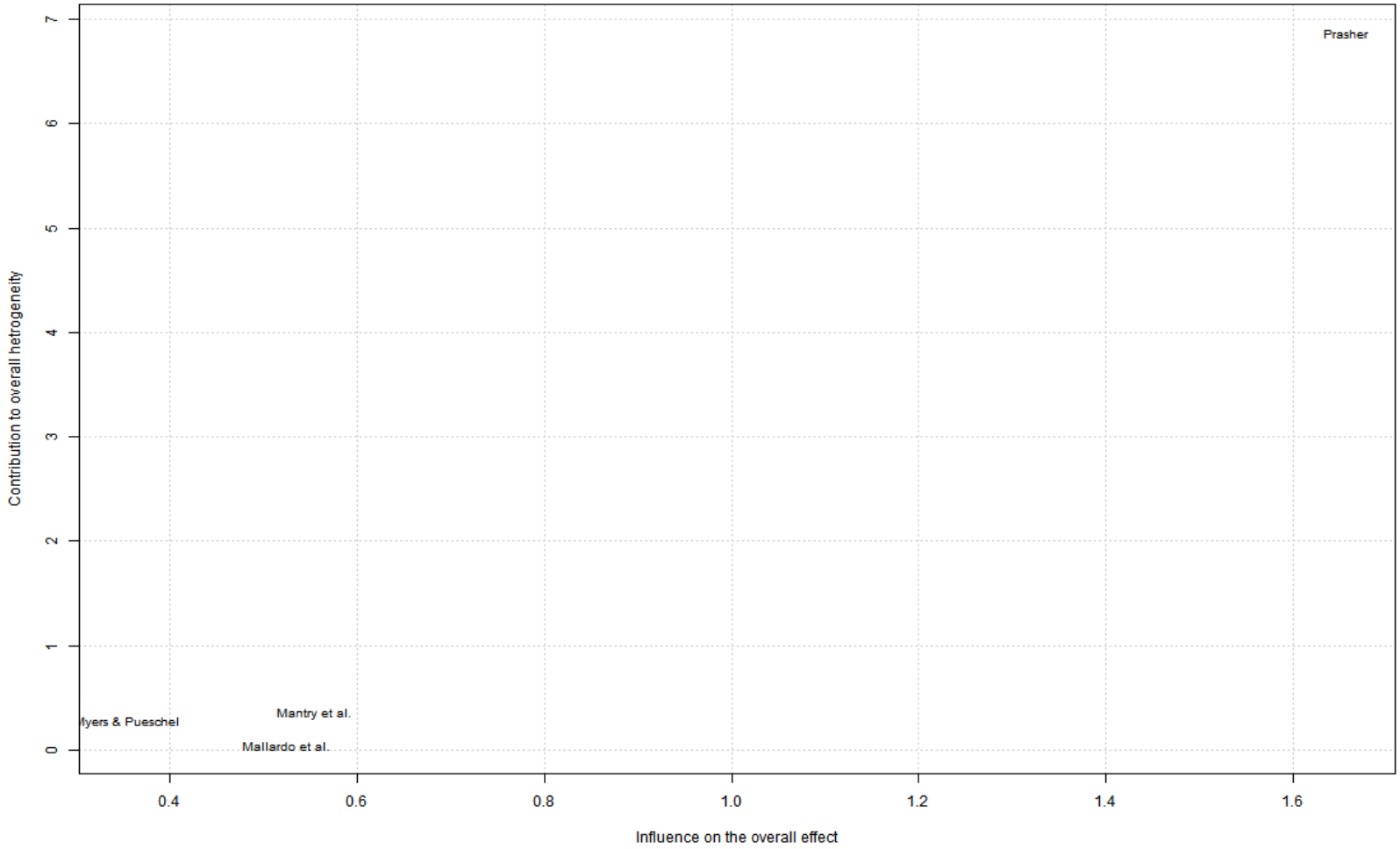
Specific anxiety profile analyses: Down syndrome (Obsessive-compulsive symptomatology/diagnosis)



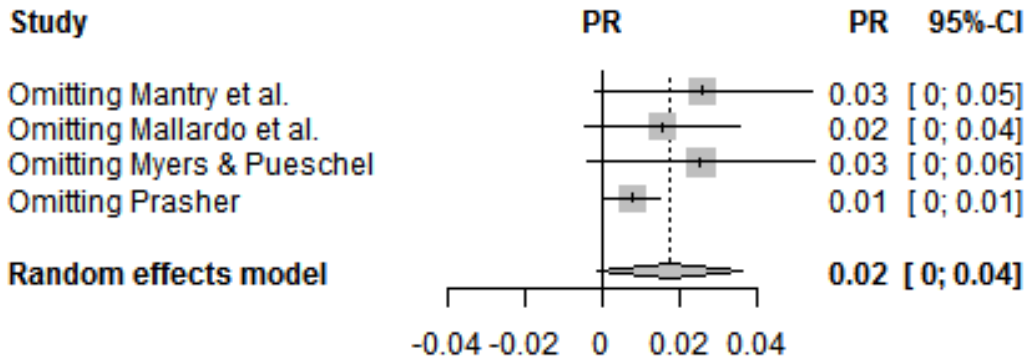
Appendices Figure 118. Forest plot for obsessive-compulsive symptomatology/diagnosis in Down syndrome using a random-effects model.



Appendices Figure 119. Forest plot for obsessive-compulsive symptomatology/diagnosis in Down syndrome using a quality-effects model.

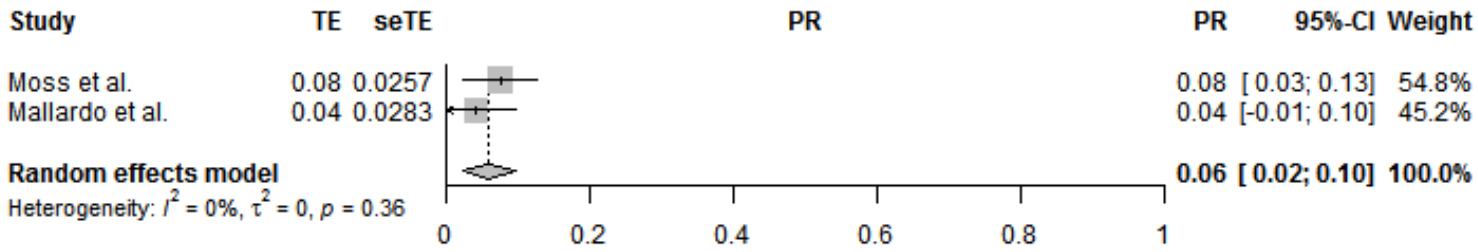


Appendices Figure 120. Baujat chart used to identify sources of heterogeneity: obsessive-compulsive symptomatology/diagnosis in Down syndrome.

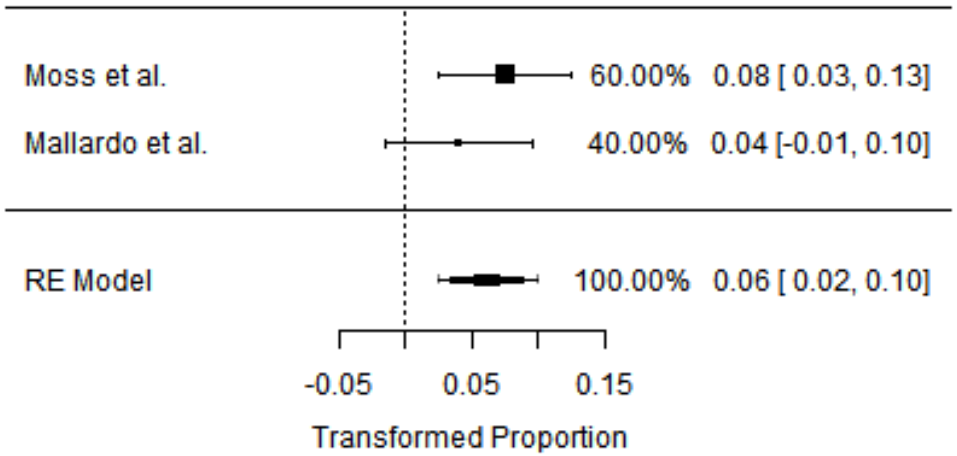


Appendices Figure 121. “Leave one out” analysis for obsessive-compulsive symptomatology/diagnosis in Down syndrome.

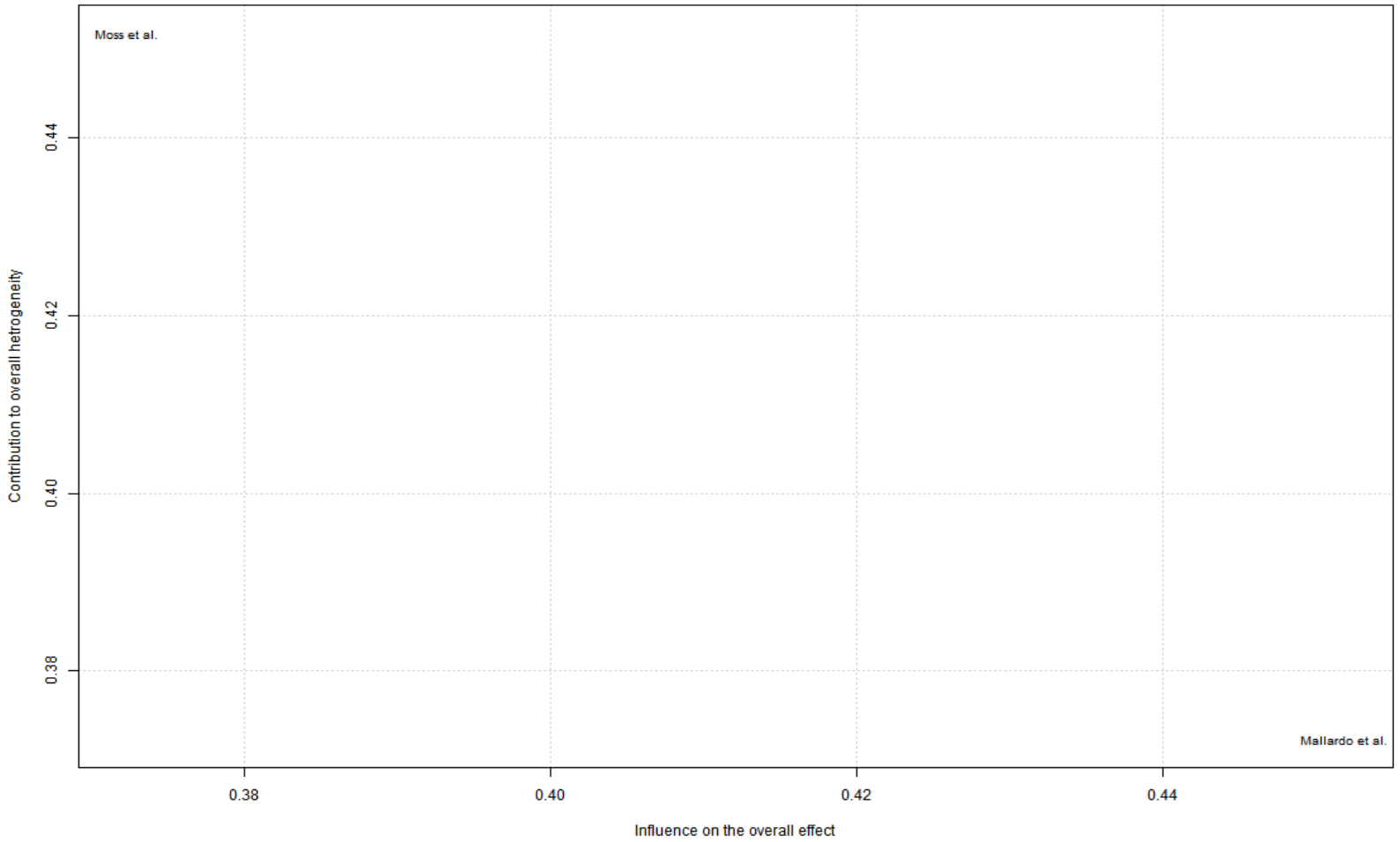
Specific anxiety profile analyses: Down syndrome (Selective mutism)



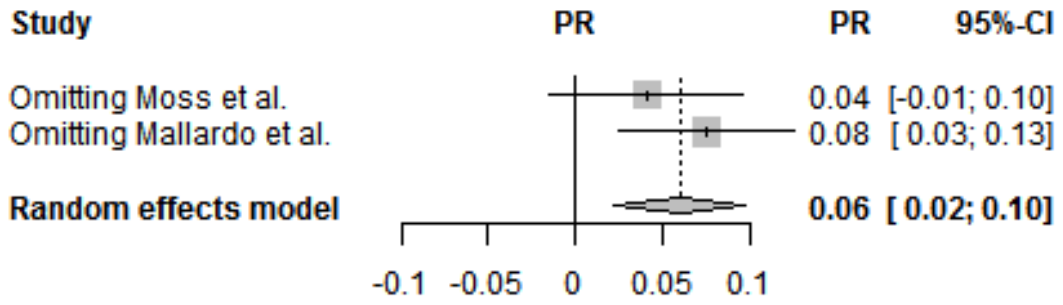
Appendices Figure 122. Forest plot for selective mutism in Down syndrome using a random-effects model.



Appendices Figure 123. Forest plot for selective mutism in Down syndrome using a quality-effects model.

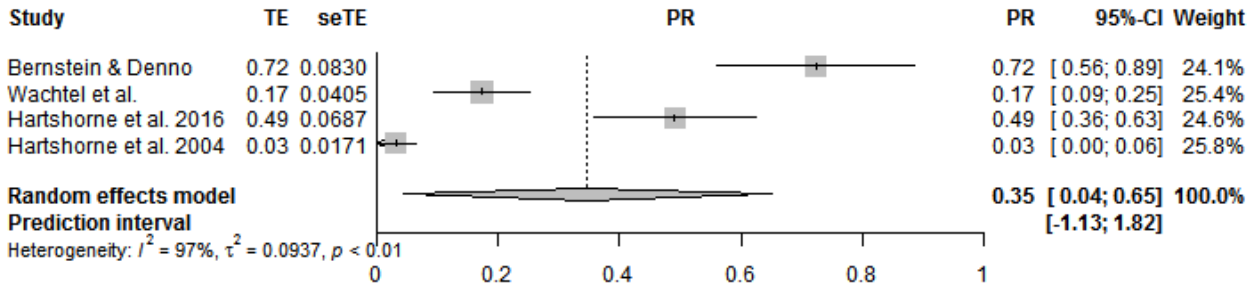


Appendices Figure 124. Baujat chart used to identify sources of heterogeneity: selective mutism in Down syndrome.

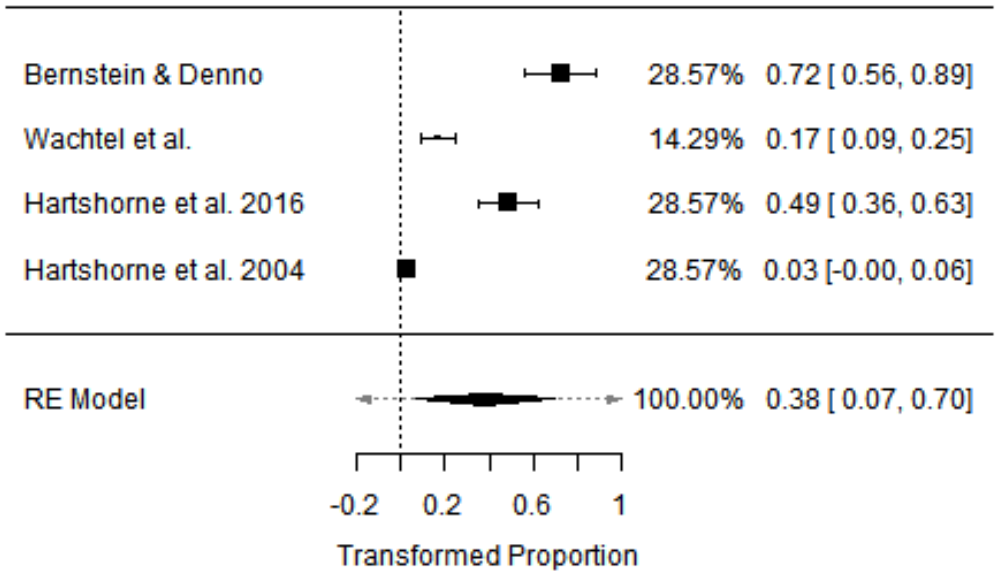


Appendices Figure 125. “Leave one out” analysis for selective mutism in Down syndrome.

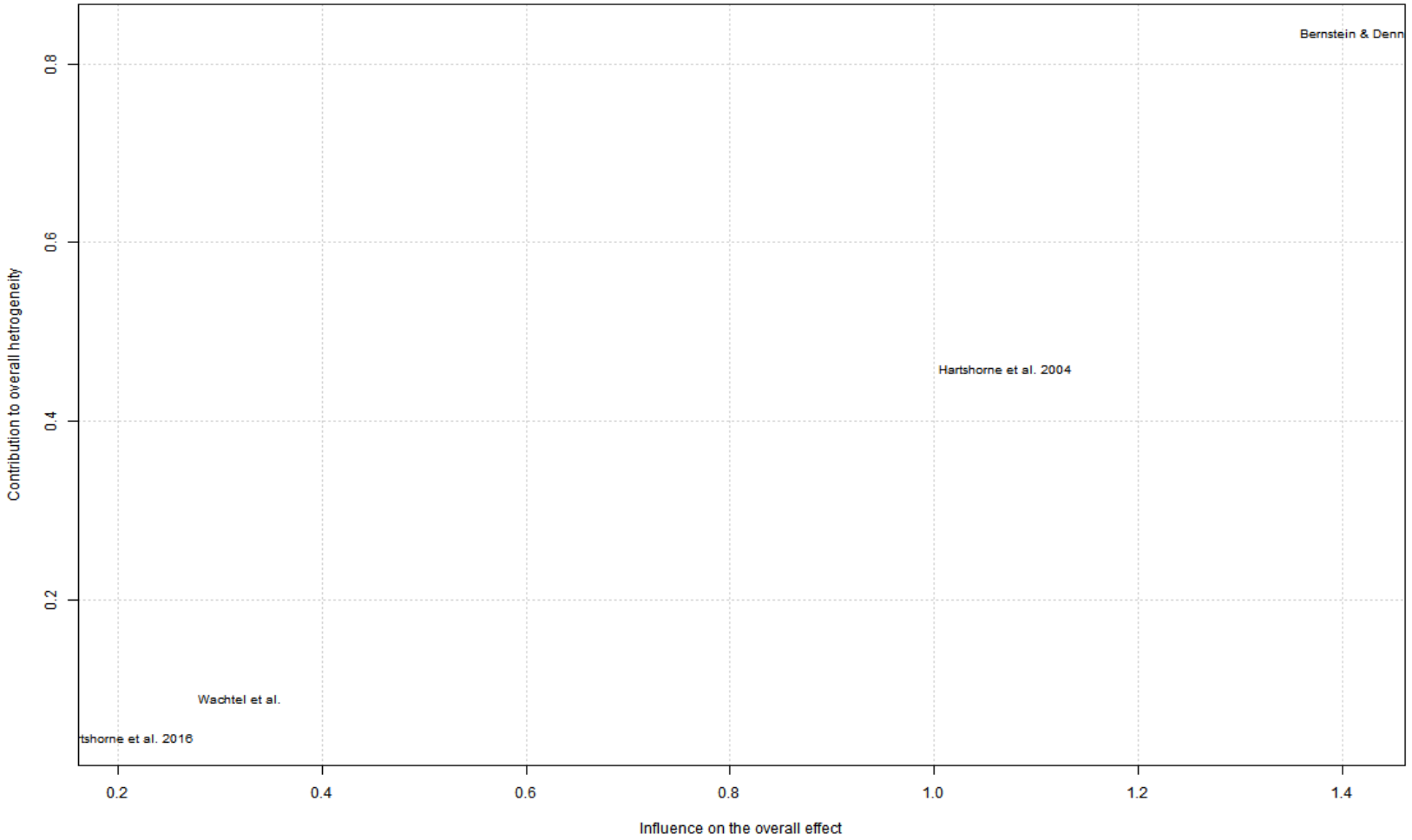
Specific anxiety profile analyses: CHARGE syndrome (Obsessive-compulsive symptomatology/diagnosis)



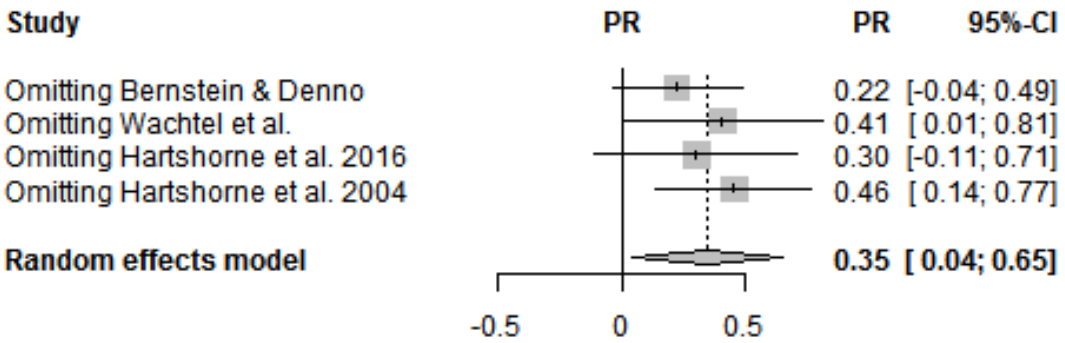
Appendices Figure 126. Forest plot for obsessive-compulsive symptomatology/diagnosis in CHARGE syndrome using a random-effects model.



Appendices Figure 127. Forest plot for obsessive-compulsive symptomatology/diagnosis in CHARGE syndrome using a quality-effects model.

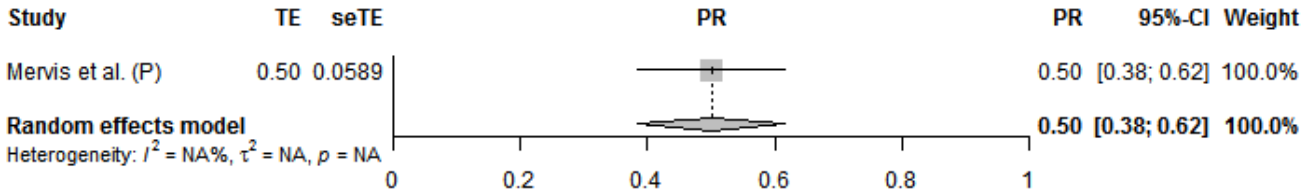


Appendices Figure 128. Baujat chart used to identify sources of heterogeneity: obsessive-compulsive symptomatology/diagnosis in CHARGE syndrome.

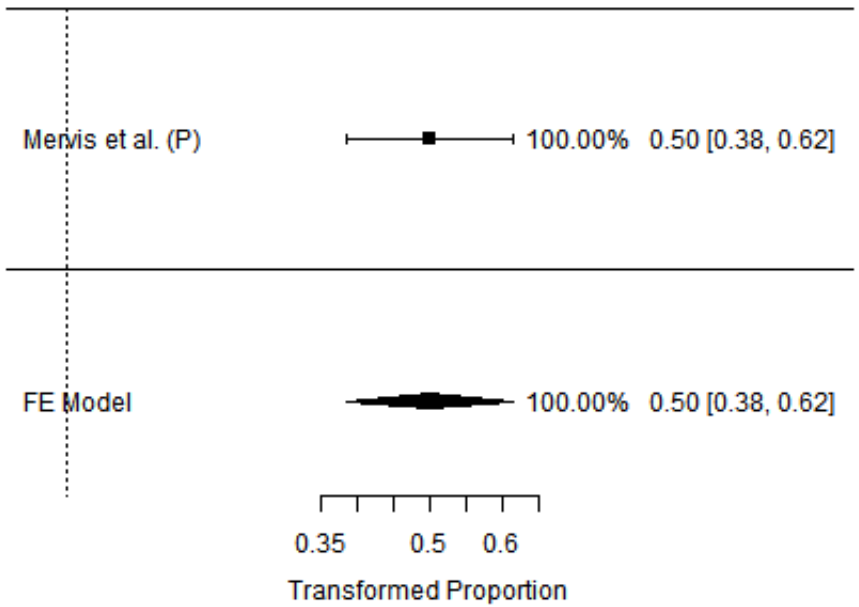


Appendices Figure 129. “Leave one out” analysis for obsessive-compulsive symptomatology/diagnosis in CHARGE syndrome.

Specific anxiety profile analyses: 7q11.23 duplication syndrome (Specific phobia)

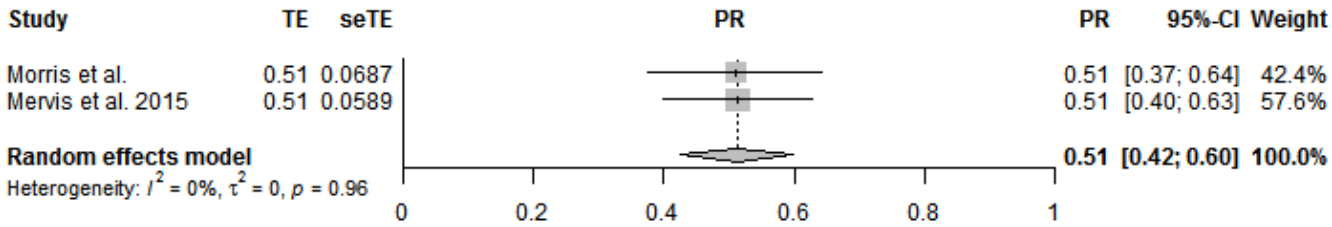


Appendices Figure 130. Forest plot for specific phobia in 7q11.23 duplication syndrome using a random-effects model.

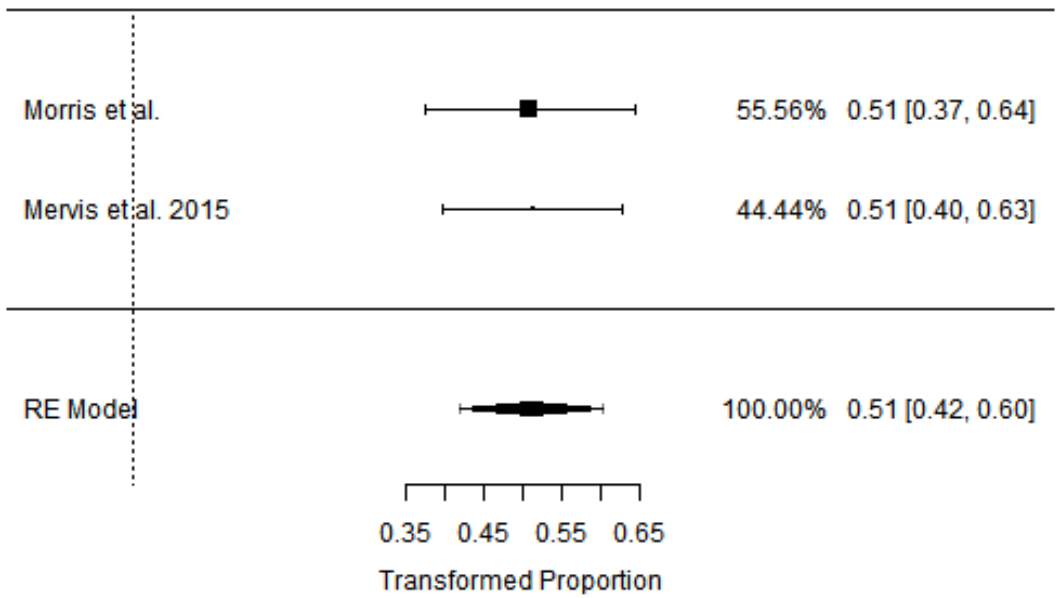


Appendices Figure 131. Forest plot for specific phobia in 7q11.23 duplication syndrome using a quality-effects model.

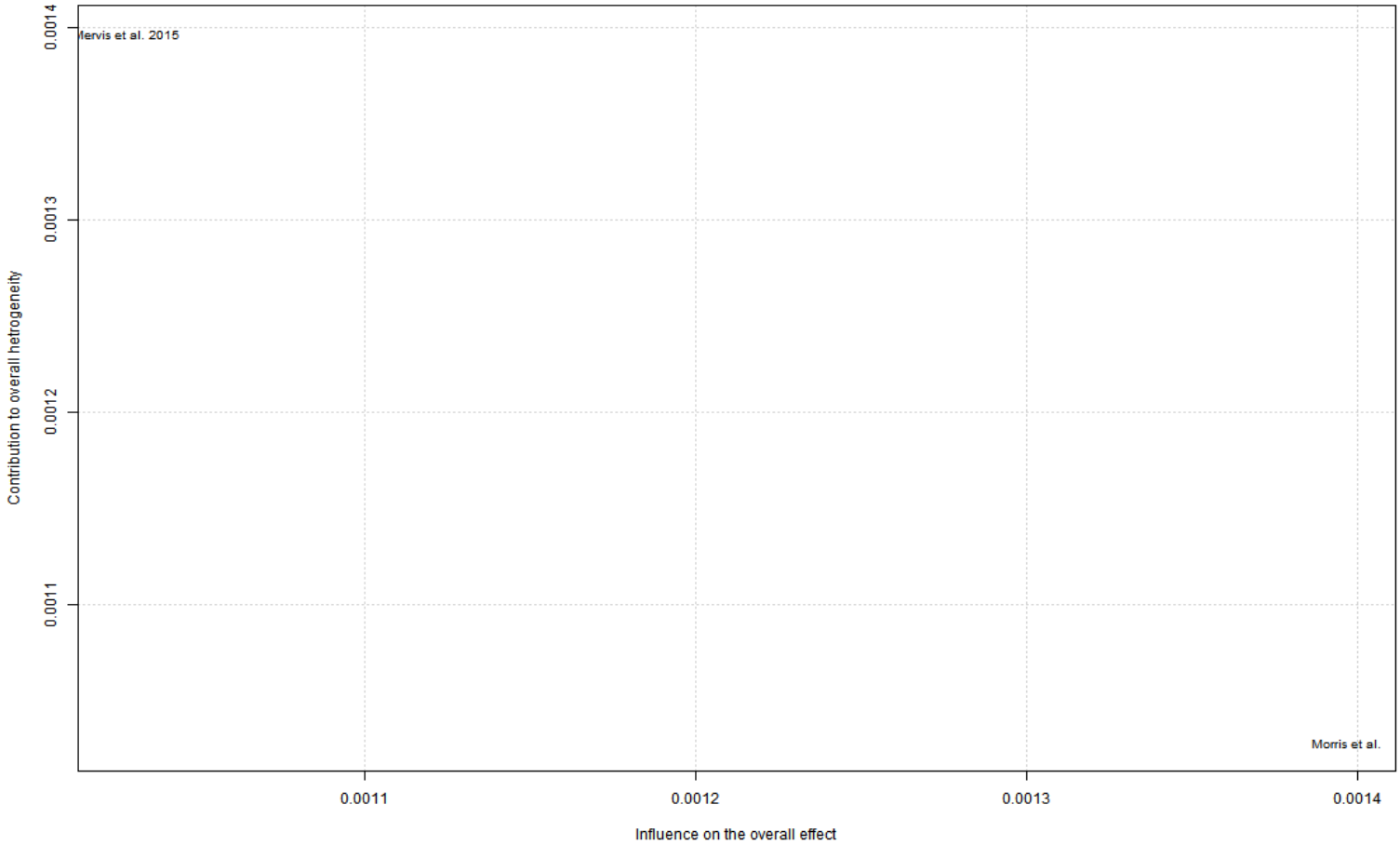
Specific anxiety profile analyses: 7q11.23 duplication syndrome (Social anxiety)



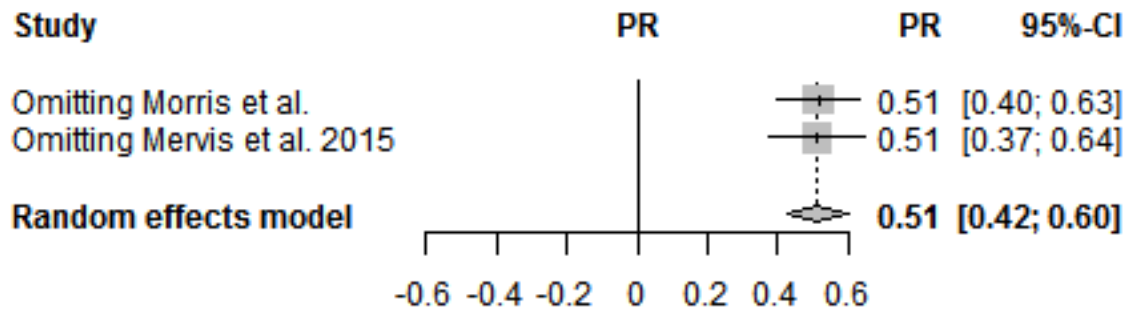
Appendices Figure 132. Forest plot for social anxiety in 7q11.23 duplication syndrome using a random-effects model.



Appendices Figure 133. Forest plot for social anxiety in 7q11.23 duplication syndrome using a quality-effects model.

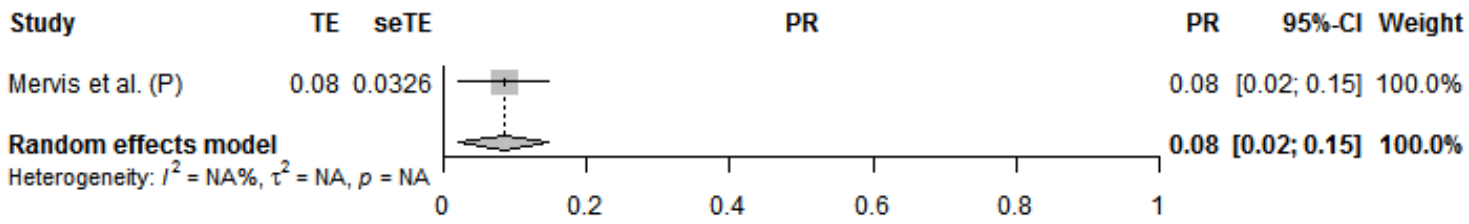


Appendices Figure 134. Baujat chart used to identify sources of heterogeneity: social anxiety in 7q11.23 duplication syndrome.

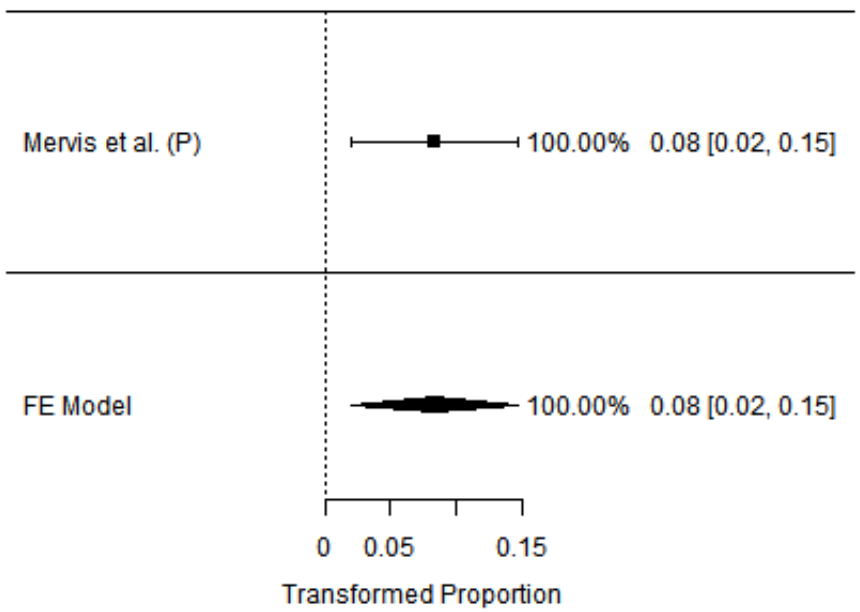


Appendices Figure 135. “Leave one out” analysis for social anxiety in 7q11.23 duplication syndrome.

Specific anxiety profile analyses: 7q11.23 duplication syndrome (Generalised anxiety)

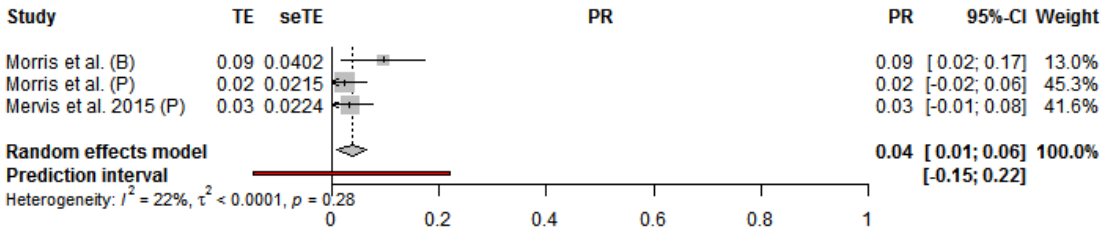


Appendices Figure 136. Forest plot for generalised anxiety in 7q11.23 duplication syndrome using a random-effects model.

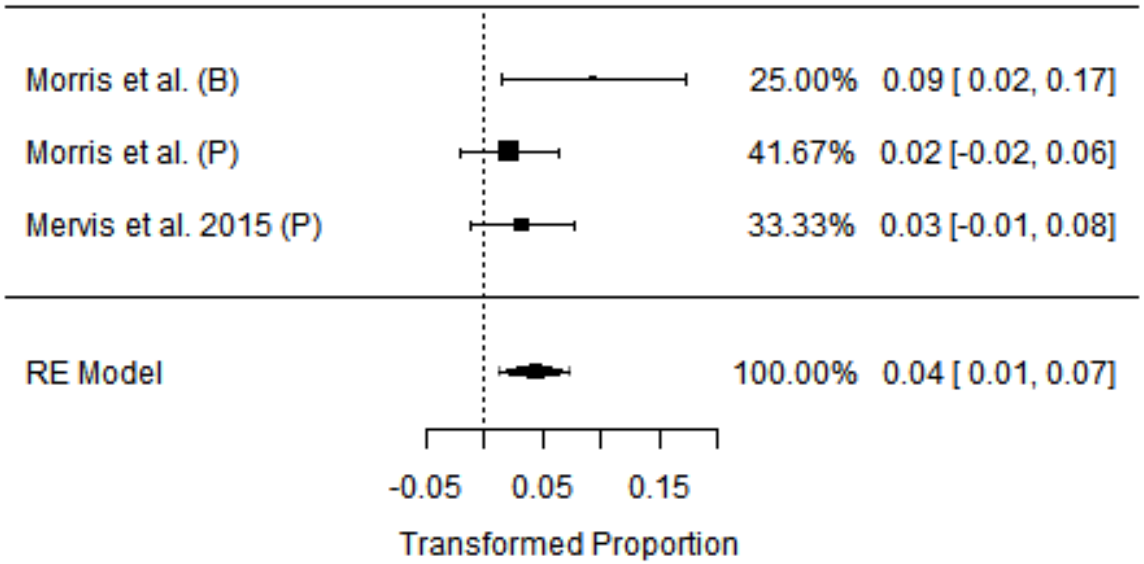


Appendices Figure 137. Forest plot for generalised anxiety in 7q11.23 duplication syndrome using a quality-effects model.

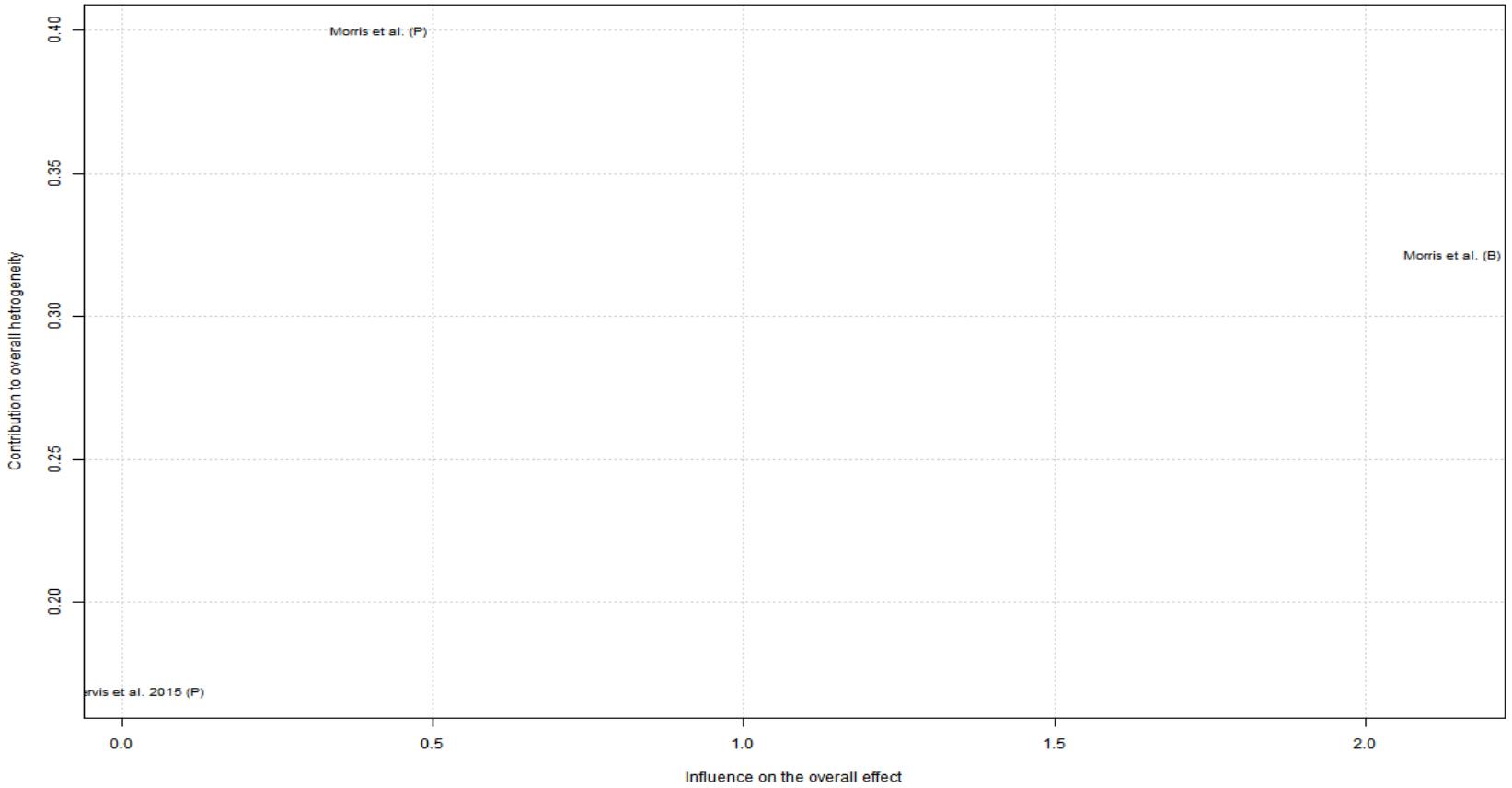
Specific anxiety profile analyses: 7q11.23 duplication syndrome (Obsessive-compulsive symptomatology/diagnosis)



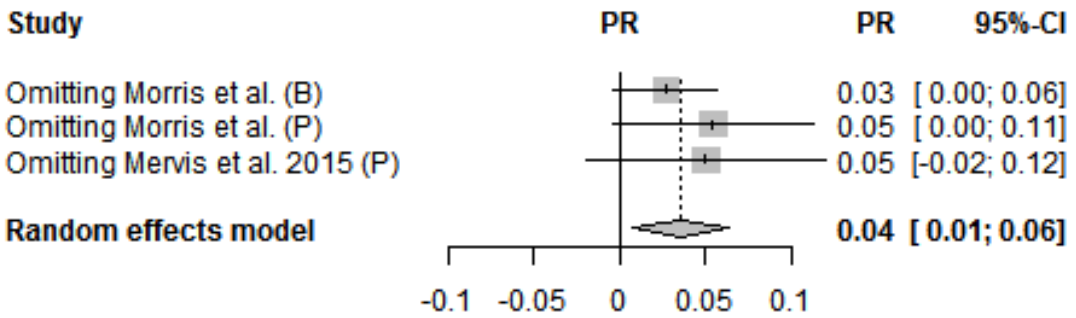
Appendices Figure 138. Forest plot for obsessive-compulsive symptomatology/diagnosis in 7q11.23 duplication syndrome using a random-effects model.



Appendices Figure 139. Forest plot for obsessive-compulsive symptomatology/diagnosis in 7q11.23 duplication syndrome using a quality-effects model.

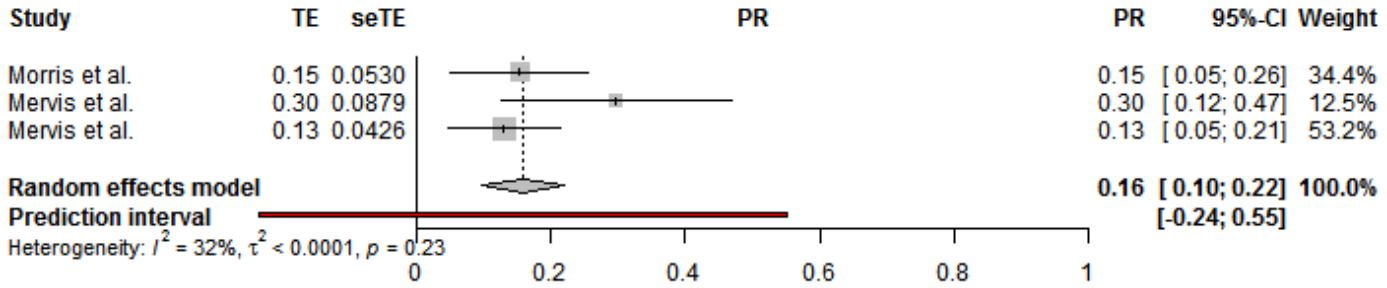


AppendicesFigure 140. Baujat chart used to identify sources of heterogeneity: obsessive-compulsive symptomatology/diagnosis in 7q11.23 duplication syndrome**.**

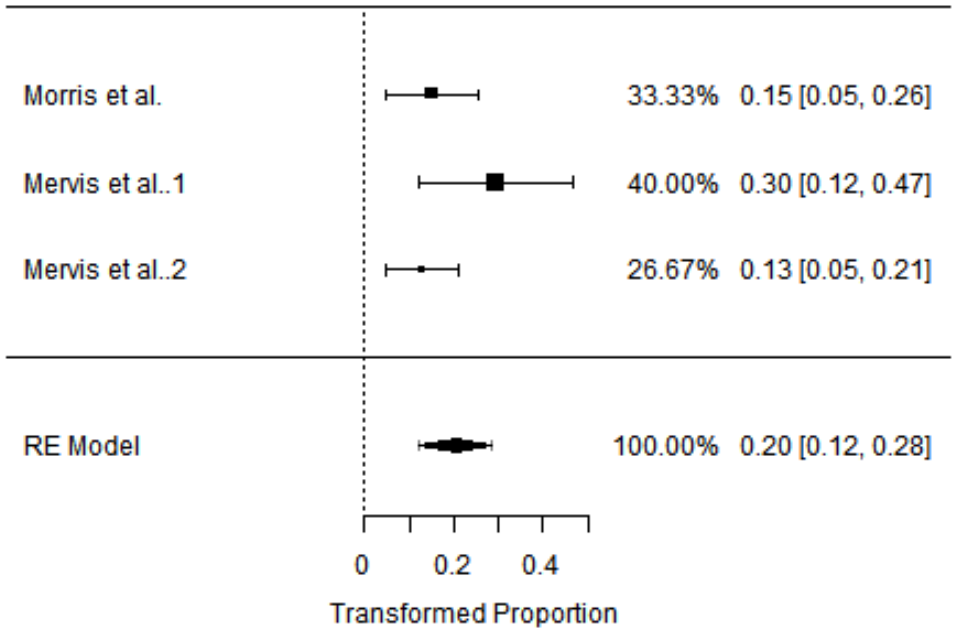


Appendices Figure 141. “Leave one out” analysis for obsessive-compulsive symptomatology/diagnosis 7q11.23 duplication syndrome.

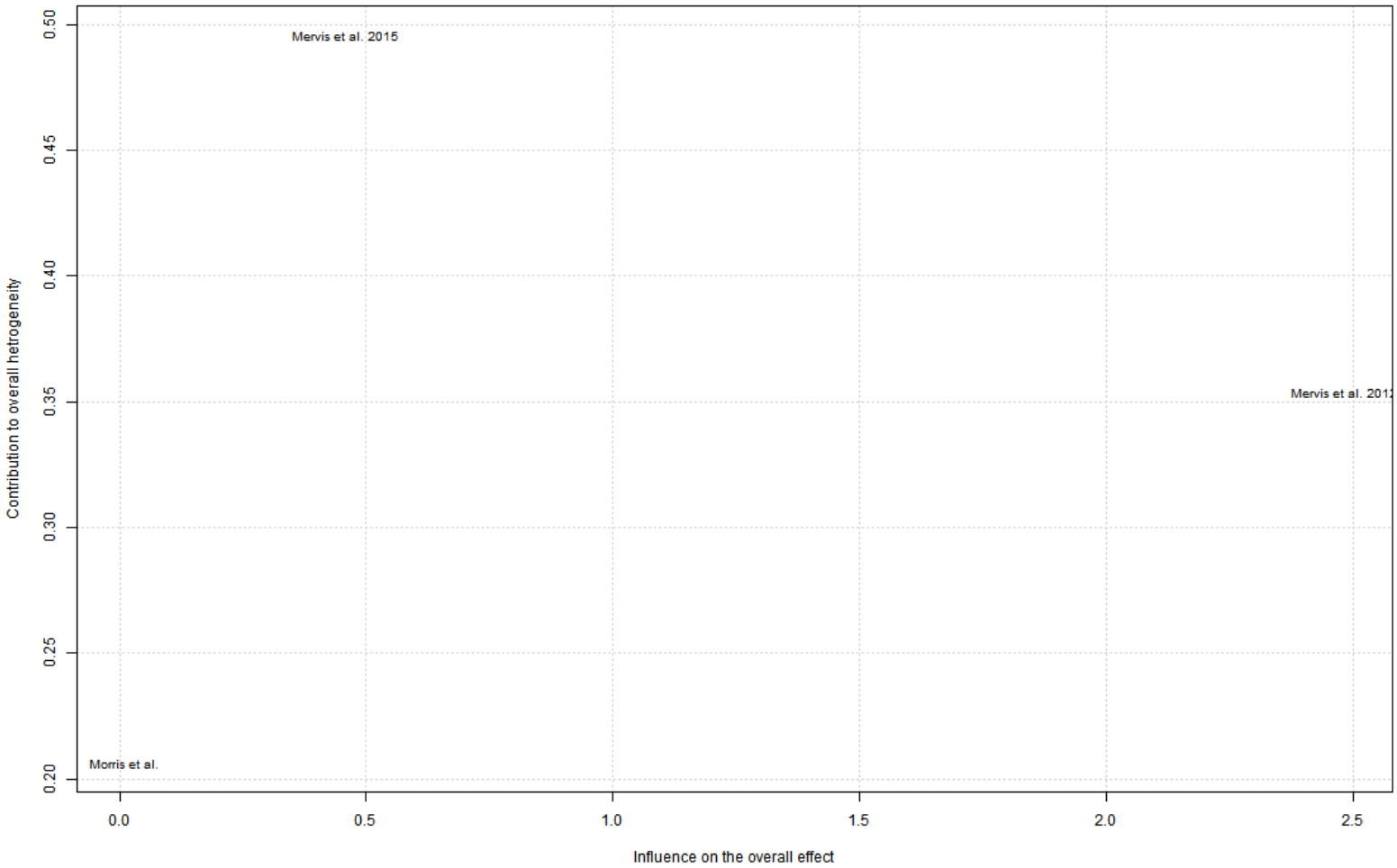
Specific anxiety profile analyses: 7q11.23 duplication syndrome (Separation anxiety)



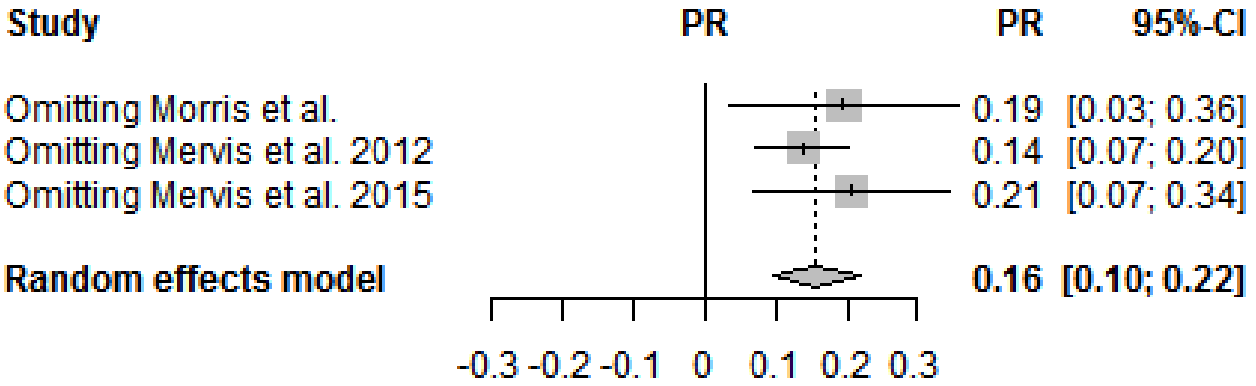
Appendices Figure 142. Forest plot for separation anxiety in 7q11.23 duplication syndrome using a random-effects model.



Appendices Figure 143. Forest plot for separation anxiety in 7q11.23 duplication syndrome using a quality-effects model.

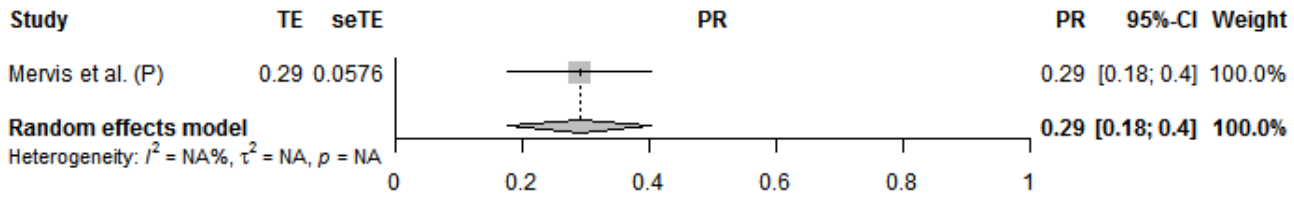


Appendices Figure 144. Baujat chart used to identify sources of heterogeneity: separation anxiety in 7q11.23 duplication syndrome.

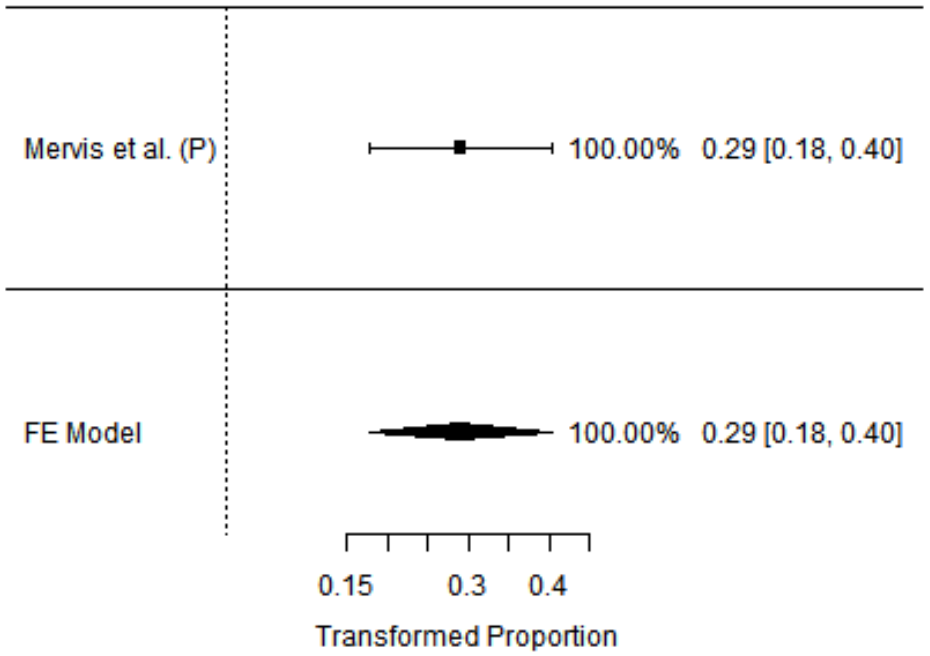


Appendices Figure 145. “Leave one out” analysis for separation anxiety in 7q11.23 duplication syndrome.

Specific anxiety profile analyses: 7q11.23 duplication syndrome (Selective mutism)

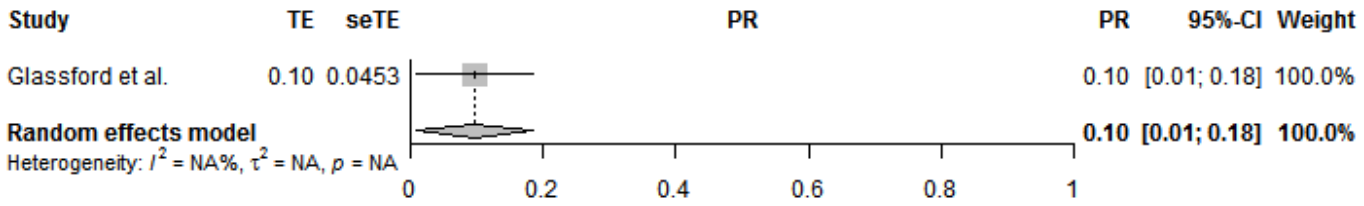


Appendices Figure 146. Forest plot for selective mutism in 7q11.23 duplication syndrome using a random-effects model.

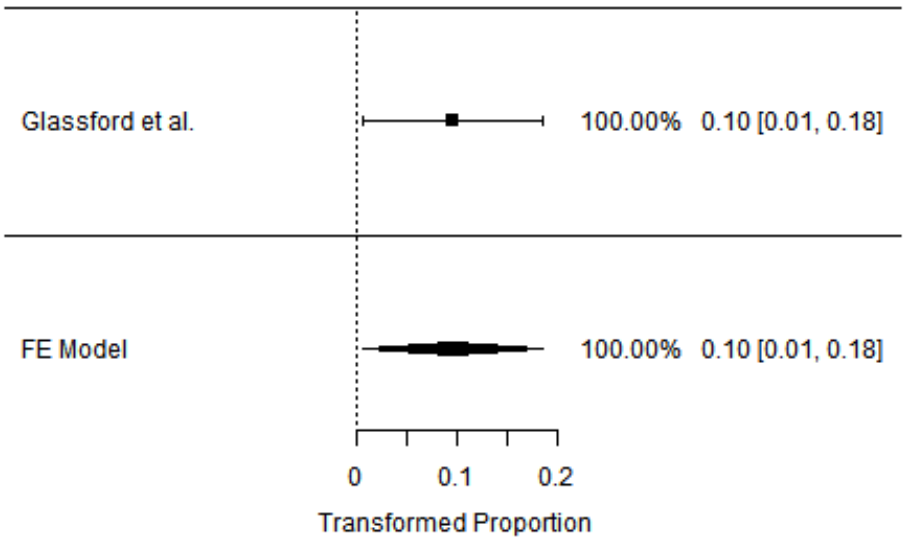


Appendices Figure 147. Forest plot for selective mutism in 7q11.23 duplication syndrome using a quality-effects model.

Specific anxiety profile analyses: 3q29 deletion syndrome (Panic attacks)

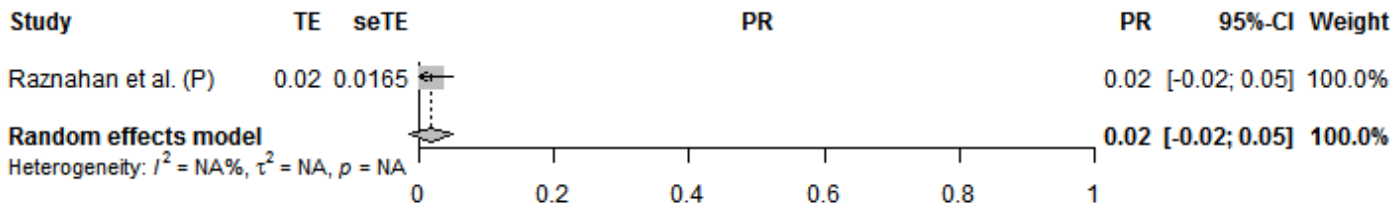


Appendices Figure 148. Forest plot for panic attacks in 3q29 deletion syndrome using a random-effects model.

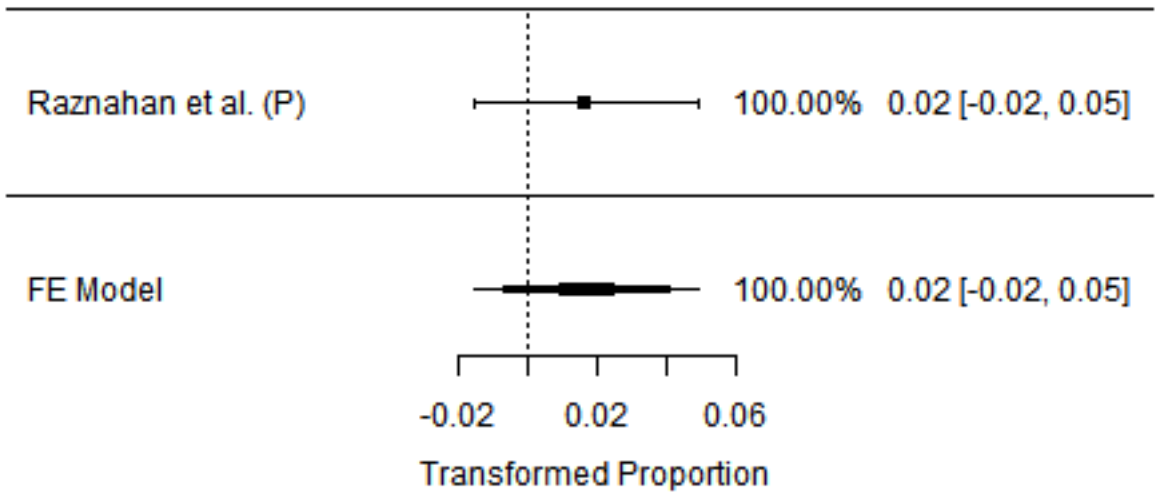


Appendices Figure 149. Forest plot for panic attacks in 3q29 deletion syndrome using a quality-effects model.

Specific anxiety disorder analyses: Tuberous sclerosis complex (Specific phobia)

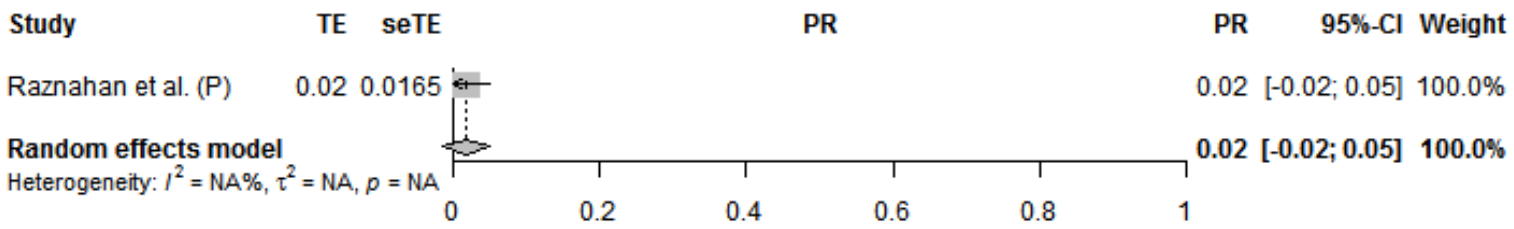


Appendices Figure 150. Forest plot for specific phobia in Tuberous sclerosis complex using a random-effects model.

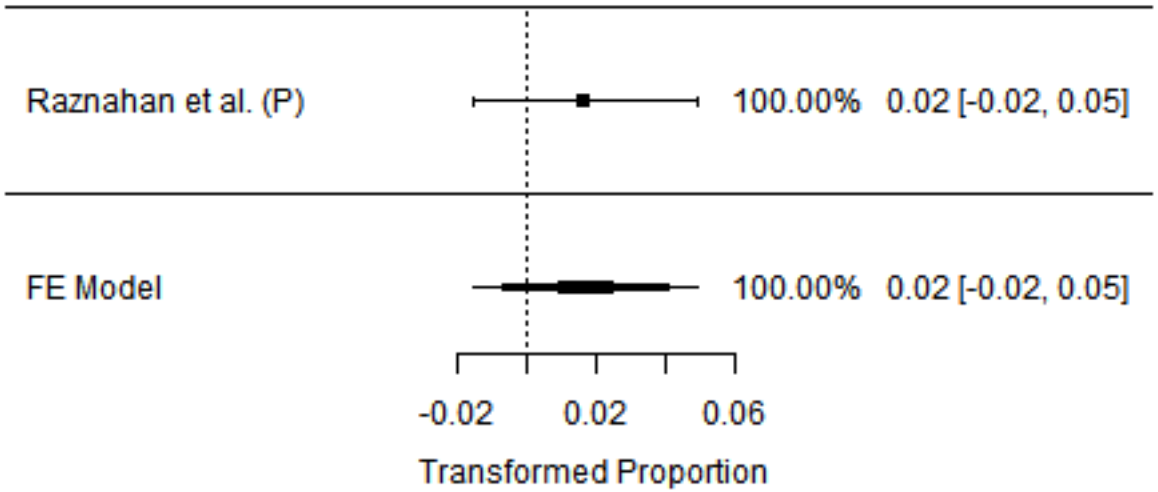


Appendices Figure 151. Forest plot for specific phobia in Tuberous sclerosis complex using a quality-effects model.

Specific anxiety disorder analyses: Tuberous sclerosis complex (Panic)

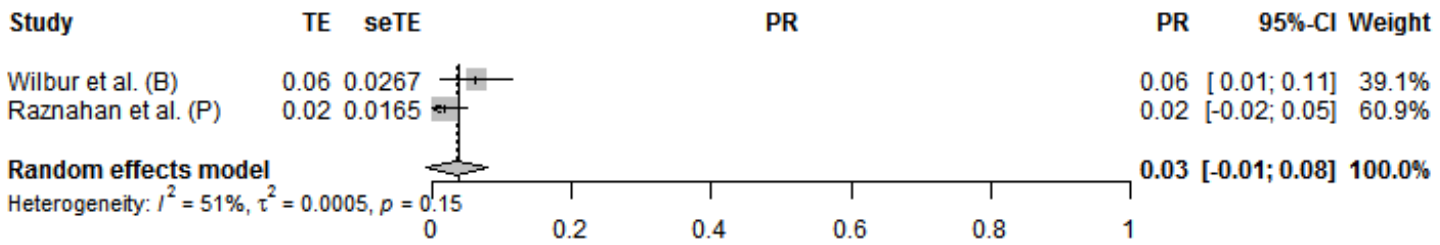


Appendices Figure 152. Forest plot for panic in Tuberous sclerosis complex using a random-effects model.

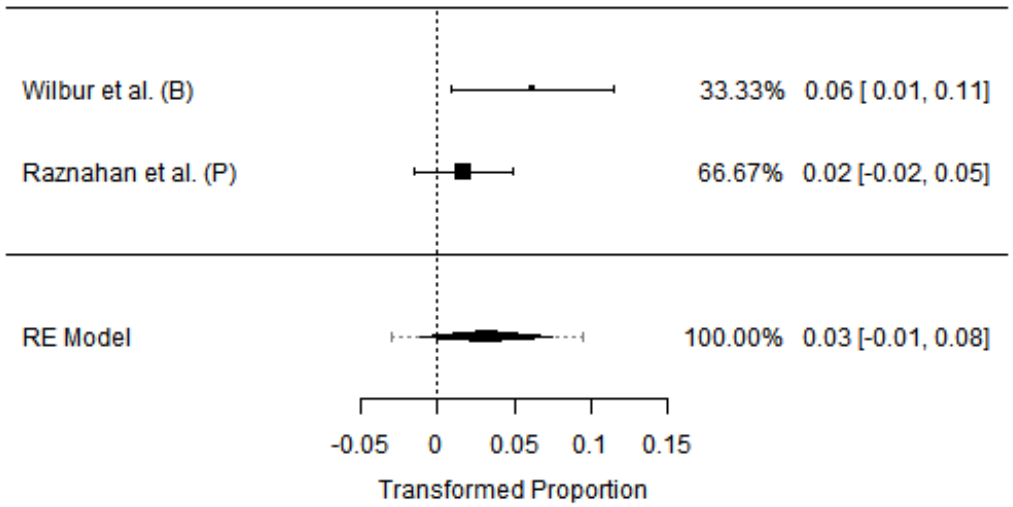


Appendices Figure 153. Forest plot for panic in Tuberous sclerosis complex using a quality-effects model.

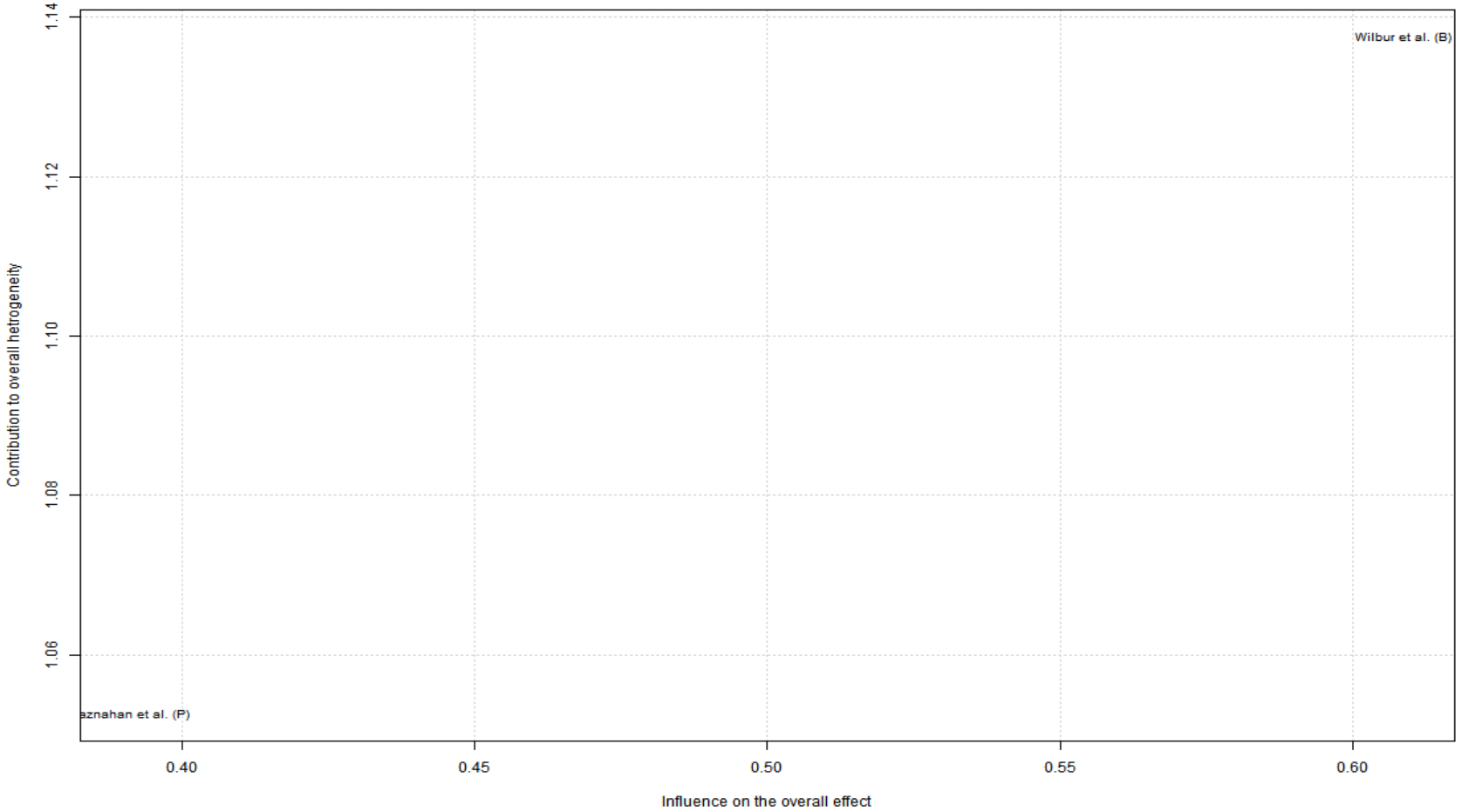
Specific anxiety disorder analyses: Tuberous sclerosis complex (Obsessive-compulsive symptomatology/diagnosis)



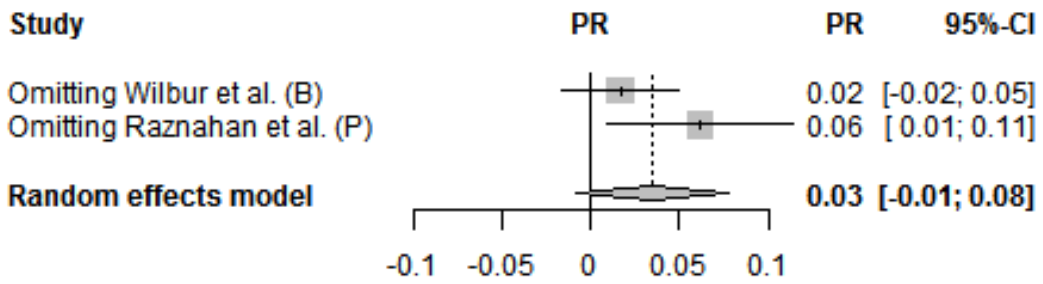
Appendices Figure 154. Forest plot for obsessive-compulsive symptomatology/diagnosis in Tuberous sclerosis complex using a random-effects model.



Appendices Figure 155. Forest plot for obsessive-compulsive symptomatology/diagnosis in Tuberous sclerosis complex using a quality-effects model.



Appendices Figure 156. Baujat chart used to identify sources of heterogeneity: obsessive-compulsive symptomatology/diagnosis in Tuberous sclerosis complex.



Appendices Figure 157. “Leave one out” analysis for obsessive-compulsive symptomatology/diagnosis in Tuberous sclerosis complex.

Subgroup analysis for specific anxiety profile analyses in 22q11.2 deletion syndrome

Appendices Table 19. Subgroup analysis of quality ratings and subsequent prevalence of anxiety between subgroups for 22q11.2 deletion syndrome.

		Anxiety prevalence for papers rated as 'poor'[6]	Anxiety prevalence for papers rated as 'good'	Number of papers[7]	χ^2	*p*
Specific phobia	Sample identification	18%	34%	18 (11)	8.09	0.0045
	Syndrome confirmation	5%	31%	18 (16)	32.08	<0.0001
	Anxiety assessment	N/A8	N/A	N/A	N/A	N/A
Social anxiety disorder	Sample identification	8%	9%	15 (7)	0.24	0.6238
	Syndrome confirmation	12%	9%	15 (14)	0.20	0.6509
	Anxiety assessment	N/A	N/A	N/A	N/A	N/A
Generalised anxiety disorder	Sample identification	13%	13%	17 (12)	0.01	0.9353
	Syndrome confirmation	32%	12%	17 (16)	4.34	0.0372
	Anxiety assessment	N/A	N/A	N/A	N/A	N/A
Separation anxiety disorder	Sample identification	4%	8%	14 (8)	5.53	0.0187
	Syndrome confirmation	4%	6%	14 (13)	0.31	0.5802
	Anxiety assessment	N/A	N/A	N/A	N/A	N/A
Obsessive-compulsive disorder	Sample identification	8%	10%	21 (12)	0.70	0.4028
	Syndrome confirmation	8%	9%	21 (19)	0.13	0.7134
	Anxiety assessment	N/A	N/A	N/A	N/A	N/A

[6] Quality ratings were collapsed into two categories, where scores of 0 and one were combined for a score of 0 and categorised as 'poor' and scores of two and three were combined for a score of one and categorised as 'good'

[7] Total number of papers in subgroup analysis (number of papers given quality rating of 'good')

[8] N/A: Subgroup analysis not performed when all studies were rated under quality rating of 'good'

Appendices Table 20. Meta-regression analysis exploring year of publication in relation to prevalence of specific anxiety profile in 22q11.2 deletion syndrome

	Year of publication					
	Estimate	S.E.	Z	*p*	Lower 95% CI	Upper 95% CI
Specific phobia	0.0018	0.0058	0.3121	0.7550	-0.0096	0.0132
Social anxiety disorder	-0.0016	0.0024	-0.6719	0.5017	-0.0062	0.0030
Generalised anxiety disorder	0.0012	0.0032	0.3673	0.7134	-0.0051	0.0074
Separation anxiety disorder	-0.0013	0.0017	-0.7627	0.4456	-0.0046	0.0020
Obsessive-compulsive disorder	-0.0034	0.0020	-1.7385	0.0821	-0.0073	0.0004

Appendices Table 21. Meta-regression analysis exploring total number of participants assessed for anxiety in relation to the prevalence of specific anxiety profile in 22q11.2 deletion syndrome

	Number of participants					
	Estimate	S.E.	Z	*p*	Lower 95% CI	Upper 95% CI
Specific phobia	0.0002	0.0006	0.4050	0.6855	-0.0009	0.0014
Social anxiety disorder	-0.0000	0.0002	-0.1508	0.8801	-0.0004	0.0003
Generalised anxiety disorder	0.0002	0.0002	0.7063	0.4800	-0.0003	0.0006
Separation anxiety disorder	-0.0004	0.0003	-1.3090	0.1905	-0.0010	0.0002
Obsessive-compulsive disorder	-0.0001	0.0002	-0.7239	0.4691	-0.0005	0.0002

Appendix 6 Chapter two references of included studies

Fragile X syndrome references

1. Crawford, H., Waite, J., & Oliver, C. (2017). Diverse Profiles of Anxiety Related Disorders in Fragile X, Cornelia de Lange and Rubinstein-Taybi Syndromes. *Journal of autism and developmental disorders*, *47*(12), 3728–3740. https://doi.org/10.1007/s10803-016-3015-y
2. Visootsak, J., Kidd, S. A., Anderson, T., Bassell, J. L., Sherman, S. L., & Berry-Kravis, E. M. (2016). Importance of a specialty clinic for individuals with fragile X syndrome. *American journal of medical genetics. Part A*, *170*(12), 3144–3149. https://doi.org/10.1002/ajmg.a.37982
3. Haessler, F., Gaese, F., Huss, M., Kretschmar, C., Brinkman, M., Peters, H., Elstner, S., Colla, M., & Pittrow, D. (2016). Characterization, treatment patterns, and patient-related outcomes of patients with Fragile X syndrome in Germany: final results of the observational EXPLAIN-FXS study. *BMC psychiatry*, *16*(1), 318. https://doi.org/10.1186/s12888-016-1020-5
4. Wheeler, A, C., Raspa, M., Bishop, E., & Bailey, Jr, D, B. (2016). Aggression in fragile X syndrome. *J Intell Disabil Res, 60*(2), 113-125. https://doi.org/10.1111/jir.12238
5. Tonnsen, B. L., Cornish, K. M., Wheeler, A. C., & Roberts, J. E. (2014). Maternal predictors of anxiety risk in young males with fragile X. *American journal of medical genetics. Part B, Neuropsychiatric genetics: the official publication of the International Society of Psychiatric Genetics*, *165B*(5), 399–409. https://doi.org/10.1002/ajmg.b.32244
6. Ouyang, L., Grosse, S. D., Riley, C., Bolen, J., Bishop, E., Raspa, M., & Bailey, D. B., Jr (2014). A comparison of family financial and employment impacts of fragile X syndrome, autism spectrum disorders, and intellectual disability. *Research in developmental disabilities*, *35*(7), 1518–1527. https://doi.org/10.1016/j.ridd.2014.04.009
7. Talisa, V. B., Boyle, L., Crafa, D., & Kaufmann, W. E. (2014). Autism and anxiety in males with fragile X syndrome: an exploratory analysis of neurobehavioral profiles from a parent survey. *American journal of medical genetics. Part A*, *164A*(5), 1198–1203. https://doi.org/10.1002/ajmg.a.36468
8. Pérez-García, D., Granero, R., Gallastegui, F., Pérez-Jurado, L. A., & Brun-Gasca, C. (2011). Behavioral features of Williams Beuren syndrome compared to Fragile X syndrome and subjects with intellectual disability without defined etiology. *Research in developmental disabilities*, *32*(2), 643–652. https://doi.org/10.1016/j.ridd.2010.12.005
9. Cordeiro, L., Ballinger, E., Hagerman, R., & Hessl, D. (2011). Clinical assessment of DSM-IV anxiety disorders in fragile X syndrome: prevalence and characterization. *Journal of neurodevelopmental disorders*, *3*(1), 57–67. https://doi.org/10.1007/s11689-010-9067-y
10. Gabis, L. V., Baruch, Y. K., Jokel, A., & Raz, R. (2011). Psychiatric and autistic comorbidity in fragile X syndrome across ages. *Journal of child neurology*, *26*(8), 940–948. https://doi.org/10.1177/0883073810395937
11. Bailey, D. B., Jr, Raspa, M., Olmsted, M., & Holiday, D. B. (2008). Co-occurring conditions associated with FMR1 gene variations: findings from a national parent survey. *American journal of medical genetics. Part A*, *146A*(16), 2060–2069. https://doi.org/10.1002/ajmg.a.32439
12. Sullivan, K., Hooper, S., & Hatton, D. (2007). Behavioural equivalents of anxiety in children with fragile X syndrome: parent and teacher report. *Journal of intellectual disability research: JIDR*, *51*(Pt 1), 54–65. https://doi.org/10.1111/j.1365-2788.2006.00899.x

13. von Gontard, A., Backes, M., Laufersweiler-Plass, C., Wendland, C., Lehmkuhl, G., Zerres, K., & Rudnik-Schöneborn, S. (2002). Psychopathology and familial stress - comparison of boys with Fragile X syndrome and spinal muscular atrophy. *Journal of child psychology and psychiatry, and allied disciplines*, *43*(7), 949–957. https://doi.org/10.1111/1469-7610.00098
14. Teisl, J. T., Reiss, A. L., & Mazzocco, M. M. (1999). Maximizing the sensitivity of a screening questionnaire for determining Fragile X at-risk status. *American journal of medical genetics*, *83*(4), 281–285.
15. Niemczyk, J., von Gontard, A., Equit, M., Bauer, K., Naumann, T., Wagner, C., & Curfs, L. (2016). Detailed assessment of incontinence in boys with fragile-X-syndrome in a home setting. *European journal of pediatrics*, *175*(10), 1325–1334. https://doi.org/10.1007/s00431-016-2767-x
16. Franke, P., Leboyer, M., Gänsicke, M., Weiffenbach, O., Biancalana, V., Cornillet-Lefebre, P., Croquette, M. F., Froster, U., Schwab, S. G., Poustka, F., Hautzinger, M., & Maier, W. (1998). Genotype-phenotype relationship in female carriers of the premutation and full mutation of FMR-1. *Psychiatry research*, *80*(2), 113–127. https://doi.org/10.1016/s0165-1781(98)00055-9
17. Freund, L. S., Reiss, A. L., & Abrams, M. T. (1993). Psychiatric disorders associated with fragile X in the young female. *Pediatrics*, *91*(2), 321–329.
18. Lachiewicz, A. M., & Dawson, D. V. (1994). Behavior problems of young girls with fragile X syndrome: factor scores on the Conners' Parent's Questionnaire. *American journal of medical genetics*, *51*(4), 364–369. https://doi.org/10.1002/ajmg.1320510413
19. Dykens, E. M., Hodapp, R. M., & Leckman, J. F. (1989). Adaptive and maladaptive functioning of institutionalized and noninstitutionalized fragile X males. *Journal of the American Academy of Child and Adolescent Psychiatry*, *28*(3), 427–430. https://doi.org/10.1097/00004583-198905000-00021
20. Sobesky, W. E., Pennington, B. F., Porter, D., Hull, C. E., & Hagerman, R. J. (1994). Emotional and neurocognitive deficits in fragile X. *American journal of medical genetics*, *51*(4), 378–385. https://doi.org/10.1002/ajmg.1320510416
21. Shaw, T. A., & Porter, M. A. (2013). Emotion recognition and visual-scan paths in Fragile X syndrome. *Journal of autism and developmental disorders*, *43*(5), 1119–1139. https://doi.org/10.1007/s10803-012-1654-1
22. Moss, J., Nelson, L., Powis, L., Waite, J., Richards, C., & Oliver, C. (2016). A Comparative Study of Sociability in Angelman, Cornelia de Lange, Fragile X, Down and Rubinstein Taybi Syndromes and Autism Spectrum Disorder. *American journal on intellectual and developmental disabilities*, *121*(6), 465–486. https://doi.org/10.1352/1944-7558-121.6.465

22q11.2 deletion syndrome references

23. Serur, Y., Sofrin Frumer, D., Daon, K., Sobol-Havia, D., Weinberger, R., Shulman, C., & Gothelf, D. (2019). Psychiatric disorders and autism in young children with 22q11.2 deletion syndrome compared to children with idiopathic autism. *European psychiatry: the journal of the Association of European Psychiatrists*, *55*, 116–121. https://doi.org/10.1016/j.eurpsy.2018.10.007
24. Cunningham, A. C., Delport, S., Cumines, W., Busse, M., Linden, D., Hall, J., Owen, M. J., & van den Bree, M. (2018). Developmental coordination disorder, psychopathology and IQ in 22q11.2 deletion syndrome. *The British journal of psychiatry: the journal of mental science*, *212*(1), 27–33. https://doi.org/10.1192/bjp.2017.6
25. Schneider, M., Van der Linden, M., Menghetti, S., Debbané, M., & Eliez, S. (2017). Negative and paranoid symptoms are associated with negative performance beliefs

and social cognition in 22q11.2 deletion syndrome. *Early intervention in psychiatry*, *11*(2), 156–164. https://doi.org/10.1111/eip.12224
26. Fjermestad, K, W., Vatne, T, M., & Gjone, H. (2015). Cognitive behavioral therapy for adolescents with 22q11.2 deletion syndrome. *Adv Ment Health Intellect Disabil*, *9*(1), 30-39. https://doi.org/10.1108/AMHID-05-2014-0017
27. Gothelf, D., Schneider, M., Green, T., Debbané, M., Frisch, A., Glaser, B., Zilkha, H., Schaer, M., Weizman, A., & Eliez, S. (2013). Risk factors and the evolution of psychosis in 22q11.2 deletion syndrome: a longitudinal 2-site study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *52*(11), 1192–1203.e3. https://doi.org/10.1016/j.jaac.2013.08.008
28. Ousley, O. Y., Smearman, E., Fernandez-Carriba, S., Rockers, K. A., Coleman, K., Walker, E. F., & Cubells, J. F. (2013). Axis I psychiatric diagnoses in adolescents and young adults with 22q11 deletion syndrome. *European psychiatry : the journal of the Association of European Psychiatrists*, *28*(7), 417–422. https://doi.org/10.1016/j.eurpsy.2013.06.002
29. Fabbro, A., Rizzi, E., Schneider, M., Debbane, M., & Eliez, S. (2012). Depression and anxiety disorders in children and adolescents with velo-cardio-facial syndrome (VCFS). *European child & adolescent psychiatry*, *21*(7), 379–385. https://doi.org/10.1007/s00787-012-0273-x
30. Young, A. S., Shashi, V., Schoch, K., Kwapil, T., & Hooper, S. R. (2011). Discordance in Diagnoses and Treatment of Psychiatric Disorders in Children and Adolescents with 22q11.2 Deletion Syndrome. *Asian journal of psychiatry*, *4*(2), 119–124. https://doi.org/10.1016/j.ajp.2011.03.002
31. Glaser, B., Debbané, M., Ottet, M. C., Vuilleumier, P., Zesiger, P., Antonarakis, S. E., & Eliez, S. (2010). Eye gaze during face processing in children and adolescents with 22q11.2 deletion syndrome. *Journal of the American Academy of Child and Adolescent Psychiatry*, *49*(7), 665–674. https://doi.org/10.1016/j.jaac.2010.04.004
32. Antshel, K. M., Shprintzen, R., Fremont, W., Higgins, A. M., Faraone, S. V., & Kates, W. R. (2010). Cognitive and psychiatric predictors to psychosis in velocardiofacial syndrome: a 3-year follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *49*(4), 333–344.
33. Gothelf, D., Feinstein, C., Thompson, T., Gu, E., Penniman, L., Van Stone, E., Kwon, H., Eliez, S., & Reiss, A. L. (2007). Risk factors for the emergence of psychotic disorders in adolescents with 22q11.2 deletion syndrome. *The American journal of psychiatry*, *164*(4), 663–669. https://doi.org/10.1176/ajp.2007.164.4.663
34. Baker, K. D., & Skuse, D. H. (2005). Adolescents and young adults with 22q11 deletion syndrome: psychopathology in an at-risk group. *The British journal of psychiatry : the journal of mental science*, *186*, 115–120. https://doi.org/10.1192/bjp.186.2.115
35. Gothelf, D., Presburger, G., Zohar, A. H., Burg, M., Nahmani, A., Frydman, M., Shohat, M., Inbar, D., Aviram-Goldring, A., Yeshaya, J., Steinberg, T., Finkelstein, Y., Frisch, A., Weizman, A., & Apter, A. (2004). Obsessive-compulsive disorder in patients with velocardiofacial (22q11 deletion) syndrome. *American journal of medical genetics. Part B, Neuropsychiatric genetics : the official publication of the International Society of Psychiatric Genetics*, *126B*(1), 99–105. https://doi.org/10.1002/ajmg.b.20124
36. Arnold, P. D., Siegel-Bartelt, J., Cytrynbaum, C., Teshima, I., & Schachar, R. (2001). Velo-cardio-facial syndrome: Implications of microdeletion 22q11 for schizophrenia and mood disorders. *American journal of medical genetics*, *105*(4), 354–362. https://doi.org/10.1002/ajmg.1359
37. Mekori-Domachevsky, E., Guri, Y., Yi, J., Weisman, O., Calkins, M. E., Tang, S. X., Gross, R., McDonald-McGinn, D. M., Emanuel, B. S., Zackai, E. H., Zalsman, G., Weizman, A., Gur, R. C., Gur, R. E., & Gothelf, D. (2017). Negative subthreshold psychotic symptoms distinguish 22q11.2 deletion syndrome from other

neurodevelopmental disorders: A two-site study. *Schizophrenia research*, *188*, 42–49. https://doi.org/10.1016/j.schres.2016.12.023
38. Maeder, J., Schneider, M., Bostelmann, M., Debbané, M., Glaser, B., Menghetti, S., Schaer, M., & Eliez, S. (2016). Developmental trajectories of executive functions in 22q11.2 deletion syndrome. *Journal of neurodevelopmental disorders*, *8*, 10. https://doi.org/10.1186/s11689-016-9141-1
39. Niarchou, M., Zammit, S., van Goozen, S. H., Thapar, A., Tierling, H. M., Owen, M. J., & van den Bree, M. B. (2014). Psychopathology and cognition in children with 22q11.2 deletion syndrome. *The British journal of psychiatry: the journal of mental science*, *204*(1), 46–54. https://doi.org/10.1192/bjp.bp.113.132324
40. Schonherz, Y., Davidov, M., Knafo, A., Zilkha, H., Shoval, G., Zalsman, G., Frisch, A., Weizman, A., & Gothelf, D. (2014). Shyness discriminates between children with 22q11.2 deletion syndrome and Williams syndrome and predicts emergence of psychosis in 22q11.2 deletion syndrome. *Journal of neurodevelopmental disorders*, *6*(1), 3. https://doi.org/10.1186/1866-1955-6-3
41. Antshel, K. M., Hendricks, K., Shprintzen, R., Fremont, W., Higgins, A. M., Faraone, S. V., & Kates, W. R. (2013). The longitudinal course of attention deficit/hyperactivity disorder in velo-cardio-facial syndrome. *The Journal of pediatrics*, *163*(1), 187–93.e1. https://doi.org/10.1016/j.jpeds.2012.12.026
42. Mosheva, M., Pouillard, V., Fishman, Y., Dubourg, L., Sofrin-Frumer, D., Serur, Y., Weizman, A., Eliez, S., Gothelf, D., & Schneider, M. (2019). Education and employment trajectories from childhood to adulthood in individuals with 22q11.2 deletion syndrome. *European child & adolescent psychiatry*, *28*(1), 31–42. https://doi.org/10.1007/s00787-018-1184-2
43. Sobin, C., Kiley-Brabeck, K., Monk, S. H., Khuri, J., & Karayiorgou, M. (2009). Sex differences in the behavior of children with the 22q11 deletion syndrome. *Psychiatry research*, *166*(1), 24–34. https://doi.org/10.1016/j.psychres.2008.03.023
44. Green, T., Gothelf, D., Glaser, B., Debbane, M., Frisch, A., Kotler, M., Weizman, A., & Eliez, S. (2009). Psychiatric disorders and intellectual functioning throughout development in velocardiofacial (22q11.2 deletion) syndrome. *Journal of the American Academy of Child and Adolescent Psychiatry*, *48*(11), 1060–1068. https://doi.org/10.1097/CHI.0b013e3181b76683
45. Midbari Kufert, Y., Nachmani, A., Nativ, E., Weizman, A., & Gothelf, D. (2016). Association between prematurity and the evolution of psychotic disorders in 22q11.2 deletion syndrome. *Journal of neural transmission (Vienna, Austria: 1996)*, *123*(12), 1491–1497. https://doi.org/10.1007/s00702-016-1607-5
46. Klaassen, P., Duijff, S., Swanenburg de Veye, H., Vorstman, J., Beemer, F., & Sinnema, G. (2013). Behavior in preschool children with the 22q11.2 deletion syndrome. *American journal of medical genetics. Part A*, *161A*(1), 94–101. https://doi.org/10.1002/ajmg.a.35685
47. Michaelovsky, E., Frisch, A., Carmel, M., Patya, M., Zarchi, O., Green, T., Basel-Vanagaite, L., Weizman, A., & Gothelf, D. (2012). Genotype-phenotype correlation in 22q11.2 deletion syndrome. *BMC medical genetics*, *13*, 122. https://doi.org/10.1186/1471-2350-13-122
48. Kates, W. R., Burnette, C. P., Bessette, B. A., Folley, B. S., Strunge, L., Jabs, E. W., & Pearlson, G. D. (2004). Frontal and caudate alterations in velocardiofacial syndrome (deletion at chromosome 22q11.2). *Journal of child neurology*, *19*(5), 337–342. https://doi.org/10.1177/088307380401900506
49. Schneider, M., Van der Linden, M., Menghetti, S., Glaser, B., Debbané, M., & Eliez, S. (2014). Predominant negative symptoms in 22q11.2 deletion syndrome and their associations with cognitive functioning and functional outcome. *Journal of psychiatric research*, *48*(1), 86–93. https://doi.org/10.1016/j.jpsychires.2013.10.010
50. Lima, K., Følling, I., Eiklid, K. L., Natvig, S., & Abrahamsen, T. G. (2010). Age-dependent clinical problems in a Norwegian national survey of patients with the

22q11.2 deletion syndrome. *European journal of pediatrics*, *169*(8), 983–989. https://doi.org/10.1007/s00431-010-1161-3
51. Papolos, D. F., Faedda, G. L., Veit, S., Goldberg, R., Morrow, B., Kucherlapati, R., & Shprintzen, R. J. (1996). Bipolar spectrum disorders in patients diagnosed with velo-cardio-facial syndrome: does a hemizygous deletion of chromosome 22q11 result in bipolar affective disorder?. *The American journal of psychiatry*, *153*(12), 1541–1547. https://doi.org/10.1176/ajp.153.12.1541
52. Feinstein, C., Eliez, S., Blasey, C., & Reiss, A. L. (2002). Psychiatric disorders and behavioral problems in children with velocardiofacial syndrome: usefulness as phenotypic indicators of schizophrenia risk. *Biological psychiatry*, *51*(4), 312–318. https://doi.org/10.1016/s0006-3223(01)01231-8
53. Shashi, V., Keshavan, M., Kaczorowski, J., Schoch, K., Lewandowski, K. E., McConkie-Rosell, A., Hooper, S. R., & Kwapil, T. R. (2010). Socioeconomic status and psychological function in children with chromosome 22q11.2 deletion syndrome: implications for genetic counseling. *Journal of genetic counseling*, *19*(5), 535–544. https://doi.org/10.1007/s10897-010-9309-x
54. Sobin, C., Kiley-Brabeck, K., & Karayiorgou, M. (2005). Associations between prepulse inhibition and executive visual attention in children with the 22q11 deletion syndrome. *Molecular psychiatry*, *10*(6), 553–562. https://doi.org/10.1038/sj.mp.4001609
55. Carlson, C., Papolos, D., Pandita, R. K., Faedda, G. L., Veit, S., Goldberg, R., Shprintzen, R., Kucherlapati, R., & Morrow, B. (1997). Molecular analysis of velo-cardio-facial syndrome patients with psychiatric disorders. *American journal of human genetics*, *60*(4), 851–859.
56. Mosheva, M., Eyal, S., Weisman, O., Gilad, R., Fishman, Y., Weinberger, R., Weizman, A., & Gothelf, D. (2018). Higher adaptive functioning and lower rate of psychotic comorbidity in married versus unmarried individuals with 22q11.2 deletion syndrome. *American journal of medical genetics. Part A*, *176*(11), 2365–2374. https://doi.org/10.1002/ajmg.a.38555
57. Briegel, W., Schneider, M., & Schwab, K. O. (2007). 22q11.2 deletion syndrome: behaviour problems of infants and parental stress. *Child: care, health and development*, *33*(3), 319–324. https://doi.org/10.1111/j.1365-2214.2006.00654.x
58. Gothelf, D., Aviram-Goldring, A., Burg, M., Steinberg, T., Mahajnah, M., Frisch, A., Fennig, S., Zalsman, G., & Weizman, A. (2007). Cognition, psychosocial adjustment and coping in familial cases of velocardiofacial syndrome. *Journal of neural transmission (Vienna, Austria: 1996)*, *114*(11), 1495–1501. https://doi.org/10.1007/s00702-007-0766-9

Down syndrome references

59. Esbensen, A. J., Hoffman, E. K., Shaffer, R., Chen, E., Patel, L., & Jacola, L. (2018). Reliability of parent report measures of behaviour in children with Down syndrome. *Journal of intellectual disability research : JIDR*, *62*(9), 785–797. https://doi.org/10.1111/jir.12533
60. Moss, J., Nelson, L., Powis, L., Waite, J., Richards, C., & Oliver, C. (2016). A Comparative Study of Sociability in Angelman, Cornelia de Lange, Fragile X, Down and Rubinstein Taybi Syndromes and Autism Spectrum Disorder. *American journal on intellectual and developmental disabilities*, *121*(6), 465–486. https://doi.org/10.1352/1944-7558-121.6.465
61. Tassé, M, J., Navas, P., Havercamp, S, M., Benson, B, A., Allain, D, C., Manickam, K., & Davis, S. (2016). Psychiatric conditions prevalent among adults with Down syndrome. *J Policy Pract Intellect Disabil, 13*(2), 173-180. https://doi.org/10.1111/jppi.12156

62. Mantry, D., Cooper, S. A., Smiley, E., Morrison, J., Allan, L., Williamson, A., Finlayson, J., & Jackson, A. (2008). The prevalence and incidence of mental ill-health in adults with Down syndrome. *Journal of intellectual disability research: JIDR*, *52*(Pt 2), 141–155. https://doi.org/10.1111/j.1365-2788.2007.00985.x
63. Mallardo, M., Cuskelly, M., White, P., & Jobling, A. (2014). Mental Health Problems in Adults with Down Syndrome and Their Association With Life Circumstances. *J Ment Health Res Intellect Disabil*, 7(3), 229-245. https://doi.org/10.1080/19315864.2013.842622
64. Patti, P, J., & Tsiouris, J, A. (2006). Psychopathology in adults with Down syndrome: Clinical findings from an outpatient clinic. *Int J Disabil Human Dev*, *5*(4), 357-364. https://doi.org/10.1515/IJDHD.2006.5.4.357
65. Glenn, S., Cunningham, C., Nananidou, A., Prasher, V., & Glenholmes, P. (2013). Using the strengths and difficulties questionnaire with adults with Down syndrome. *Research in developmental disabilities*, *34*(10), 3343–3351. https://doi.org/10.1016/j.ridd.2013.06.034
66. Myers, B. A., & Pueschel, S. M. (1991). Psychiatric disorders in persons with Down syndrome. *The Journal of nervous and mental disease*, *179*(10), 609–613. https://doi.org/10.1097/00005053-199110000-00004
67. Prasher, V, P. (1995). Prevalence of Psychiatric Disorders in Adults with Down Syndrome. *Eur J Psychiatry*, *9*(2), 77-82.
68. Way, E, L., & Rojahn, J. (2012). Psycho-social Characteristics of Children with Prenatal Alcohol Exposure, Compared to Children with Down Syndrome and Typical Children. *J Dev Phys Disabil*, *24,* 247-268. https://doi.org/10.1007/s10882-012-9269-1
69. Haveman, M. J., Maaskant, M. A., van Schrojenstein Lantman, H. M., Urlings, H. F., & Kessels, A. G. (1994). Mental health problems in elderly people with and without Down's syndrome. *Journal of intellectual disability research: JIDR*, *38 (Pt 3)*, 341–355. https://doi.org/10.1111/j.1365-2788.1994.tb00400.x
70. Collacott, R. A., Cooper, S. A., & McGrother, C. (1992). Differential rates of psychiatric disorders in adults with Down's syndrome compared with other mentally handicapped adults. *The British journal of psychiatry: the journal of mental science*, *161*, 671–674. https://doi.org/10.1192/bjp.161.5.671
71. Lund J. (1988). Psychiatric aspects of Down's syndrome. *Acta psychiatrica Scandinavica*, *78*(3), 369–374. https://doi.org/10.1111/j.1600-0447.1988.tb06350.x
72. McCarthy, J., & Boyd, J. (2001). Psychopathology and young people with Down's syndrome: childhood predictors and adult outcome of disorder. *Journal of intellectual disability research: JIDR*, *45*(Pt 2), 99–105. https://doi.org/10.1046/j.1365-2788.2001.00335.x

Rett syndrome references

73. Halbach, N. S., Smeets, E. E., Schrander-Stumpel, C. T., van Schrojenstein Lantman de Valk, H. H., Maaskant, M. A., & Curfs, L. M. (2008). Aging in people with specific genetic syndromes: Rett syndrome. *American journal of medical genetics. Part A*, *146A*(15), 1925–1932. https://doi.org/10.1002/ajmg.a.32361
74. Anderson, A., Wong, K., Jacoby, P., Downs, J., & Leonard, H. (2014). Twenty years of surveillance in Rett syndrome: what does this tell us?. *Orphanet journal of rare diseases*, *9*, 87. https://doi.org/10.1186/1750-1172-9-87
75. Cianfaglione, R., Clarke, A., Kerr, M., Hastings, R. P., Oliver, C., Moss, J., Heald, M., & Felce, D. (2015). A national survey of Rett syndrome: behavioural characteristics. *Journal of neurodevelopmental disorders*, *7*(1), 11. https://doi.org/10.1186/s11689-015-9104-y

76. Sansom, D., Krishnan, V. H., Corbett, J., & Kerr, A. (1993). Emotional and behavioural aspects of Rett syndrome. *Developmental medicine and child neurology*, *35*(4), 340–345. https://doi.org/10.1111/j.1469-8749.1993.tb11646.x
77. Mount, R. H., Charman, T., Hastings, R. P., Reilly, S., & Cass, H. (2002). The Rett Syndrome Behaviour Questionnaire (RSBQ): refining the behavioural phenotype of Rett syndrome. *Journal of child psychology and psychiatry, and allied disciplines*, *43*(8), 1099–1110. https://doi.org/10.1111/1469-7610.00236
78. Robertson, L., Hall, S. E., Jacoby, P., Ellaway, C., de Klerk, N., & Leonard, H. (2006). The association between behavior and genotype in Rett syndrome using the Australian Rett Syndrome Database. *American journal of medical genetics. Part B, Neuropsychiatric genetics: the official publication of the International Society of Psychiatric Genetics*, *141B*(2), 177–183. https://doi.org/10.1002/ajmg.b.30270

CHARGE syndrome references

79. Bernstein, V., & Denno, L. S. (2005). Repetitive behaviors in CHARGE syndrome: differential diagnosis and treatment options. *American journal of medical genetics. Part A*, *133A*(3), 232–239. https://doi.org/10.1002/ajmg.a.30542
80. Wachtel, L, E., Hartshorne, T, S., & Dailor, A, N. (2007). Psychiatric Diagnoses and Psychotropic Medications in CHARGE Syndrome: A Pediatric Survey. *J Dev Phys Disabil*, *19,* 471-483. https://doi.org/10.1007/s10882-007-9064-6
81. Hartshorne, N., Hudson, A., MacCuspie, J., Kennert, B., Nacarato, T., Hartshorne, T., & Blake, K. (2016). Quality of life in adolescents and adults with CHARGE syndrome. *American journal of medical genetics. Part A*, *170*(8), 2012–2021. https://doi.org/10.1002/ajmg.a.37769
82. Hartshorne, T, S., & Cypher, A, D. (2004). Challenging Behavior in CHARGE Syndrome. *Mental Health Aspects of Developmental Disabilities*, *7*(2), 41-52.

7q11.23 duplication syndrome references

83. Morris, C. A., Mervis, C. B., Paciorkowski, A. P., Abdul-Rahman, O., Dugan, S. L., Rope, A. F., Bader, P., Hendon, L. G., Velleman, S. L., Klein-Tasman, B. P., & Osborne, L. R. (2015). 7q11.23 Duplication syndrome: Physical characteristics and natural history. *American journal of medical genetics. Part A*, *167A*(12), 2916–2935. https://doi.org/10.1002/ajmg.a.37340
84. Mervis, C. B., Klein-Tasman, B. P., Huffman, M. J., Velleman, S. L., Pitts, C. H., Henderson, D. R., Woodruff-Borden, J., Morris, C. A., & Osborne, L. R. (2015). Children with 7q11.23 duplication syndrome: psychological characteristics. *American journal of medical genetics. Part A*, *167*(7), 1436–1450. https://doi.org/10.1002/ajmg.a.37071
85. Mervis, C. B., Dida, J., Lam, E., Crawford-Zelli, N. A., Young, E. J., Henderson, D. R., Onay, T., Morris, C. A., Woodruff-Borden, J., Yeomans, J., & Osborne, L. R. (2012). Duplication of GTF2I results in separation anxiety in mice and humans. *American journal of human genetics*, *90*(6), 1064–1070. https://doi.org/10.1016/j.ajhg.2012.04.012

3q29 deletion syndrome reference

86. Glassford, M. R., Rosenfeld, J. A., Freedman, A. A., Zwick, M. E., Mulle, J. G., & Unique Rare Chromosome Disorder Support Group (2016). Novel features of 3q29 deletion syndrome: Results from the 3q29 registry. *American journal of medical genetics. Part A*, *170A*(4), 999–1006. https://doi.org/10.1002/ajmg.a.37537

Tuberous Sclerosis Complex references

87. de Vries, P. J., Belousova, E., Benedik, M. P., Carter, T., Cottin, V., Curatolo, P., Dahlin, M., D'Amato, L., d'Augères, G. B., Ferreira, J. C., Feucht, M., Fladrowski, C., Hertzberg, C., Jozwiak, S., Kingswood, J. C., Lawson, J. A., Macaya, A., Marques, R., Nabbout, R., O'Callaghan, F., … TOSCA Consortium and TOSCA Investigators (2018). TSC-associated neuropsychiatric disorders (TAND): findings from the TOSCA natural history study. *Orphanet journal of rare diseases*, *13*(1), 157. https://doi.org/10.1186/s13023-018-0901-8
88. Wilbur, C., Sanguansermsri, C., Chable, H., Anghelina, M., Peinhof, S., Anderson, K., Steinbok, P., Singhal, A., Datta, A., & Connolly, M. B. (2017). Manifestations of Tuberous Sclerosis Complex: The Experience of a Provincial Clinic. *The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques*, *44*(1), 35–43. https://doi.org/10.1017/cjn.2016.311
89. Chung, T. K., Lynch, E. R., Fiser, C. J., Nelson, D. A., Agricola, K., Tudor, C., Franz, D. N., & Krueger, D. A. (2011). Psychiatric comorbidity and treatment response in patients with tuberous sclerosis complex. *Annals of clinical psychiatry: official journal of the American Academy of Clinical Psychiatrists*, *23*(4), 263–269.
90. de Vries, P. J., Hunt, A., & Bolton, P. F. (2007). The psychopathologies of children and adolescents with tuberous sclerosis complex (TSC): a postal survey of UK families. *European child & adolescent psychiatry*, *16*(1), 16–24. https://doi.org/10.1007/s00787-006-0570-3
91. Raznahan, A., Joinson, C., O'Callaghan, F., Osborne, J. P., & Bolton, P. F. (2006). Psychopathology in tuberous sclerosis: an overview and findings in a population-based sample of adults with tuberous sclerosis. *Journal of intellectual disability research : JIDR*, *50*(Pt 8), 561–569. https://doi.org/10.1111/j.1365-2788.2006.00828.x
92. Smalley, S. L., Burger, F., & Smith, M. (1994). Phenotypic variation of tuberous sclerosis in a single extended kindred. *Journal of medical genetics*, *31*(10), 761–765. https://doi.org/10.1136/jmg.31.10.761
93. Kothare, S. V., Singh, K., Hochman, T., Chalifoux, J. R., Staley, B. A., Weiner, H. L., Menzer, K., & Devinsky, O. (2014). Genotype/phenotype in tuberous sclerosis complex: associations with clinical and radiologic manifestations. *Epilepsia*, *55*(7), 1020–1024. https://doi.org/10.1111/epi.12627
94. Kingswood, J. C., d'Augères, G. B., Belousova, E., Ferreira, J. C., Carter, T., Castellana, R., Cottin, V., Curatolo, P., Dahlin, M., de Vries, P. J., Feucht, M., Fladrowski, C., Gislimberti, G., Hertzberg, C., Jozwiak, S., Lawson, J. A., Macaya, A., Nabbout, R., O'Callaghan, F., Benedik, M. P., … TOSCA consortium and TOSCA investigators (2017). TuberOus SClerosis registry to increase disease Awareness (TOSCA) - baseline data on 2093 patients. *Orphanet journal of rare diseases*, *12*(1), 2. https://doi.org/10.1186/s13023-016-0553-5
95. Kopp, C. M., Muzykewicz, D. A., Staley, B. A., Thiele, E. A., & Pulsifer, M. B. (2008). Behavior problems in children with tuberous sclerosis complex and parental stress. *Epilepsy & behavior : E&B*, *13*(3), 505–510. https://doi.org/10.1016/j.yebeh.2008.05.010

Appendix Seven. Invitation letter for questionnaire study

The Cerebra Centre for Neurodevelopmental Disorders

UNIVERSITY OF BIRMINGHAM

Appendix 7 Invitation letter for Chapter three (questionnaire study)

Dear **[insert name of parent],**

A new research project is being carried out by Dr Jane Waite at Aston University, in partnership with the Cerebra Centre for Neurodevelopmental Disorders at the University of Birmingham, Coventry University and Birmingham Women's and Children's Hospital. We wanted to let you know about this study so that you and the person you care for can decide whether you'd like to take part. The research is a questionnaire study looking at emotion and behaviour in children and adults with **neurodevelopmental disorders, such as [insert syndrome name].**

This research is being carried out to inform the development of a new assessment tool to measure emotional well-being and distress in people with learning disabilities. It is hoped that this tool will be used when children are seen by health professionals in the NHS. In the future, this assessment tool may improve care for individuals with learning disabilities, particularly individuals who have communication difficulties. Each parent/carer who completes the questionnaire will receive a £5 voucher for their participation (maximum of one voucher per family).

If you and your child/person you care for would like to learn more about the new study and decide whether you would like to take part, the information sheets and questionnaire can be accessed and completed online (see back of this letter for details). Alternatively, you can request the information sheet and a paper copy of the questionnaire from Dr Joanne Tarver at Aston University (see enclosed expression of interest form for details).

When the research team have analysed the information you send to them, you will be provided with a personalised feedback about the person you care for.

If you are unclear about any aspect of the study or have any questions, then contact Dr Joanne Tarver (0121 204 4386; j.tarver@aston.ac.uk) at Aston University.

Thank you for your time and the research team look forward to hearing from you

The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.Bham.ac.uk **E-mail**: cndd-enquiries@contacts.bham.ac.uk
Phone: 0121 414 7206

Appendix Seven. Invitation letter for questionnaire study

The Cerebra Centre for Neurodevelopmental Disorders

UNIVERSITY OF BIRMINGHAM

[signature removed]

Chris Oliver, Professor of Neurodevelopmental Disorders

The Cerebra Centre for Neurodevelopmental Disorders,
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Appendix Seven. Invitation letter for questionnaire study

The Cerebra Centre for Neurodevelopmental Disorders

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Instructions for taking part online

Important information before you start the questionnaire online:

The information sheet for this study will be provided when you visit the link below. Please read this information sheet before deciding whether you would like to take part. The information sheet will provide details about how the research team will protect your data, as well as other important information about the study.

To access the questionnaire study online go to:

[insert link]

Password to access survey:

ID number:

[insert participants ID number]

Thank you for your support!

If you would rather request a paper copy of the questionnaire, complete the expression of interest form that is enclosed with this letter.

The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
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Phone: 0121 414 7206

Appendix Seven. *Invitation letter for questionnaire study*

Aston University
Birmingham

Dear **[insert name of parent],**

A new research project is being carried out by Dr Jane Waite at Aston University, in partnership with the Cerebra Centre for Neurodevelopmental Disorders at the University of Birmingham, Coventry University and Birmingham Women's and Children's Hospital. We wanted to let you know about this study so that you and the person you care for can decide whether you'd like to take part. The research is a questionnaire study looking at emotion and behaviour in children and adults with **neurodevelopmental disorders, such as [insert syndrome name].**

This research is being carried out to inform the development of a new assessment tool to measure emotional well-being and distress in people with learning disabilities. It is hoped that this tool will be used when children are seen by health professionals in the NHS. In the future, this assessment tool may improve care for individuals with learning disabilities, particularly individuals who have communication difficulties.

If you and your child/person you care for would like to learn more about the new study and decide whether you would like to take part, the information sheets and questionnaire can be accessed and completed online (see back of this letter for details). Alternatively, you can request the information sheet and a paper copy of the questionnaire from Dr Jane Waite at Aston University (see enclosed expression of interest form for details).

When the research team have analysed the information you send to them, you will be provided with a personalised feedback about the person you care for.

If you are unclear about any aspect of the study or have any questions, then contact Dr Jane Waite (0121 204 4307; j.waite@aston.ac.uk) at Aston University.

Thank you for your time and the research team look forward to hearing from you

[signature removed]

Chris Oliver
Professor of Neurodevelopmental Disorders

The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.Bham.ac.uk **E-mail**: cndd-enquiries@contacts.bham.ac.uk
Phone: 0121 414 7206

Appendix Seven. *Invitation letter for questionnaire study*

Aston University
Birmingham

Instructions for taking part online

Important information before you start the questionnaire online:

The information sheet for this study will be provided when you visit the link below. Please read this information sheet before deciding whether you would like to take part. The information sheet will provide details about how the research team will protect your data, as well as other important information about the study.

To access the questionnaire study online go to: **https://tinyurl.com/y4tnu375**

Password to access survey (case sensitive): **Cerebra**

Your ID number:

Scan this QR code with your phone's camera to access the questionnaire:

Thank you for your support!

If you would rather request a paper copy of the questionnaire, complete the expression of interest form that is enclosed with this letter.

The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.Bham.ac.uk **E-mail**: cndd-enquiries@contacts.bham.ac.uk
Phone: 0121 414 7206

Appendix Seven. *Invitation letter for questionnaire study*

[insert Trust letterhead]

Dear **[insert name of parent],**

Re: **[insert child's name; NHS number; DoB]**

We are contacting you because (insert name of trust) are supporting a new research project that you may wish to participate in. This new research project is being carried out by Dr Jane Waite at Aston University, in partnership with the Cerebra Centre for Neurodevelopmental Disorders at the University of Birmingham, and Aston University. We have not passed your details to anyone outside of your NHS service, and your personal details will only be shared with the research lead at Aston University if you decide to take part.

The research is a questionnaire study looking at emotion and behaviour in children and adults with **neurodevelopmental disorders, such as [insert syndrome/diagnosis if appropriate].** This research is being carried out to inform the development of a new assessment tool to measure emotional well-being and distress in people with learning disabilities. It is hoped that this tool will be used when children are seen by health professionals in the NHS. In the future, this assessment tool may improve care for individuals with learning disabilities, particularly individuals who have communication difficulties. Each parent/carer who completes the questionnaire will receive a £5 voucher for their participation (maximum of one voucher per family).

If you would like to learn more about the new study and decide whether you would like to take part, the information sheets and questionnaire can be accessed and completed online (see back of this letter for details). Alternatively, you can request the information sheet and a paper copy of the questionnaire from the lead researcher, Dr Joanne Tarver, at Aston University (see enclosed expression of interest form for details).

When the research team have analysed the information you send to them, they will provide you with personalised feedback about the person you care for.

If you are unclear about any aspect of the study or have any questions then contact Dr Joanne Tarverat Aston University, 0121204 4386; j.waite@aston.ac.uk.

Thank you for your time and we look forward to hearing from you.

The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.Bham.ac.uk **E-mail**: cndd-enquiries@contacts.bham.ac.uk
Phone: 0121 414 7206

Appendix Seven. *Invitation letter for questionnaire study*

Yours sincerely

Insert name of local clinical team contact

The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.Bham.ac.uk **E-mail**: cndd-enquiries@contacts.bham.ac.uk
Phone: 0121 414 7206

Appendix Seven. *Invitation letter for questionnaire study*

Instructions for taking part online

Important information before you start the questionnaire online:

The information sheet for this study will be provided when you visit the link below. Please read this information sheet before deciding whether you would like to take part. The information sheet will provide details about how the research team will protect your data, as well as other important information about the study.

To access the questionnaire study online go to:

[insert link]

Password to access survey:
Cerebra

ID number:

[insert participants ID number]

Thank you for your support!

If you would rather request a paper copy of the questionnaire, complete the expression of interest form that is enclosed with this letter.

The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.Bham.ac.uk **E-mail**: cndd-enquiries@contacts.bham.ac.uk
Phone: 0121 414 7206

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Dr Jane Waite
Lecturer in Psychology
Aston University
Aston Triangle
Birmingham
B4 7ET

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

18 May 2018

Dear Dr Waite
Appendix 8 Ethical approval for Chapter three (questionnaire study)

HRA and Health and Care

Study title:	**Developing the Clinical Anxiety Screen for people with Severe to Profound Intellectual Disabilities (CIASP-ID)**
IRAS project ID:	**240250**
Protocol number:	**CIASPID_4.12.16_V1**
REC reference:	**18/WA/0139**
Sponsor	**Aston University**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

How should I continue to work with participating NHS organisations in England and Wales? You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).

It is important that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details of the research management function for each organisation can be accessed here.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?

HRA and HCRW Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) has been sent to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?

HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your nonNHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including: Registration of research

- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

I am a participating NHS organisation in England or Wales. What should I do once I receive this letter?

You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Name: Matthew Richards
Tel: 0121 204 5069
Email: m.richards3@aston.ac.uk

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **240250**. Please quote this on all correspondence.

Yours sincerely

Simon Connolly
Senior Assessor

Email: hra.approval@nhs.net

Copy to: Mr Matthew Richards, Aston University
Ms Kelly Hard, Birmingham Women's and Children's NHS Foundation Trust

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Contract/Study Agreement template [Clinical Research Agreement]	V1	19 March 2018
Copies of advertisement materials for research participants [AppendixE_Advert_Interview]	V1	12 November 2017
Copies of advertisement materials for research participants [AppendixZa_Advert]	V1	12 November 2017
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Aston EL-PL]		
GP/consultant information sheets or letters [AppendixZu_GPLetter_13.2.17_V3_clean]	3	13 February 2017
GP/consultant information sheets or letters [AppendixZv_Parent_GPLetterFollowup_18.4.18_V1]	1	18 April 2018
GP/consultant information sheets or letters [AppendixZw_PersonLD_GPLetterFollowup_18.4.18_V1]	1	18 April 2018
GP/consultant information sheets or letters [AppendixZx_GPLetterParent_18.4.18_V1]	1	18 April 2018
HRA Schedule of Events	1	17 May 2018
HRA Statement of Activities	1	17 May 2018
Interview schedules or topic guides for participants [AppendixS_Interview_24.4.18_V2_clean]	2	24 April 2018
Interview schedules or topic guides for participants [AppendixU_ClinicianInterview_24.4.18_V2_Clean]	2	24 April 2018
IRAS Application Form		24 April 2018
Letter from funder [Outcome Letter]	V1	01 June 2017
Letter from sponsor [Sponsorship Letter]	V1	22 March 2018
Letters of invitation to participant [AppendixZs_Invite_NHS_FeasibilityStudy]	V1	12 November 2017
Letters of invitation to participant [AppendixD_Invite_CNDD]	V1	12 November 2017
Letters of invitation to participant [AppendixJ_EoI_Interview]	V1	12 November 2017
Letters of invitation to participant [AppendixN_Invite_NHS_Interview]	V1	12 November 2017
Letters of invitation to participant [AppendixP_ClinicianInvite]	V1	04 December 2017
Letters of invitation to participant [AppendixV_InviteSG_Questionnaire]	V1	04 December 2017
Letters of invitation to participant [AppendixW_Invite_Database_Questionnaire]	V1	12 November 2017
Letters of invitation to participant [AppendixX_Invite_NHS_Questionnaire]	V1	12 November 2017
Letters of invitation to participant [AppendixZ_EoI_Questionnaire]	V1	12 November 2017
Non-validated questionnaire [AppendixZn_FollowupQs]	V1	12 November 2017
Non-validated questionnaire [AppendixZg_BackgroundQ_24.4.18_V2_clean]	2	24 April 2018

Other [AppendixZt_Pre Visit Risk Assessment]	V1	04 January 2018
Other [Notice of Minor Amendment]		15 May 2018
Participant consent form [Appendix G Able participant (adult or child & parent) Interview]	3	15 May 2018
Participant consent form [Appendix H Adult lacking capacity	3	15 May 2018
Interview]		
Participant consent form [Appendix I Parent/guardian of child lacking capacity interview]	3	15 May 2018
Participant consent form [Appendiz Zp Able participants (Adult or child & parent) Feasibility]	3	15 May 2018
Participant consent form [Appendix Zq Adult lacking capacity Feasibility]	3	15 May 2018
Participant consent form [Appendix Zr Parent/guardian of child lacking capacity Feasibility]	3	15 May 2018
Participant consent form [AppendixZd_Consent_Over16_Q_18.4.18_V2_clean]	2	18 April 2018
Participant consent form [AppendixZe_Consent_Under16_NotAble_Q_18.4.18_V2_cleandoc]	2	18 April 2018
Participant consent form [AppendixZf_Consent_Able_Q_18.4.18_V2_clean]	2	18 April 2018
Participant consent form [AppendixR_Consent_Clinician]	V1	12 November 2017
Participant information sheet (PIS) [AppendixK_Consultee_Information_24.4.18_V2_clean]	2	24 April 2018
Participant information sheet (PIS) [AppendixZc_Questionnaire_18.4.18_V2_clean]	2	18 April 2018
Participant information sheet (PIS) [Appendix Zo Feasibility Study]	3	15 May 2018
Participant information sheet (PIS) [AppendixL_SymbolInfoSheet]	V1	18 November 2017
Participant information sheet (PIS) [AppendixM_Capacity Protocol]	V2	06 April 2012
Participant information sheet (PIS) [AppendixQ_ClinicianInfo]	V1	12 November 2017
Participant information sheet (PIS) [AppendixF_Info_Interview_18.4.18_V2_clean]	2	18 April 2018
Research protocol or project proposal [Research_Protocol_V2_18.4.18_clean]	2	18 April 2018
Summary CV for Chief Investigator (CI) [CV_JaneWaite]	V1	12 November 2017
Summary CV for student [CV_AShiraz]	V1	08 January 2018
Summary CV for student [CV_HannahPitt]	V1	08 January 2018
Summary CV for supervisor (student research) [CV_ChrisOliver]	V1	08 January 2018
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Flowchart_V2_18.4.18_Clean]	2	18 April 2018
Validated questionnaire [AppendixA_WQ]	V1	12 November 2017
Validated questionnaire [AppendixB_WADL]	V1	04 January 2018
Validated questionnaire [AppendixC_VABS]	V1	12 September 2017
Validated questionnaire [AppendixT_SCQ]	V1	12 November 2017
Validated questionnaire [AppendixZh_HQ]	V1	12 November 2017
Validated questionnaire [AppendixZi_CBQ]	V1	12 November 2017

Validated questionnaire [AppendixZj_EDAQ]	V1	12 November 2017
Validated questionnaire [AppendixZk_ADAMS]	V1	12 November 2017
Validated questionnaire [AppendixZl_MIPQ]	V1	12 November 2017
Validated questionnaire [AppendixZm_PainChecklist]	V1	01 March 2004

Summary of assessment

The following information provides assurance to you, the sponsor and the NHS in England and Wales that the study, as assessed for HRA and HCRW Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England and Wales to assist in assessing, arranging and confirming capacity and capability.

Assessment criteria

Section	Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	Minor amendment made to documents subsequent to REC favourable opinion.
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	Agreement to be in place between sponsor and participating NHS organisation using a Aston University template. Statement of activities and schedule of events provided.
4.2	Insurance/indemnity arrangements assessed	Yes	No comments
4.3	Financial arrangements assessed	Yes	Funding available to participating NHS organisations as detailed in schedule of events.
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments

5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
Section	**Assessment Criteria**	**Compliant with Standards**	**Comments**
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	Minor amendment made to documents subsequent to REC favourable opinion.
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England and Wales

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.

There will be a single participating NHS organisation. They will contact potential participants in the study and provide information about the study. They will also facilitate data collection from medical records. NHS staff will take part as participants in one element of the study.

All other research activities will be conducted by university researchers. Potential participants will also come from outside the NHS. This approval only covers activities and recruitment within the NHS.

The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England and Wales in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. Where applicable, the local LCRN contact should also be copied into this correspondence.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England and Wales which are not provided in IRAS or on the HRA or HCRW websites, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net, or HCRW at Research-permissions@wales.nhs.uk. We will work with these organisations to achieve a consistent approach to information provision.

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and Wales, and the minimum expectations for education, training and experience that PIs should meet (where applicable).
A local collaborator will be in place at the participating NHS organisation. GCP training is not a generic training expectation, in line with the HRA/HCRW/MHRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken
Where arrangements are not already in place researchers will require a letter of access to conduct research activities or access identifiable data derived from health records within NHS care facilities. If conducting any research activities with service users in facilities of the NHS provider then appropriate occupational health and DBS checks should be confirmed.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales to aid study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

Appendix 9 Background Questionnaire

BACKGROUND INFORMATION

Please tick or write your response to these questions concerning background details:

Please answer the following about the person you care for:

1. **Today's date:** _____
2. **Gender:** Male ☐ Female ☐
3. **Date of Birth**: ___/___/____ **Age:**_____
4. **Is the person you care for verbal?** (i.e. more than 30 signs/words in their vocabulary)

   Yes/No (delete as appropriate)

5. **Is the person you care for able to walk unaided?**

   Yes/No (delete as appropriate)

6. **Has the person you care for been diagnosed with a syndrome/neurodevelopmental condition?** Yes/No (delete as appropriate)

If yes, please indicate which syndrome in 5a. and answer questions 6 to 8. If no, please move on to question 9

6.a

Cornelia de Lange syndrome	☐	Cri du Chat syndrome	☐
Prader-Willi syndrome	☐	Angelman syndrome	☐
Fragile X syndrome	☐	Smith-Magenis syndrome	☐
Lowe syndrome	☐	Soto Syndrome	☐
Rubinstein-Taybi syndrome	☐	9q34 deletion	
8p23deletion	☐	Tuberous Sclerosis	☐
Autism	☐		

Other _____

7. **What is the genetic mechanism causing the syndrome in the person you care for?**

Uni-parental disomy	☐	Sequence repetition	☐
Deletion	☐	Translocation	☐
Unknown	☐	Other	

_____

8. **When was the person you care for diagnosed?**
   _____
9. **Who diagnosed the person you care for?**

Paediatrician	☐	Clinical Geneticist	☐

GP ☐ Other

_____

10. Has the person you care for had any medical/health difficulties in the last six months? If yes, please give details:

_____

_____

_____

_____

We may need to contact your child's/person you care for's GP in order to clarify any information regarding your child's health status (see consent form and information sheet for more information). If you are happy for us to do this, please complete the relevant details below:

11. Name of your child's/person you care for's

GP_____

GP

Address_____

_____

_____**GP Telephone**

number_____

Is your child's GP the same as your GP?

Yes/No (delete as appropriate)

If no, please give us your GP details:

12. GP_____

GP

Address_____

_____

_____**GP Telephone**

number_____

The following questions ask for background information <u>about you and your family</u>.
Please tick the appropriate boxes or write in the spaces provided.

1. Are you male or female? Male ☐ Female ☐

2. What was your age in years on your last birthday? _____years

3. Please tick the highest level of your educational qualifications.

No formal educational qualifications..... ☐

Fewer than 5 GCSE's or O Level's (grades A-C), NVQ 1, or BTEC First Diploma……. ….
☐
5 or more GCSE's or O Level's (grades A-C), NVQ 2, or equivalent……..……..
☐
3 or more 'A' Levels, NVQ 3, BTEC National, or equivalent..... ☐
Polytechnic/University degree, NVQ 4, or equivalent..... ☐
Masters/Doctoral degree, NVQ 5, or equivalent……..... ☐

4. What is your relationship to your child with a genetic syndrome (e.g. mother, father, stepmother, grandmother, adoptive parent)? _____

5. In total how many people currently live in your home? _____ Adults _____ Children

6. Does your child with a genetic syndrome normally live with you?Yes ☐ No ☐

If no, then where do they live? _____

7. What is your current marital status?

Married, and living with spouse..... ☐

Living with partner..... ☐

Divorced/Separated/Widowed/Single and NOT living with a partner..... ☐

If living with partner/spouse, please answer the following questions, if not, please go to question 12.

8. Is your partner male or female? Male ☐ Female ☐

9. What was their age in years on their last birthday? _____ years

10. Please tick the highest level of your partner/spouse's educational qualifications.

No formal educational qualifications..... ☐

Fewer than 5 GCSE or O Level (grades A-C), NVQ 1, or BTEC First Diploma…☐

5 or more GCSE or O Level (grades A-C), NVQ 2, or equivalent……☐

3 or more 'A' Levels, NVQ 3, BTEC National, or equivalent.....☐

Polytechnic/University degree, NVQ 4, or equivalent.....☐

Masters/Doctoral degree, NVQ 5, or equivalent…….....☐

11. What is your partner/spouse's relationship to your child with a genetic syndrome (e.g., mother, father, stepmother, adoptive parent)?

_____

12. Recent data from research with families of children with special needs has shown that a family's financial resources are important in understanding family member's views and experiences. With this in mind, we would be very grateful if you could answer the additional question below. We are not interested in exactly what your family income is, but we would like to be able to look at whether those with high versus lower levels of financial resources have different experiences.

What is your current total annual family income? Please include a rough estimate of total salaries and other income (including benefits) before tax and national insurance/pensions.

Please tick one box only:

Less than £15,000.....☐

£15,001 to £25,000.....☐

£25,001 to £35,000.....☐

£35,001 to £45,000.....☐

£45,001 to £55,000.....☐

£55,001 to £65,000.....☐

£65,001 or more.....☐

Appendix 10 Wessex Questionnaire

Wessex Questionnaire

These items refer to the person you care for. For each question (A, B, C, D etc …), please enter the appropriate code in each box.

A) Wetting (nights)	**1** = frequently	**2** = occasionally	**3** = never	☐
B) Soiling (nights)	**1** = frequently	**2** = occasionally	**3** = never	☐
C) Wetting (days)	**1** = frequently	**2** = occasionally	**3** = never	☐
D) Soiling (days)	**1** = frequently	**2** = occasionally	**3** = never	☐
E) Walk with help*	**1** = not at all	**2** = not up stairs	**3** = up stairs and elsewhere	☐

*(note: if this person walks *by himself/herself* upstairs and elsewhere, please also code '3' for 'walk with help')

F) Walk by himself	**1** = not at all	**2** = not up stairs	**3** = up stairs and elsewhere	☐
G) Feed himself	**1** = not at all	**2** = with help	**3** = without help	☐
H) Wash himself	**1** = not at all	**2** = with help	**3** = without help	☐
I) Dress himself	**1** = not at all	**2** = with help	**3** = without help	☐

J) Vision	**1** = blind or almost	**2** = poor	**3** = normal	☐
K) Hearing	**1** = deaf or almost	**2** = poor	**3** = normal	☐
L) Speech	**1** = never a word	**2** = odd words only	**3** = sentences and normal	**4** = can talk but doesn't ☐

If this person talks in sentences, is his/her speech:

1 = Difficult to understand even by acquaintances, impossible for strangers?

2 = Easily understood for acquaintances, difficult for strangers?

3 = Clear enough to be understood by anyone? ☐

M) Reads	**1** = nothing	**2** = a little	**3** = newspapers and/or books	☐
N) Writes	**1** = nothing	**2** = a little	**3** = own correspondence	☐
O) Counts	**1** = nothing	**2** = a little	**3** = understands money values	☐

Appendix 11 Social Communication Questionnaire

Social Communication Questionnaire (SCQ) removed due to copyright restrictions

Appendix 12 Anxiety, Depression and Mood Scale (ADAMS)

Instructions The Anxiety Depression and Mood Scale (ADAMS) contains a list of behaviors that can be found among individuals with intellectual disability. Please describe the individual's behavior over the last 6 months.

0 behavior has not occurred, or is not a problem
1 behavior occurs occasionally, or is a mild problem
2 behavior occurs quite often, or is a moderate problem
3 behavior occurs a lot, or is a severe problem

	not a problem	mild problem	moderate problem	severe problem
1. Nervous	0	1	2	3
2. Problems initiating communication	0	1	2	3
3. Does not relax or settle down	0	1	2	3
4. Has periods of over-activity	0	1	2	3
5. Sleeps more than normal	0	1	2	3
6. Withdraws from other people	0	1	2	3
7. Tense	0	1	2	3
8. Engages in ritualistic behaviors	0	1	2	3
9. Depressed mood	0	1	2	3
10. Sad	0	1	2	3
11. Worried	0	1	2	3
12. Has developed difficulty staying on task or completing work	0	1	2	3
13. Shy	0	1	2	3
14. Easily fatigued (not due to being overweight).	0	1	2	3
15. Anxious	0	1	2	3
16. Repeatedly checks items	0	1	2	3
17. Easily distracted	0	1	2	3
18. Lacks energy	0	1	2	3
19. Avoids others, spends much of time alone	0	1	2	3
20. Easily upset if ritualistic behaviors are interrupted	0	1	2	3
21. Lacks emotional facial expressions	0	1	2	3
22. Has shown difficulty in starting routine tasks	0	1	2	3
23. Listless	0	1	2	3
24. Experiences panic attacks	0	1	2	3
25. Avoids eye contact	0	1	2	3
26. Trembles when frightening situations are not present	0	1	2	3
27. Avoids peers	0	1	2	3
28. Tearful	0	1	2	3

Appendix 13 Diagnostic Assessment for Severely Handicapped (DASH-II) anxiety subscale

Diagnostic Assessment for the Severely Handicapped (DASH-II) removed due to copyright restrictions

Appendix 14 Sensory Profile 2: visual, tactile, and auditory subscales

Sensory Profile 2 removed due to copyright restrictions

Appendix 15 Repetitive Behaviour Questionnaire (RBQ)

Repetitive Behaviour Questionnaire (2): Scoring

	Does your child:	***Never** or **rarely***	***One** or more times daily*	***15** or more times daily (or at least once an hour)*	***30** or more times daily (or twice an hour)*
1.	Arrange toys or other items in rows or patterns?	**1**	**2**	**3**	**4**
2.	Repetitively fiddle with toys or other items? (e.g. spin, twiddle, bang, tap, twist, or flick anything repeatedly?)	**1**	**2**	**3**	**4**
3.	Spin him/herself around and around?	**1**	**2**	**3**	**4**
4.	Rock backwards and forwards, or side to side, either when sitting or when standing?	**1**	**2**	**3**	**4**
5.	Pace or move around repetitively? (e.g. walk to and fro across a room, or around the same path in the garden?)	**1**	**2**	**3**	**4**
6.	Make repetitive hand and/or finger movements? (e.g. flap, wave, or flick, his/her hands or fingers repetitively?)	**1**	**2**	**3**	**4**
	Does your child:	***Never** or **rarely***	***Mild** or **occasional***	***Marked** or **notable***	
7.	Have a fascination with specific objects? (e.g. trains, road signs or other things?)	**1**	**2**	**3**	
8.	Like to look at objects from particular or unusual angles?	**1**	**2**	**3**	
9.	Have a special interest in the smell of people or objects?	**1**	**2**	**3**	
10.		**1**	**2**	**3**	

11.	Have a special interest in the feel of different surfaces?	**1**	**2**	**3**
12.	Have any special objects he/she likes to carry around? (e.g. a teddy, a blanket, a book, or a stick?) Collect or hoard items of any sort?	**1**	**2**	**3**

	Does your child:	***Never** or rarely*	***Mild** or **occasional** (does not affect others)*	***Marked** or **notable** (affects others on a regular basis))*
13.	Insist on things at home remaining the same? (e.g. furniture staying in the same place, things being kept in certain places, or arranged in certain ways?)	**1**	**2**	**3**
14.	Get upset about minor changes to objects (e.g. flecks of dirt on his clothes, minor scratches on toys)	**1**	**2**	**3**
15.	Insist that aspects of daily routine must remain the same?	**1**	**2**	**3**
16.	Insist on doing things in a certain way or redoing things until they are "just right"?	**1**	**2**	**3**
.	**Does your child:**	***Never** or rarely*	***Mild** or **occasional** (will tolerate alternatives when necessary)*	***Marked** or **notable** (will not tolerate any alternatives))*
17.	Play the same music, game or video, or read the same book repeatedly?	**1**	**2**	**3**
18.	Insist on wearing the same clothes or refuse to wear new clothes?	**1**	**2**	**3**
19.				

	Insist on eating the same foods, or a very small range of foods, at every meal?	**1**	**2**	**3**
	What sort of activity will your child choose if they are left to occupy themselves?	*A **range** of different and flexible selfchosen activities*	***Some** varied and flexible interests but commonly chooses the same activities*	***Almost always** chooses from a restricted range of repetitive activities*
20.		**1**	**2**	**3**

Appendix 16 Responses to Uncertainty and Low Environmental Structure (RULES) Questionnaire

Responses to Uncertainty and Low Environmental Structure (RULES)

For each of the following statements, please rate how well the statement describes your child by selecting among one of five responses and circling the number corresponding to that response.

1. My child gets tense when unexpected events or transitions occur in his/her environment.

1	2	3	4	5
Not at all		Somewhat		Very much

2. My child has a hard time coping with even minor changes.

1	2	3	4	5
Not at all		Somewhat		Very much

3. My child says, "It is unfair" when he/she cannot know what will happen next.

1	2	3	4	5
Not at all		Somewhat		Very much

4. My child always wants to know ahead of the time what the plan is.

1	2	3	4	5
Not at all		Somewhat		Very much

5. My child becomes upset if he/she has to enter a new situation.

1	2	3	4	5
Not at all		Somewhat		Very much

6. My child seeks reassurance prior to entering an unfamiliar situation.

1	2	3	4	5
Not at all		Somewhat		Very much

7. My child cries when he/she finds him/herself in an unfamiliar situation.

1	2	3	4	5
Not at all		Somewhat		Very much

8. My child gets down on himself if he does not know what will happen next.

1	2	3	4	5

9. My child performs best in highly structured environments.

1	2	3	4	5
Not at all		Somewhat		Very much

10. My child tantrums when an unexpected event occurs.

1	2	3	4	5
Not at all		Somewhat		Very much

11. My child avoids unstructured situations.

1	2	3	4	5
Not at all		Somewhat		Very much

12. My child cannot relax if he/she does not know what will happen next.

1	2	3	4	5
Not at all		Somewhat		Very much

13. My child cannot sleep if he anticipates an upcoming change.

1	2	3	4	5
Not at all		Somewhat		Very much

14. My child becomes fidgety during transitions.

1	2	3	4	5
Not at all		Somewhat		Very much

15. My child freezes up in the face of unexpected events.

1	2	3	4	5
Not at all		Somewhat		Very much

16. Transitions are difficult for my child.

1	2	3	4	5
Not at all		Somewhat		Very much

17. My child complains of physical symptoms (e.g., headaches, stomachaches) when he/she is about to enter a new situation.

1	2	3	4	5
Not at all		Somewhat		Very much

Appendix 17 Health Questionnaire

Health Questionnaire

Instructions:

- Have these medical problems affected the person you care for in the past **MONTH**
- Please rate as **0** – if your child has not been affected by this problem in the past month, **1** - if they have been mildly affected, **2** – if the problem has moderately affected your child and **3** - if your child has been severely affected by the problem.

	No	**Mild**	**Mod-erate**	**Se v-ere**
1. Eye Problems (e.g. glaucoma / blocked tear duct/s).....	**0**	**1**	**2**	**3**
2. Ear Problems (e.g. infections, glue ear).....	**0**	**1**	**2**	**3**
3. Dental Problems (e.g. toothache / gum problems / mouth ulcers / delayed eruption of teeth).....	**0**	**1**	**2**	**3**
4. Cleft Palate.....	**0**	**1**	**2**	**3**
5. Gastrointestinal Difficulties (e.g. reflux / stomach problems).....	**0**	**1**	**2**	**3**
6. Bowel Problems (e.g. obstruction).....	**0**	**1**	**2**	**3**
7. Heart Abnormalities or Circulatory Problems (e.g. congenital heart lesions or murmur)……...	**0**	**1**	**2**	**3**
8. Problems with Genitalia (e.g. prostate / testicular problems i.e. undescended testes)...	**0**	**1**	**2**	**3**
9. Hernia (e.g. inguinal or hiatal).....	**0**	**1**	**2**	**3**
10. Limb Abnormalities (e.g. malformed arm).....	**0**	**1**	**2**	**3**
11. Epilepsy / Seizures / Neurological Referrals.....	**0**	**1**	**2**	**3**
12. Lung or Respiratory Problems (asthma / bronchitis).....	**0**	**1**	**2**	**3**

13. Liver or Kidney Problems.....	**0**	**1**	**2**	**3**
14. Diabetes or Thyroid Function Problems.....	**0**	**1**	**2**	**3**
15. Skin Problems (e.g. tinea, eczema, psoriasis, dry skin).....	**0**	**1**	**2**	**3**
16. Other (please specify problem and severity from 0-3) ……..	**0**	**1**	**2**	**3**

Appendix 18 Anxiety Triggers Questionnaire (ATQ)

Anxiety Triggers Questionnaire

Person being assessed ……
Name of person completing form ……
Relation to person ……
Date ……

Anxiety is characterised by feelings of fear and worry about a perceived threat or anticipation about future events. There are many different causes that can trigger anxiety and these can vary from person to person.

A. Please indicate how often the triggers below are involved when the person you care for experiences anxiety. Please do not spend too long thinking about each question.
Please circle the most appropriate option. If you think an item is not applicable to the person you care for, please circle 0 and move onto the next question.
In the **LAST SIX MONTHS**, the person I care for has experienced anxiety related to:

	Never	Rarely	About half of the time	Most of the time	Always
1. Receiving criticism from others	0	1	2	3	4
2. Worries across multiple contexts and situations *(not related to one specific event)*	0	1	2	3	4
3. When other people are upset or cross with someone else	0	1	2	3	4
4. Heights *(e.g. escalators/stairs, being at the top of a tall building)*	0	1	2	3	4
5. Changes to routine *(e.g. unexpected trip to the shops, different route home than usually take)*	0	1	2	3	4
6. Being around people who are unpredictable *(e.g. young children/babies)*	0	1	2	3	4
7. Animals *(e.g. dogs, snakes, birds)*	0	1	2	3	4
8. Anticipation about future events *(e.g. birthday parties, holidays)*	0	1	2	3	4
9. New situations *(e.g. starting a new school/job)*	0	1	2	3	4
10. Visiting the doctor/hospital/dentist	0	1	2	3	4
11. Loud or unexpected noises *(e.g. fireworks)*	0	1	2	3	4
12. When injured or in pain	0	1	2	3	4

13. Getting something wrong *(e.g. giving the wrong answer to a question)*	0	1	2	3	4
14. Others being upset or cross with them	0	1	2	3	4
15. Thunder/lightning	0	1	2	3	4
	Never	Rarely	About half of the time	Most of the time	Always
16. Mechanical noises or noises in the environment *(e.g. vacuum cleaner, car gear changes)*	0	1	2	3	4
17. Using public transport *(e.g. buses, trains)*	0	1	2	3	4
18. Being in unpredictable situations *(e.g. a power cut)*	0	1	2	3	4
19. Social situations *(e.g. talking to groups of others, meeting new people, concern about being judged by others)*	0	1	2	3	4
20. Injections, needles and blood	0	1	2	3	4
21. Crowds	0	1	2	3	4
22. Sensory sensitivities	0	1	2	3	4
23. High demands (*e.g. being given a difficult puzzle or crossword*)	0	1	2	3	4
24. Clowns	0	1	2	3	4

B. How often do the following events increase the likelihood of anxiety occurring for the person you care for?

	Never	Rarely	About half of the time	Most of the time	Always
1. Feeling tired	0	1	2	3	4
2. Experiencing pain or illness	0	1	2	3	4
3. Feeling hungry	0	1	2	3	4
4. Negative mood	0	1	2	3	4

C. List the top 5 triggers of anxiety (A-E) for the person you care for in the table below. This may include triggers not outlined in the above checklist. There are spaces for five triggers, but only fill in as many as relevant. For each trigger, please indicate at which time-point anxiety is presented.

Time-point Key:

Prior to the event: worrying and feeling anxious in the lead up to an event or worrying that an event may happen *(e.g. worrying about an upcoming social event, continual checking of weather forecasts to see if a storm is coming)*

During event: immediate fear response when faced with event *(e.g. becoming extremely anxious when seeing a dog in the park)*

After the event: worrying about events that have occurred for a period of time after the event *(e.g. ruminating for a few hours/days after receiving criticism from another person)*

Circle all the options that apply.

Triggers	Time Point		
	Prior to event	During event	After the event
A.	1	2	3
B. **.....**	1	2	3
C. **.....**	1	2	3
D. **.....**	1	2	3
E. **.....**	1	2	3

Local site logo to be added here

Appendix 19 Chapter three information sheet

Interview study: Understanding emotional well-being and distress in people with learning disabilities

Please read this information carefully before deciding whether you wish to take part in the study. If you have any further questions or would like a verbal explanation of this research study, please contact Dr Jane Waite (Lead Researcher) on 0121 204 4307 or j.waite@aston.ac.uk.

When you have decided whether you/ the person you care for would like to take part in the study, please [complete the enclosed consent forms and return them to us in the prepaid envelope provided/click next below to complete the consent forms]. Please note, if you are returning consent forms to the research team whilst social distancing measures are in place, there may be some delay in getting back to you whilst the team have restricted access to research offices (to be removed once social distancing is lifted).

Background

We would like to invite you to take part in an interview study being conducted by researchers from Aston University, the Cerebra Centre for Neurodevelopmental Disorders, at the University of Birmingham, and Coventry University. This research work, being led by Dr Jane Waite and Prof Chris Oliver, focuses on the development of an assessment tool that can be used in clinical practice to measure emotional well-being and distress. We know that the current assessments for emotional distress is currently under recognised in people with learning disabilities, so we hope that the current research will improve the identification of these difficulties.

Aims of the study

The study aims to develop an effective clinical assessment tool for emotional well-being and distress for use within NHS settings. The research team is aiming to recruit 400 parents and carers so that they can further develop the assessment tool.

What will happen if you/ the person you care for decide(s) to participate?

Why have you been chosen?

You have been approached about this study because you are a parent or carer of a person with a learning disability. We are interested in your responses on this questionnaire because we are aware that your child/person you care for may experience communication difficulties that may make it harder for clinicians and professionals to detect when your child is experiencing distress. We feel we can learn from your responses to help us develop better assessment tools for people with learning disabilities.

Where will the research take place?
You can complete the study at a location and time convenient to you.

What will you be required to do in the study?
You will be asked to complete some consent forms and then take part in a questionnaire study that will ask questions about behaviours and emotions you observe in the person you care for. You can complete this online or request a paper copy. If possible, we would also ask you to ask a second person who knows your child well (such as a partner, or support worker) to complete the questionnaire about your child too. However, if you are unable to ask a second person to complete the questionnaire that's OK.

Who will be involved in collecting and analysing the data?
Members of the research team at Aston University and the University of Birmingham.

How long will participation in the study take?
Taking part in the study will take approximately 60 minutes at your convenience. You don't have to complete the questionnaire in one go as you can save your answers as you go along and take a break.

We will be collecting information from participants between September 2019 and September 2021. We will spend some time understanding the information we have collected and writing reports. This means that the questionnaire study will be finished in September 2023.

Are there any risks that individuals taking part in the study might face?
We will be asking you to think about times when the person you care for may feel distressed. This can sometimes be upsetting for parents and carers.

Your decision to participate in this study will not impact your right to access services.

As this is an online survey you will be asked to type your name and contact details onto the online consent forms. The online survey is created through 'Qualtrics' and hosted on highly secure servers that complies with General Data Protect Regulations. However, as with all online activity, there is a risk that unauthorised individuals (hackers) may access data. If you are uncomfortable with this risk, or simply would prefer a paper copy of the questionnaires, please contact the research team who can put one in the post to you.

What are the potential benefits for participants from taking part?

You will receive a £5 online voucher in return for your completed participation. We are unable to give vouchers for partially completed questionnaires and only one voucher will be given per family (e.g. if a partner or support worker also completes the survey, you will not receive another £5 voucher). We will contact you soon after you have completed your survey to issue your voucher. You will also receive a personalised feedback regarding your child/ the person you care for. This study will help us to find out more about the lives of people with learning disabilities and the difficulties people face. The results may lead to the development of more effective assessment tools to help identify emotional distress earlier on.

Where will data be stored?
All data will be stored on highly secure servers for up to one month once you have entered it onto the online survey (Qualtrics). Data will then be downloaded and stored at Aston University.

A code will be attached to the data you provide to maintain confidentiality. Your personal data (name and contact details) will only be used to arrange study visits or collect data by phone. Analysis of your data will be undertaken using coded data.

The data we collect will be stored in a secure document store (paper records) at Aston University, or electronically on an Aston University password protected computer server or secure cloud storage device.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

Personal identifying information will be treated as strictly confidential and handled in accordance with the provisions of the General Data Protection Regulation (see Appendix A). Anonymised data, that cannot be linked to you, will be shared with Prof Chris Oliver's research team at the University of Birmingham.

If you/ the person you care for decide(s) to participate, what will happen after that participation?

You and your child/person you care for will receive an individual feedback report describing the results of the assessments. We will also send a copy of the feedback to your child's/person you care for's GP. If requested, we can give this report to other interested individuals who you tell us about. [We will also send you information about Prof Chris Oliver's participant database that you may want to join (optional)].

Research findings will be published in newsletters of the support groups and educational institutions, and in scientific journals. Data will also be included in student dissertations. The findings will also be presented at relevant conferences. Data published and presented will not be linked to you as all identifying information will have been removed.

Sometimes after you have participated, the results may suggest to us that it would be useful for us to find out more information to make sure the overall results of the

study are as useful as possible. If this happens, we would contact you before the end of the study to ask if you would be willing to provide extra information.

Any request for advice concerning the participant will be passed on to Dr Jane Waite (a Clinical Psychologist), who will sign-post you to support.

What will happen to the data afterwards?

Aston University is organising this study and is acting as data controller for the study. Aston University will keep identifiable information about you for six years after the study has finished. You can find out more about how we use your information in Appendix A [Link to Appendix A].

It is often important to find out how things change over time. By keeping your details we would be able to trace the results of the previous assessments that you have done with us back to you. This means that if you take part in other studies with us we would be able to look at how things have changed over time.

Who would have access to my details?
Only approved members of Dr Waite's research team would have access to your details. Your details would not be shared by with anyone outside the research team.

When would I be contacted?
You would only be contacted by an approved member of the research team when we are starting another study or phase of a study that we think you might like to participate in or when we need to clarify some information that you have provided us with from participation in a research study.

What happens if I decide that I want my details to be added to the database but then I change my mind?
All you would need to do is contact Dr Jane Waite at j.waite@aston.ac.uk or at the School of Life and Health Sciences at the University of Aston, Aston Triangle, Birmingham, B4 7ET. Your details would be removed from the database immediately.

Confidentiality
The confidentiality of participants will be ensured. However, in line with the University's Child Protection Procedures, the researchers have a duty to disclose any concerns about the welfare of children or young people to the University's Child Protection Officer. At this point, confidentiality may be broken to ensure safety of the child and those around them.

As part of the study we will write to your GP and your child's/person you care for's GP to notify them that you are both taking part in the study. We will write to your child's GP during the study if we have concerns that your child may be experiencing a mental health difficulty. We will write to your GP if we were concerned that you were experiencing a mental health difficulty and we would encourage you to make a follow-up appointment with them.

Withdrawal
Even after consent has been granted, you can request to be withdrawn from the study and for your research data to be destroyed at any time. However, once anonymised data, which cannot be linked to you, is published in academic papers, we will not be able to remove this data.

What if I have a concern about my participation in the study?

If you have any concerns about your participation in this study, please speak to the research team and they will do their best to answer your questions. Contact details can be found at the end of this information sheet.

If the research team are unable to address your concerns or you wish to make a complaint about how the study is being conducted you should contact the Aston University Research Integrity Office at research_governance@aston.ac.uk or telephone 0121 204 3000.

You can also discuss any concerns with the Patient Advice and Liaison Service (PALS) at Birmingham Children's Hospital (0121 333 8403; bwc.pals@nhs.net).

Review
This project has received a favourable opinion by Wales REC 3 Research Ethics Committee.

Further information
If you would like any more information about the study please contact Dr Jane Waite on (0121 204 4307, j.waite@aston.ac.uk) or [insert name and contact details of research assistant at Aston University].

You can also seek independent advice regarding taking part in research by contacting the Patient Advice and Liaison Service (PALS) at (insert site specific PALS information here).

Appendix A: Transparency Statement

Aston University takes its obligations under data and privacy law seriously and complies with the General Data Protection Regulation ("GDPR") and the Data Protection Act 2018 ("DPA").

Aston University is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study. Aston University will process your personal data in order to register you as a participant and to manage your participation in the study. It will process your personal data on the grounds that it is necessary for the performance of a task carried out in the public interest (GDPR Article 6(1)(e). Aston University may process special categories of data about you which includes details about your health. Aston University will process this data on the grounds that it is necessary for statistical or research purposes (GDPR Article 9(2)(j)). Aston University will keep identifiable information about you for 6 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

You can find out more about how we use your information at www.aston.ac.uk/dataprotection or by contacting our Data Protection Officer at dp_officer@aston.ac.uk.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

IMPORTANT:

You need to decide whether your child/the person you care for can understand enough about the study to make an 'informed' decision independently about whether they would like to participate and to communicate this decision to you. If you are unsure whether your child/person you care for can understand enough to decide independently then we can provide you with some guidelines to help you to assess this. We can also provide you with a picture information sheet, if you feel this is appropriate for your child, or materials to support communicating information about the study to your child/person you care for. Please contact the research team if you would like to request this. Please contact Dr Jane Waite 0121 414 4307 or j.waite@aston.ac.uk to request a copy of this.

[This page will either be provided to individuals in the paper copy of the questionnaire to help individuals locate the correct consent form or will be a bridging page between the information sheets and consent forms in the online study. For the online study the options will be changed to a tick box format to allow the participant to select the option that is most appropriate for their child and be directed to the correct consent forms. Please note that while three potential options are described below, where the age of the participant is known at the point of recruitment, only two options will be provided to make this easier for families to understand].

Please choose from one of the following options:

1. My child/ the person I care for is able to understand what is involved in the study and what will be required from them if they participate and has communicated their decision to me:

If you think that the person is ***is* able** to understand enough about the study in order to make an 'informed' decision and they decide that they would like to participate then please complete **Section 1 of Consent Form A coloured YELLOW** enclosed, or that you complete it with them, on their behalf. A parent/carer will need to complete **Section 2 of Consent From A coloured YELLOW** to indicate that they also agree to participate in the study.

2. My child/ the person I care for is under 16 and cannot understand what is involved in the study and what will be required from them if they participate and has communicated their decision to me:

If you are reading this information on behalf of someone you care for who is **under the age of 16** and you decide that the person ***is not*** able to make an 'informed' decision about whether or not they would like to participate, please complete **Consent Form B coloured GREEN.**

3. My child/ the person I care for is over the age of 16 and cannot understand what is involved in the study or cannot communicate their decision to me:

If you are reading this information on behalf of someone you care for who is **over the age of 16** and you decide that the person ***is not*** able to make an 'informed' decision about whether or not they would like to participate, then we would like to invite you to act as a 'personal consultee' (or 'nominated consultee' where an unpaid carer e.g. parent, legal guardian etc is not able to act as a 'personal consultee') for that person. Please read the enclosed 'Personal and Nominated Consultee Information Sheet' coloured **PINK**. Once you have finished reading the 'Personal and Nominated Consultee Information Sheet' please decide whether you feel able to act as a personal or nominated consultee for the person you care for.

If you decide that the person would decide to participate, please complete **Consent Form *C* coloured BLUE** enclosed and return it to us alongside the questionnaire pack in the prepaid envelope provided.

Appendix 20 Chapter three consent form for individuals with capacity to consent

Consent Form A : For [children and adults] with intellectual disabilities who are able to provide [assent/consent] to participate in the study

Questionnaire study: Understanding emotional well-being and distress in people with learning disabilities

SECTION 1: Please complete this section if you are a person with a learning disability. If needed, your parent and carer can read this form to you and you can let them know your answers.

Please circle

1. Has somebody else explained the project to you? YES/NO
2. Do you understand what the project is about? YES/NO
3. Have you asked all of the questions you want? YES/NO
4. Have you had your questions answered in a way you understand? YES/NO
5. If your Dr sees your results is that OK? YES/NO
6. Do you understand it is OK to stop taking part at any time? YES/NO
7. Are you happy to take part? YES/NO

If any answers are 'no' or you don't want to take part, don't sign your name!

If you do want to take part, you can write your name below.

You can also choose if you want to say 'yes' to these questions:

8. If another person who looks after my health asks to see your results is that OK?

   YES/NO

9. Are you happy for us to contact you again in the future?

   YES/NO

Your name:_____

Date:_____

The person who explained this project to you needs to sign too. If you are under the age of 16, this should be your parent/guardian.

Print name:_____ Sign: [paper versions only]:
_____

Date:_____

SECTION 2: Please complete this section if you are a parent/carer/guardian of a person with a learning disability who has provided their assent/consent to participate in the study.

Please initial box for 'yes'

1. I confirm that I have read and understand the information sheet (Version 7 dated 20.04.2021) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation and that of my child/person I care for is voluntary and that I am free to withdraw at any time without giving any reason, without my or that of my child's/person I care for's legal rights being affected. ☐

3. I understand that data will be temporarily stored on highly secure servers at Aston University; however, as with all online activity there is a small risk of unauthorised access to my data (hackers). I am comfortable with this risk. ☐

4. I understand that the feedback report from this study will also be shared with my child's/person I care for's GP. ☐

5. I agree to take part in the above study. ☐

Optional clause: The statement below is optional: Please initial 'yes' or 'no'

	YES	NO
1. I agree to the research team sharing his/her research data with an professionals or clinicians working with them should they request to see them.	☐	☐
2. I agree to be contacted about the next stage of this research project t consider whether I would like to take part.	☐	☐

3. I agree to my personal data being processed for the purposes of inviting me

   to participate in future research projects. I understand that I may opt out of receiving these invitations at any time

Print Name: _____ Telephone number: _____

Address: _____Email: _____

Relationship to participant:_____ Signature [paper versions only]: _____

Date: _____

FOR OFFICE USE ONLY (do not complete if you are a participant) [paper copies]

Name of person receiving consent:_____

Role within the study team:_____ Signature: _____

Date:_____

Appendix 21 Chapter three consent form for individuals aged 16 years or older without capacity to consent

Consent Form C(a): For a personal/nominated consultee of a person over the age of 16 who is not able to provide consent.

Questionnaire Study: Understanding emotional well-being and distress in people with learning disabilities

Before deciding whether to participate, please ensure you read the information on acting as a personal consultee in the (attached document/link) for the person you care for.

SECTION 1: Please read the following statements:
Please initial box for 'yes'

1. I have been consulted about (name of participant) _____'s participation in the above research project. I confirm that I have read and understand the information sheet (Version 7 dated 20.04.2021) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. In my opinion he/she would have no objection to taking part in the above study ☐
3. I understand that I can request he/she is withdrawn from the study at any time without giving any reason and without his/her legal rights being affected. I understand that I can also withdraw my participation at any time without giving a reason and without my legal rights being affected. ☐
4. I understand that data will be temporarily stored on highly secure servers at Aston University; however, as with all online activity there is a small risk of unauthorised access to my data (hackers). I am comfortable with this risk. ☐
5. I understand that the feedback report arising from this study will be shared with the GP of the person for whom I am acting as consultee. ☐
6. I agree to take part in the above study. ☐

Optional clause: The statement below is optional:

Please initial 'yes' or 'no'

	YES	NO
4. I agree to the research team sharing his/her research data with any professionals or clinicians working with them should they request to see them.	☐	☐
5. I agree to be contacted about the next stage of this research project to consider whether the person for whom I am acting as consultee would like to take part.	☐	☐
6. I agree to my personal data being processed for the purposes of inviting me to participate in future research projects. I understand that I may opt out of receiving these invitations at any time.	☐	☐

Print Name: _____

Telephone number:_____ Mobile number (optional):_____

Address:_____Email: _____

Relationship to participant _____Signature [paper versions only]: _____

Date: _____

FOR OFFICE USE ONLY (do not complete if you are a participant) [paper copies]

Name of person receiving consent:_____

Role within the study team:_____ Signature: _____

Date:_____

Appendix 22 Chapter three consent form for individuals under 16 years old

Consent Form A : For parents/carers whose child is under the age of 16 and is not able to make an informed decision about participation in the study.

Questionnaire study: Understanding emotional well-being and distress in people with learning disabilities

Please initial box for 'yes'

6. I confirm that I have read and understand the information sheet (Version 7 dated 20.04.2021) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

7. I confirm that my child is not able to understand the all the information needed to decide about participating in this study, but that I have shared as much information as possible with my child about the study. ☐

8. I understand that my participation and that of my child/person I care for is voluntary and that I am free to withdraw at any time without giving any reason, without my or that of my child's/person I care for's legal rights being affected. ☐

9. I understand that data will be temporarily stored on highly secure servers at Aston University; however, as with all online activity there is a small risk of unauthorised access to my data (hackers). I am comfortable with this risk. ☐

10. I understand that the feedback report arising from this study will also be shared with my child's GP. ☐

11. I agree to take part in the above study. ☐

Optional clause: The statement below is optional:

Please initial 'yes' or 'no'

	YES	NO
7. I agree to the research team sharing his/her research data with any other professionals or clinicians working with them should they request to see them.	☐	☐
8. I agree to be contacted about the next stage of this research project to consider whether I would like to take part.	☐	☐
9. I agree to my personal data being processes for the purposes of inviting me to participate in future research projects. I understand that I may opt out of receiving these invitations at any time.	☐	☐

Print Name: _____
Date:_____

Telephone number: _____Mobile number (optional):_____

Address: _____Email: _____

Relationship to participant:_____ Signature [paper versions only]: _____

Questionnaire study consent form for individuals under 16 years old
Appendix Ze; IRAS ID: 240250
Consent_Under16_NotAble_Q_20.04.2021_V7

FOR OFFICE USE ONLY (do not complete if you are a participant) [paper copies]

Name of person receiving consent:_____

Role within the study team:_____ Signature: _____

Date:_____

Appendix 23 Findings from ATQ broken down by diagnosis

Appendices Table 22 Endorsement of anxiety triggers across diagnoses - most highly endorsed within diagnosis highlighted in **bold**.

Anxiety Triggers Questionnaire item	ASD *n* (%)	AS	Cd LS	CdC S	FX S	DS	TS C	KS	PW S	PTL S	P T H S	SYNG AP1	ID	P K S	PMS	LS	RTS
Receiving criticism from others	9 (24)	4 (10)	2 (12)	1 (11)	3 (30)	1 (14)	1 (25)	0 (0)	1 (25)	3 (75)	1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Worries across multiple contexts and situations	19 (50)	3 (8)	3 (18)	3 (33)	4 (40)	1 (14)	0 (0)	1 (20)	2 (50)	2 (50)	1 (50)	0 (0)	0 (0)	0 (0)	**2 (67)**	**1 (100)**	**1 (100)**
When other people are upset or cross with someone else	20 (53)	18 (46)	6 (35)	3 (33)	6 (60)	3 (43)	2 (50)	2 (40)	1 (25)	**4 (100)**	1 (50)	1 (50)	1 (25)	0 (0)	**2 (67)**	**1 (100)**	0 (0)
Heights	3 (8)	6 (15)	4 (24)	1 (11)	4 (40)	1 (14)	0 (0)	2 (40)	0 (0)	1 (25)	1 (50)	1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Changes to routine	30 (79)	12 (31)	**11 (65)**	**4 (44)**	4 (40)	3 (43)	2 (50)	**4 (80)**	1 (25)	1 (25)	1 (50)	1 (50)	2 (50)	0 (0)	**2 (67)**	0 (0)	**1 (100)**
Being around people who are unpredictable (young children/babies)	29 (76)	13 (33)	7 (41)	**4 (44)**	5 (50)	**4 (57)**	1 (25)	1 (20)	0 (0)	2 (50)	1 (50)	1 (50)	1 (25)	0 (0)	**2 (67)**	0 (0)	**1 (100)**
Animals	18 (47)	6 (15)	7 (41)	1 (11)	2 (20)	3 (43)	0 (0)	0 (0)	0 (0)	2 (50)	1 (50)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)
Anticipation about future events	11 (29)	4 (10)	7 (41)	3 (33)	5 (50)	2 (29)	1 (25)	3 (60)	2 (50)	2 (50)	1 (50)	**2 (100)**	1 (25)	0 (0)	1 (33)	0 (0)	**1 (100)**

New situations	20 (53)	10 (26)	9 (53)	3 (33)	5 (50)	3 (43)	2 (50)	3 (60)	1 (25)	2 (50)	1 (50)	1 (50)	0 (0)	0 (0)	1 (33)	**1 (100)**	**1 (100)**
Visiting the doctor/hospital	20 (53)	15 (38)	10 (59)	3 (33)	5 (50)	3 (43)	2 (50)	2 (40)	**3 (75)**	2 (50)	1 (50)	**2 (100)**	2 (50)	0 (0)	1 (33)	**1 (100)**	0 (0)
Loud/unexpected noises	28 (74)	8 (21)	9 (53)	3 (33)	6 (60)	2 (29)	**3 (75)**	2 (40)	0 (0)	3 (75)	**2 (100)**	**2 (100)**	**4 (100)**	0 (0)	1 (33)	**1 (100)**	0 (0)
When injured/in pain	18 (47)	15 (38)	7 (41)	3 (33)	2 (20)	3 (43)	1 (25)	3 (60)	2 (50)	1 (25)	**2 (100)**	**2 (100)**	2 (50)	0 (0)	1 (33)	0 (0)	**1 (100)**
Getting something wrong	6 (16)	2 (5)	2 (12)	1 (11)	1 (10)	0 (0)	1 (25)	2 (40)	1 (25)	2 (50)	1 (50)	**2 (100)**	1 (25)	0 (0)	1 (33)	**1 (100)**	0 (0)
Others being upset/cross with them	18 (47)	**20 (51)**	5 (29)	3 (33)	5 (50)	1 (14)	1 (25)	2 (40)	1 (25)	2 (50)	**2 (100)**	1 (50)	2 (50)	0 (0)	**2 (67)**	**1 (100)**	**1 (100)**
Thunder/lightening	7 (18)	6 (15)	3 (18)	3 (33)	1 (10)	0 (0)	2 (50)	1 (20)	2 (50)	1 (25)	1 (50)	1 (50)	2 (50)	0 (0)	0 (0)	**1 (100)**	0 (0)
Mechanical noises/noises in the environment	19 (50)	3 (8)	6 (35)	2 (22)	1 (10)	0 (0)	0 (0)	2 (40)	0 (0)	2 (50)	1 (50)	**2 (100)**	2 (50)	0 (0)	0 (0)	**1 (100)**	0 (0)
Using public transport	14 (37)	4 (10)	6 (35)	1 (11)	3 (30)	1 (14)	0 (0)	1 (20)	0 (0)	2 (50)	1 (50)	**2 (100)**	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)
Being in unpredictable situations	17 (45)	7 (18)	6 (35)	3 (33)	4 (40)	1 (14)	2 (50)	3 (60)	2 (50)	2 (50)	1 (50)	1 (50)	1 (25)	0 (0)	1 (33)	**1 (100)**	**1 (100)**
Social situations	18 (47)	8 (21)	6 (35)	2 (22)	6 (60)	1 (14)	1 (25)	1 (20)	1 (25)	2 (50)	1 (50)	**2 (100)**	0 (0)	0 (0)	1 (33)	0 (0)	0 (0)

Appendix Twenty-Three. *Findings from ATQ broken down by diagnosis*

Injections, needles, blood	17 (45)	17 (44)	8 (47)	3 (33)	3 (30)	3 (43)	**3 (75)**	2 (40)	1 (25)	3 (75)	1 (50)	1 (50)	3 (75)	0 (0)	0 (0)	0 (0)	**1 (100)**
Crowds	29 (76)	16 (41)	**11 (65)**	2 (22)	**7 (70)**	**4 (57)**	2 (50)	3 (60)	1 (25)	2 (50)	1 (50)	**2 (100)**	1 (25)	0 (0)	1 (33)	0 (0)	0 (0)
Sensory sensitivities	**32 (84)**	10 (26)	8 (47)	1 (11)	6 (60)	3 (43)	0 (0)	3 (60)	1 (25)	2 (50)	1 (50)	1 (50)	2 (50)	0 (0)	1 (33)	**1 (100)**	0 (0)
High demands	18 (47)	8 (21)	5 (29)	0 (0)	5 (50)	3 (43)	0 (0)	3 (60)	1 (25)	2 (50)	1 (50)	1 (50)	1 (25)	0 (0)	1 (33)	**1 (100)**	**1 (100)**
Clowns	0 (0)	2 (5)	2 (12)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	1 (50)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)

Anxiety Triggers Questionnaire item	Del5	CHAMP1	Lissencephaly	Global delay and LD	Global delay and atypical ASD	MEF2C	CP	DS, ES and ASD	CdCS and 8q+	SS	CDLK5	No reported diagnosis
Receiving criticism from others	**1 (100)**	0 (0)	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Worries across multiple contexts and situations	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
When other people are upset or cross with someone else	**1 (100)**	**1 (100)**	0 (0)	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	**1 (100)**	0 (0)	0 (0)
Heights	**1 (100)**	0 (0)	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Changes to routine	**1 (100)**	**1 (100)**	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	0 (0)	**1 (100)**
Being around people who are unpredictable (young children/babies)	**1 (100)**	0 (0)	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Animals	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Anticipation about future events	0 (0)	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)
New situations	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	0 (0)	0 (0)	**1 (100)**	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)

Appendix Twenty-Three. *Findings from ATQ broken down by diagnosis*

Visiting the doctor/hospital	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	0 (0)	0 (0)	**1 (100)**	0 (0)	0 (0)	**1 (100)**	0 (0)	0 (0)
Loud/unexpected noises	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	0 (0)	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	**1 (100)**
When injured/in pain	**1 (100)**	0 (0)	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	**1 (100)**	**1 (100)**	0 (0)	0 (0)
Getting something wrong	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Others being upset/cross with them	**1 (100)**	**1 (100)**	0 (0)	0 (0)	**1 (100)**	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Thunder/lightening	0 (0)	**1 (100)**	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mechanical noises/noises in the environment	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Using public transport	**1 (100)**	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Being in unpredictable situations	**1 (100)**	**1 (100)**	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)
Social situations	**1 (100)**	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)
Injections, needles, blood	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	**1 (100)**	0 (0)	**1 (100)**	0 (0)	0 (0)	0 (0)
Crowds	**1 (100)**	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Appendix Twenty-Three. *Findings from ATQ broken down by diagnosis*

Sensory sensitivities	**1 (100)**	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
High demands	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Clowns	**1 (100)**	**1 (100)**	**1 (100)**	**1 (100)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Appendix 24 Findings from Principal Component Analysis

Principal Component Analysis: Anxiety Triggers Questionnaire

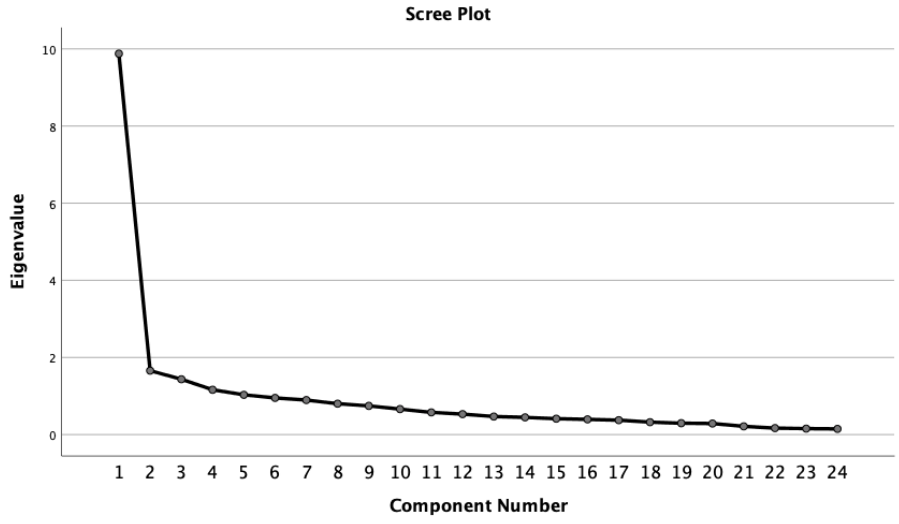
A principal component analysis (PCA) was conducted on the items of the Anxiety Triggers Questionnaire (ATQ) to explore whether there were clusters of triggers that grouped together, reducing the items into a smaller set of constructs. This is an appropriate method of analysis when findings may be used to perform further analysis such as multiple regression analyses. The PCA was conducted to see if subscales of items could become the dependent variables of the regression analyses conducted in Chapter three. Specific correlates of anxiety could then be explored to see if they predicted the different proposed clusters of triggers.

Firstly, correlations between items were explored. One item showed correlations $r<0.3$, indicating that this particular item is measuring something different to other items and so was removed from subsequent analysis. Sample adequacy was explored utilising the Kaiser-Meyer-Olkin (KMO) measure, resulting in a value of 0.897 [classified as meritorious; Kaiser (1974)], indicating good linear relationships between variables and that PCA may be useful. Bartlett's test of sphericity identified a statistically significant result ($p<.001$), indicating that the data was suitable for a PCA. For the researcher's data, independence between components could not be assumed and so the obliquely rotated solution was chosen as a more reasonable representation of reality.

When choosing components to retain in the analysis, Eigenvalues, variance explained, and a scree plot were considered.

If the eigenvalue-one criterion was followed (Kaiser, 1960), five components would be extracted.

If the proportion of variance was considered based on the suggestion that a component is only retained if it explains at least 5-10% of total variance, four components would be extracted or four-seven components if the cut-off was 60-70% for cumulative variance. If the scree plot (Cattell, 1966) was considered, one component would be extracted (see below). Due to the arbitrary cut-offs and discrepancy across different extraction criteria, exploratory analysis was run to explore the impact of different numbers of components as subscales for the regression analyses. The concepts of "simple and complex structure" were considered, complex structure was observed due to many components loading onto the same individual variables. Therefore, it was concluded that the final rotated solution did not make theoretical sense and it was decided that a single total score for the ATQ would be appropriate to use as a dependent variable in subsequent regression analyses, as consistent with the findings from the scree plot below.



Appendix Twenty-Five.

Invitation letter for interview study

The Cerebra Centre for Neurodevelopmental Disorders
UNIVERSITY OF BIRMINGHAM

Appendix 25 Chapter four invitation letter

Dear **[insert name of parent],**

A new research project is being carried out at Aston University, in partnership with the Cerebra Centre for Neurodevelopmental Disorders at the University of Birmingham, Coventry University and Birmingham Women's and Children's Hospital.

The research is an interview study looking at emotion and behaviour in children and adults with **neurodevelopmental disorders, such as [insert syndrome/diagnosis if appropriate].** The research team are hoping to speak with parents and carers about the behaviours their child shows when their child is experiencing anxiety or distress.

This research is being carried out to inform the development of a new assessment tool to measure emotional well-being and distress in people with learning disabilities. It is hoped that this tool will be used when children are seen by health professionals in the NHS. In the future, this assessment tool may improve care for individuals with learning disabilities, particularly individuals who have communication difficulties.

If you and your child/person you care for would like to learn more about the new study and decide whether you would like to take part, the information sheets and questionnaire can be accessed and completed online (see back of this letter for details). Alternatively, you can request the information sheet and a paper copy of the questionnaire from the lead researcher, Dr Jane Waite, at Aston University (see enclosed expression of interest form for details).

When the research team have analysed the information you send to them, they will provide you with personalised feedback about the person you care for.

If you are unclear about any aspect of the study or have any questions then contact Dr Jane Waite at Aston University, 0121 204 4307; j.waite@aston.ac.uk.

Thank you for your time and we look forward to hearing from you.

[signature removed]

The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.Bham.ac.uk **E-mail**: cndd-enquiries@contacts.bham.ac.uk **Phone**: 0121 414 7206

Appendix Twenty-Five.

Invitation letter for interview study

The Cerebra Centre for Neurodevelopmental Disorders
UNIVERSITY OF BIRMINGHAM

Chris Oliver
Professor of Neurodevelopmental Disorders

Instructions for taking part online

Important information before you find out more about this study:

The information sheet for this study will be provided when you visit the link below. Please read this information sheet before deciding whether you would like to take part. The information sheet will provide details about how the research team protect your data, as well as other important information about the study.

To access the information sheets and complete the consent forms online go to:

[insert link]

Password to access survey: CHealth21

ID number: XXXX

[insert participants ID number]

Thank you for your support!

If you would rather request a paper copy of the forms, complete the expression of interest form that is enclosed with this letter and return it to Dr Waite at Aston University.

Please note that while we will endeavour to speak with all families who express an interest in participating, the study will close once maximum participation is reached.

The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.Bham.ac.uk **E-mail**: cndd-enquiries@contacts.bham.ac.uk **Phone**: 0121 414 7206

Appendix 26 Chapter four information sheet

Interview study: Understanding emotional well-being and distress in people with learning disabilities

Please read this information carefully before deciding whether you wish to take part in the study. If you have any further questions or would like a verbal explanation of this research study, please contact Dr Jane Waite (Lead Researcher) on 0121 204 4307 or j.waite@aston.ac.uk.

When you are happy that you have the information to be able to decide whether you/the person you care for would like to take part in the study, please [complete the enclosed consent forms and return them to us in the prepaid envelope provided] or [click next below to complete the consent forms].

Background

We would like to invite you to take part in an interview study being conducted by researchers from Aston University, the Cerebra Centre for Neurodevelopmental Disorders, at the University of Birmingham, and Coventry University. This research work, being led by Dr Jane Waite and Prof Chris Oliver, focuses on the development of an assessment tool that can be used in clinical practice to identify children with learning disabilities who are experiencing anxiety. We hope that this research will improve the identification and treatment of anxiety.

Aims of the study

The study aims to develop an effective clinical assessment tool for anxiety in people with learning disabilities, for use within NHS settings. The research team would like to conduct interviews with parents and carers to help develop this tool.

What will happen if you/ the person you care for decide(s) to participate?

Why have I been chosen?
You have been chosen to take part in this study because the records held by [insert organisation] indicate that you are the parent or carer of a person with a learning disability, and that the person you care for may experience anxiety. We are hoping to speak with around 30 parents of children who experience worry or anxiety.

Where will the research take place?
The research will take place over the telephone at a time that is convenient for you.

How long will participation in the study take?
Taking part in the study will take no longer than 1.5 hours over the telephone at your convenience. This can be broken into two separate calls if you would prefer.

We will be collecting information from participants between April 2018 and August 2018. After this we will spend some time understanding the information we have collected and writing reports. This means that the interview study will be finished in August 2019.

Who will be involved in collecting and analysing the data?
Members of the research team at Aston University and the University of Birmingham.

What will you be required to do in the study?
You will be asked to take part in an interview that will be conducted by researchers over the phone. We would like to discuss the behaviour of your child/person you care for, including behaviours they might show when they are worried or anxious. We will ask you questions to guide the interview and would require you to provide short answers.

Will assessments/interviews be recorded?
During the interview the interviewer's questions and your responses will be audio recorded, if you are comfortable with this. Aston University will hold the copyright for the audio recordings so that the confidentiality of these recordings will be protected. Aston University cannot edit or copy these recordings without your permission.

Are there any risks that individuals taking part in the study might face?
We will be asking you to think about times when your child/the person you care for may feel distressed. This can sometimes be upsetting for parents and carers.

Your decision to participate in this study will not impact your right to access services.

What are the potential benefits for participants from taking part?
You will receive a personalised feedback regarding your child/the person you care for. This study will help us to find out more about the lives of people with neurodevelopmental disorders and the difficulties that these people face. The results may lead to the development of more effective assessment tools to help identify difficulties earlier on.

Where will data be stored?

All electronic personal data (i.e. your name, address etc.) will be kept on a password protected hard-drive in locked cabinets in Dr Jane Waite's research lab. Paper copies consent forms will be stored in a locked cabinet.

The audio recordings are considered to contain personal identifying information. We will therefore store the recordings separately to other information we have collected about you (e.g. your full names, your address, your contact details). These recordings will not be labelled with your names or any other personal identifying information but will be labelled with your special reference number.

We will store anonymised data taken from the interview recordings separately from your personal data (e.g. name/address) and interview recordings, and these data will only be able to be linked via a unique code. Anonymised data will stored in locked cabinets in Dr Jane Waite's research lab and will be shared with Prof Chris Oliver's research team at the University of Birmingham. Personal identifying information will be treated as strictly confidential and handled in accordance with the provisions of the General Data Protection Regulation.

If you/ the person you care for decide(s) to participate, what will happen after that participation?

You and your child/person you care for will receive an individual feedback report describing the results of the assessments. We will also send a copy of the feedback report to your child's/person you care for's GP. If requested, we can give this report to other interested individuals who you tell us about. [We will also send you information about Prof Chris Oliver's participant database that you may want to join (optional)].

Research findings will be published in newsletters of the support groups and educational institutions, in scientific journals, and as part of student dissertations. The findings will also be presented at relevant conferences. Data published and presented will not be linked to you as all identifying information will have been removed.

Sometimes after you have participated, the results may suggest to us that it would be useful for us to find out more information to make sure the overall results of the study are as useful as possible. If this happens, we would contact you before the end of the study to ask if you would be willing to provide extra information.

Any request for advice concerning the participant will be passed on to Dr Jane Waite who is a Clinical Psychologist, who will sign-post you to support.

What will happen to the data afterwards?

This interview study is part of a much larger study developing a clinical tool for people with intellectual disability. This larger study is ongoing for seven years. Any audio recordings we have made of you will be deleted as soon as the recordings have been transcribed. Anonymised transcripts of the interviews, that cannot be linked to you, will be deleted at the end of the study.

Six months after you have taken part in the study, your personal details that are held at Aston University will be ***destroyed unless you tell us otherwise.*** This means that we would no longer be able to trace the results of your assessments back to you or

provide you with updates about the larger study. ***The section below on 'The Regular Participant Database Information'*** gives information about a database that we use to store the personal details of some participants. Please read this section to decide if you would like to join that database.

Regular Participant Database Information:

What is the regular participant database?
Dr Jane Waite has a database that she keeps at Aston University where she stores the names and contact details of some previous participants. If you would like then we can add your details to this database. Dr Waite would use this information for two things:

1) She will contact you with information about future research work to find out whether you would like to participate.
2) It is often important to find out how things change over time. By keeping your details we would be able to trace the results of the previous assessments that you have done with us back to you. This means that if you take part in other studies with us we would be able to look at how things have changed over time.

Who would have access to my details?
Only approved members of Dr Waite's research team would have access to your details. Your details would not be shared by with anyone outside the research team.

When would I be contacted?
You would only be contacted by an approved member of the research team when we are starting another study or phase of a study that we think you might like to participate in or when we need to clarify some information that you have provided us with from participation in a research study.

What happens if I decide that I want my details to be added to the database but then I change my mind?
All you would need to do is contact Dr Jane Waite or at j.waite@aston.ac.uk or at the School of Life and Health Sciences at the University of Aston, Aston Triangle, Birmingham, B4 7ET. Your details would be removed from the database immediately.

Confidentiality

The confidentiality of participants will be ensured. However, in line with the University's Child Protection Procedures, the experimenters have a duty to disclose any concerns about the welfare of children or young people to Aston University's Child Protection Officer. At this point, confidentiality may be broken to ensure safety of the child and those around them.

As part of the study we will write to your GP and your child's/person you care for's GP to notify them that you are both taking part in the study. We will write to your child's GP during the study if we have concerns that your child may be experiencing a mental health difficulty. We will write to your GP if we were concerned that you were experiencing a mental health difficulty and we would encourage you to make a follow-up appointment with them.

Withdrawal
Even after consent has been granted, you can request to be withdrawn from the study and for your research data to be destroyed at any time. However, once anonymised data, which cannot be linked to you, is published in academic papers, we will not be able to remove this data.

Who do I contact if I wish to make a complaint about the way in which the research is conducted?
If you have any concerns about anything to do with this study, please speak to the research team and we will do our best to answer your questions. Contact details can be found at the end of this information sheet.

If the research team are unable to address your concerns or you wish to make a complaint about how it is being conducted then you should contact the Aston University Director of Governance, Mr John Walter, at j.g.walter@aston.ac.uk or telephone 0121 204 4869.

You can also discuss any concerns with the Patient Advice and Liaison Service (PALS) at Birmingham Children's Hospital (0121 333 8403; bwc.pals@nhs.net).

Review
This project has received a favourable opinion by Wales REC 3 ethics committee.

Further information
If you would like any more information about the study please contact Dr Jane Waite on (0121 204 4307, j.waite@aston.ac.uk) or [insert name and contact details of research assistant at Aston University].

You can also seek independent advice regarding taking part in research by contacting the Patient Advice and Liaison Service (PALS) at Birmingham Children's Hospital (0121 333 8403; bwc.pals@nhs.net).

IMPORTANT:

You need to decide whether your child/the person you care for can understand enough about the study to make an 'informed' decision independently about whether they would like to participate and to communicate this decision to you. If you are unsure whether your child/person you care for can understand enough to decide independently then we can provide you with some guidelines to help you to assess this. We can also provide you with a picture information sheet, if you feel this is appropriate for your child, or materials to support communicating information about the study to your child/person you care for. Please contact the research team if

you would like to request this. Please contact Dr Jane Waite 0121 414 4307 or j.waite@aston.ac.uk **to request a copy of this.**

[This page will either be provided to individuals in the paper copy of the questionnaire to help individuals locate the correct consent form or will be a bridging page between the information sheets and consent forms in the online study. For the online study the options will be changed to a tick box format to allow the participant to select the option that is most appropriate for their child and be directed to the correct consent forms. Please note that while three potential options are described below, where the age of the participant is known at the point of recruitment, only two options will be provided to make this easier for families to understand].

Please choose from one of the following options:

4. My child/ the person I care for is <u>able to understand</u> what is involved in the study and what will be required from them if they participate and has communicated their decision to me:

If you think that the person is ***is* able** to understand enough about the study in order to make an 'informed' decision and they decide that they would like to participate then please complete **Section 1 of <u>Consent Form A coloured YELLOW</u>** enclosed, or that you complete it with them, on their behalf. A parent/carer will need to complete **Section 2 of <u>Consent From A coloured YELLOW</u>** to indicate that they also agree to participate in the study.

5. My child/ the person I care for is <u>under 16</u> and <u>cannot understand</u> what is involved in the study and what will be required from them if they participate and has communicated their decision to me:

If you are reading this information on behalf of someone you care for who is **<u>under the age of 16</u>** and you decide that the person ***<u>is not</u>*** able to make an 'informed' decision about whether or not they would like to participate, please complete **<u>Consent Form B coloured GREEN.</u>**

6. My child/ the person I care for is <u>over the age of 16</u> and <u>cannot understand</u> what is involved in the study or cannot communicate their decision to me:

If you are reading this information on behalf of someone you care for who is **<u>over the age of 16</u>** and you decide that the person ***<u>is not</u>*** able to make an 'informed' decision about whether or not they would like to participate, then we would like to invite you to act as a 'personal consultee' (or 'nominated consultee' where an unpaid carer e.g. parent, legal guardian etc is not able to act as a 'personal consultee') for that person. Please read the enclosed 'Personal and Nominated Consultee Information Sheet' coloured **PINK**. Once you have finished reading the 'Personal and Nominated Consultee Information Sheet' please decide whether you feel able to act as a personal or nominated consultee for the person you care for.

If you decide that the person would decide to participate, please complete **Consent Form *C* coloured BLUE** enclosed and return it to us alongside the questionnaire pack in the prepaid envelope provided.

Aston University

Appendix G
Consent_Able_Interview_15.5.18_V3
IRAS ID: 240250

Appendix 27 Chapter four consent forms

Consent Form A : For [children and adults] with intellectual disabilities who are able to provide [assent/consent] to participate in the study

Interview study: Understanding emotional well-being and distress in people with learning disabilities

SECTION 1: Please complete this section if you are a person with a learning disability. If needed, your parent and carer can read this form to you and you can let them know your answers Please circle

1. Has somebody else explained the project to yo YES/NO
2. Do you understand what the project is about? YES/NO
3. Have you asked all of the questions you want? YES/NO
4. Have you had your questions answered in a way you understand? YES/NO
5. If your Dr sees your results is that OK? YES/NO
6. Do you understand it is OK to stop taking part at any time? YES/NO
7. Are you happy to take part? YES/NO

If any answers are 'no' or you don't want to take part, don't sign your name!

If you do want to take part, you can write your name below.

You can also choose if you want to say 'yes' to these questions:

8. Is it OK for sound recordings to be made during the study? YES/NO
9. If another person who looks after my health asks to see your results is that OK? YES/NO
10. Are you happy for us to contact you again in the future? YES/NO

Your name:_____

Date:_____

Aston University

Appendix G
Consent_Able_Interview_15.5.18_V3
IRAS ID: 240250

The person who explained this project to you needs to sign too. If you are under the age of 16, this should be your parent/guardian.

Print name:_____ Sign: [paper versions only]: _____

Date:_____

SECTION 2: Please complete this section if you are a parent/carer/guardian of a person with a learning disability who has provided their [assent/consent] to participate in the study.

Please initial box for 'yes'

1. I confirm that I have read and understand the information sheet (Version xxxx dated yyyy) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily ☐

2. I understand that my participation and that of my child/person I care for is voluntary and that I am free to withdraw at any time without giving any reason, without my or that of my child's/person I care legal rights being affected. ☐

3. I understand that the feedback report from this study will be shared with my child's/person I care for's GP. ☐

4. I agree to take part in the above study. ☐

Aston University

Appendix G
Consent_Able_Interview_15.5.18_V3
IRAS ID: 240250

Optional clause: The statement below is optional: Initial 'yes' or 'no' **YES** **NO**

1. I understand that as part of the above study, audio recordings of participants may be made and stored for further revie iv permission ☐ ☐
2. for audio recordings to be made and stored.

3. I understand that the Aston University will store any audio recordings collected during the study but that this does not entitle the Aston University to edit, copy or use the recordings for teaching purpose without my written permission. ☐ ☐

4. I agree for my details to be retained on Dr Jane Waite's participar database (Aston University) and I understand that I can request that my details be removed at any time. ☐ ☐

5. I give permission for Aston University to share my results with any other professionals or clinicians working with me and the pers I care for should they request to see them. ☐ ☐

Print Name: _____ Date: _____

Telephone number: _____Mobile number (optional):_____

Address: _____Email: _____

Relationship to participant:_____ Signature [paper versions only]: _____

FOR OFFICE USE ONLY (do not complete if you are a participant) [paper copies]

Name of person receiving consent:_____

Aston University

Appendix G
Consent_Able_Interview_15.5.18_V3
IRAS ID: 240250

Role within the study team:_____ Signature: _____

Date:_____

Aston University

Appendix H
Consent_Over16_Interview_15.5.18_V3
IRAS ID: 240250

Consent Form C(a): For a personal/nominated consultee of a person over the age of 16 who is not able to provide consent.

Interview study: Understanding emotional well-being and distress in people with learning disabilities

Before deciding whether to participate, please ensure you read the information on acting as a personal/nominated consultee in the (attached document/link) for the person you care for.

SECTION 1: Please read the following statements:

Please initial box for 'yes'

1. I have been consulted about (name of participant) _____'s participation in the above research project. I have read and understand the information sheet (Version xxxx dated yyyy) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. In my opinion he/she would have no objection to taking part in the above st ☐
3. I understand that I can request he/she is withdrawn from the study at any time without giving any reason and without his/her legal rights being affected. I understand that I can also withdraw my participation at any time without giving a reason and without my legal rights being affected. ☐
4. I understand that the feedback report from this study will be shared with the GP of the person for whom I am acting as a consultee. ☐
5. I agree to take part in the above study. ☐

Aston University

Appendix H
Consent_Over16_Interview_15.5.18_V3
IRAS ID: 240250

Optional clause: The statement below is optional:

Initial 'yes' or 'no' below **YES NO**

1. I understand that as part of the above study, audio recordings of participants may be made and stored for further review. I give permission for audio recordings to be stored and reviewed. ☐ ☐

2. I understand that the University of Aston will store of any audio recordings collected during the study but that this does not entitle the University of Aston to edit, copy or use the recordings for teaching purposes without my written permission. ☐ ☐

3. I agree to the research team sharing his/her research data with any other professionals or clinicians working with them should they request to see them. ☐ ☐

4. I agree for my details to be retained on Dr Jane Waite's participant database (Aston University) and I understand that I can request that my details be removed at any time. ☐ ☐

Print Name: _____

Telephone number:_____ Mobile number (optional): _____

Address:_____Email: _____

Relationship to participant _____Signature [paper versions only]: _____

Date: _____

FOR OFFICE USE ONLY (do not complete if you are a participant) [paper copies]

Name of person receiving consent:_____

Appendix H
Consent_Over16_Interview_15.5.18_V3
IRAS ID: 240250

Role within the study team:_____ Signature: _____

Date:_____

Aston University

Appendix I.
Consent_Under16_NotAble_Interview_15.5.18_V3
IRAS ID: 240250

<u>Consent Form B:</u> For parents/carers whose child is under the age of 16 and is <u>not</u> able to make an informed decision about participation in the study.

Interview study: Understanding emotional well-being and distress in people with learning disabilities

SECTION 1: Please complete this section if you are a parent/carer of a child (under 16 years) with a learning disability who is not able to provide an informed decision about taking part.

Please initial box for 'yes' (leave blank for 'no')

1. I have read and understand the information sheet (Version 2 dated 18.04.18) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I confirm that my child is not able to understand the all the information needed to decide about participating in this study, but that I have shared as much information as possible with my child about the study. ☐

3. I understand that my participation and that of my child/person I care for is voluntary and that I am free to withdraw at any time without giving any reason, without my or that of my child's/person I care for's legal rights being affected. ☐

4. I understand that the feedback report from this study will be shared with my child's GP. ☐

5. I agree to take part in the above study. ☐

Aston University

Appendix I.
Consent_Under16_NotAble_Interview_15.5.18_V3
IRAS ID: 240250

Optional clause: The statement below is optional: Initial 'yes' or 'no' below

	YES	NO
1. I understand that as part of the above study, audio recordings of participants may be made and stored for further review. I give permission for audio recordings to be made and stored.	☐	☐
2. I understand that the Aston University will store of any audio recordings collected during the study but that this does not entitle the Aston University to edit, copy or use the recordings for teaching purposes without my written permission.	☐	☐
3. I agree to the research team sharing my research data with any professionals or clinicians working with me and the person I care for should they request to see them.	☐	☐
4. I agree for my details to be retained on Dr Jane Waite's participant database (Aston University) and I understand that I can request that my details be removed at any time.	☐	☐

Print Name: _____Name of person you care for: _____

Address:_____Email: _____

Telephone number:_____ Mobile Number (optional):_____

Relationship to participant: _____

Signature : _____Date: _____

FOR OFFICE USE ONLY (do not complete if you are a participant) [paper copies]

Name of person receiving consent:_____

Role within the study team:_____ Signature: _____

Date:_____

Aston University

Appendix R_Consent_Clinician_12.11.17_V1
IRAS ID: 240250

The development of an assessment tool for anxiety and pain in children with neurodevelopmental disorders

Consent Form

Please complete this section if you are a clinician who is providing consent to participate in the study.

Please initial box

1. I confirm that I have read and understand the information sheet (Version 1 dated 12.11.17) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason without my rights being affected. ☐

3. I understand that all information collected during the study will be confidential. Only members of the research team at Aston University will know who has participated in the study. ☐

4. I understand that as part of the above study, voice recordings of participants may be made and stored for further review. ☐

5. I understand that Aston University will hold the copyright of any voice recordings collected during the study but that this does not entitle the University to edit, copy or use these recordings for teaching purposes without my written permission. ☐

6. I agree to take part in the above study. ☐

Print Name: _____

Job Role:_____NHS Site: _____

Email: _____ Telephone number: _____

Signature:_____ Date: _____

FOR OFFICE USE ONLY (do not complete if you are a participant)

Name of person receiving consent:_____

Role within the study team:_____ Signature: _____

Date:_____

Appendix 28 Chapter four parent/carer interview schedule

Anxiety: Bottom-up Interview

Overview: This semi-structured interview has been developed to capture and characterise the nature of anxiety in children and adults with Williams Syndrome. It also has the potential to be adapted for use in the intellectual disability field with other genetic syndromes. It aims to gather information regarding the antecedents of anxiety, behavioural responses and the resulting impact using open-ended questions with parents/carers. The interview has three main sections: general introductory items, items relating to anxiety bursts (Section B) and generalised anxiety items (Section C). The general introductory items are used to determine whether Section B or Section C is more suitable for each individual interview. The purpose of having two separate sections is to tailor the interview to best fit the emotions and behaviours being described by the parent/carer in order to save time and burden on participants whilst collecting the necessary and relevant data efficiently.
If a parent/carer discusses symptoms relating to both anxiety bursts and generalised anxiety in the introductory section, then the full interview including both Section B and Section C will be administered. There is an additional section which contains several items regarding comorbidity between anxiety and depression (Section D). These items should be incorporated within the interview, at an appropriate time within the flow of the discussion, in cases where parents/carers indicate the presence of depressive symptoms and low moods in Section A.
Format of the interview: All participants will be asked questions from Section A and depending on their answers should subsequently be asked questions from Section B, Section C or both. Questions from Section D may also be included where appropriate. The interview is fluid, therefore parent/carers should be encouraged to talk freely and the order and direction of the interview may vary between participants. During the interview, questions which are not deemed relevant may be omitted by the researcher and extra prompts may be added if the researcher considers that further information is necessary. All questions asked should be kept within the guidelines given although the interview will be guided by the participants and the order of questions may be changed to best suit the direction of the interview. Participants will not be subjected to leading questions.

Scoring: There is a separate coding sheet for this interview. Scoring for each question can be found in the right hand column of the scoring sheet. These should be filled out based on the information given by the parent/carer, placing an 'X' in the relevant boxes and giving descriptive answers where spaces have been provided. Further notes can be made in the 'notes' column. Prompts may be given in order to aid the researcher in scoring each item although the scoring categories will not be disclosed to the participant. Further clarification of the scoring categories and other useful information has been provided in the right hand column of the interview. Coding categories have been based on validated and relevant measures in the literature although some have been adapted following the pilot interviews and related feedback. 'Other' categories have been included where relevant in order to ensure important information is not overlooked or missed.
Composite scores will be calculated using Z scores (i.e. an anxiety composite score will be calculated using the frequency, duration and severity scores, coping

behaviour composite score will be calculated using safety and avoidance behaviour scores).
Checklists will also be coded using a ranking system whereby the top 5 (symptoms) and top 3 (impact ratings) most frequently described items will be calculated.

SECTION A

Useful prompt to be used when appropriate: 'can you tell me a little more about that?'

Opening Question	Sub Questions	Information
1. I am interested in any difficult or negative emotions that (X) may experience. Can you tell me about them?	- Are there any other emotions that (X) experiences? - Which one of them do you see as being the most problematic? - Does (X) ever get anxious, worried or apprehensive? - *If yes:* is there a constant level of anxiety or does anxiety occur in bursts whereby the symptoms increases suddenly and then return to normal?	*(If anxiety present: answer Q2 + Q3 if anxiety not present: move to Q4)*
2. Does the onset of anxiety seem to be linked to any triggers or causes? Please list all the possible triggers.	- What do you think are the causes? Have you noticed any patterns? (when anxiety occurs)	*Internal + External* i.e. setting events/common triggers
3. Why do you think that this/these issues may be difficult for (X)?		E.g: dog phobia – is it the dog or the loud noise when a dog barks
4. Does (X) ever suffer from a low mood or feel down and depressed?		
5. Does (X) take any mood related medication? 6. Is (X) involved in any behavioural programmes or interventions?	- Do you think these may impact (X)'s emotions?	

- If parent/carer describes X's anxiety as occurring in bursts, move to **SECTION B.**

- If parent/carer describes X's anxiety as occurring persistently (i.e. no specific triggers/bursts and occurs in multiple contexts/situations), move to **SECTION C.**

SECTION B *Useful prompt to be used when appropriate:* 'can you tell me a little more about that?'		
Opening Question	**Sub Questions**	**Information**
1. Can you describe a recent example or period of time when (X) showed this anxiety?	- What happened? - How *frequently* does this sort of anxiety occur?	
1a. Is this typical for (X)?		*(If yes, answer Q3, if no, move to Q2)*
2. Can you describe a typical example of when (X) shows anxiety?	7. How *frequently*?	
3. How many minutes tend to pass between the start of the anxiety burst and when it reaches its peak/highest point?		
4. How long would you say the entire episode tends to last? (minutes/hours)		
5. How severe would you say the anxiety shown during these events is?	- Are the symptoms very noticeable? - How distressed does (X) become? - Did (X) overcome the anxiety or did it continue for a long period?	**N/A: (0)** **Mild:** only noticeable to family/people who know X very well, slightly distressing but no lasting impact, overcome fairly easily few physical symptoms **(1)** **Moderate:** often noticeably anxious to others (i.e. teachers/friends),

		moderately distressing, often takes time to overcome anxiety feelings, persistent physical symptoms, impacts well-being **(2)** **Severe:** always noticeable to others/strangers, severely distressing continues for long period, interferes with ability to function, severe physical symptoms, often or almost totally unable to overcome **(3)**
6. At what age did (X) begin showing the anxiety?		
7. Did anything happen around the time that the anxiety began to develop?	- Were there any specific triggers or events? - Did it happen gradually over time or suddenly?	
8. Is there a particular time of day when the anxiety is more likely to occur?	- When is the anxiety at its worse? - When is it milder?	
9. Is there anything that (X) does that makes you realise he/she is beginning to feel anxious?	- Are there any warning signs right before the onset of the emotion? - Is there a pattern of behaviour?	*Looking for behaviours/emotions that are expressed*

10. When (X) feels anxious, how do they behave during this time?	- Do you see any physical changes in their body? - Do you see changes in how they moves? - Do you see any changes in their face? - Do you see any changes in their speech pattern? - Do these behaviours occur in an order/sequence? - Do the behaviours that (X) shows differ between events/bursts? Or are the same behaviours always shown?	*(If yes, specify)*
11. What do you think (X) is thinking when they are feeling anxious? Why do you think that?	- What behaviours does (X) show? - What does (X) say to make you think this? - Do you think they are feeling any other emotions?	E.g. feels scared
12. Is there anything (X) does himself/herself that helps reduce their anxiety?	- How often do they use these strategies? - Do they work? How well?	**List all strategies** *Code avoidance strategies and safety strategies separately* -Never -Sometimes: *several times a month* -Often: *several times a week* -Always: *several times a day*

13. Is there anything that you can do that helps to reduce (X)'s anxiety?	- How often do you try using these techniques? - Do these strategies work? How often?	**List three most often used strategies** -Never -Sometimes: *several times a month* -Often: *several times a week* -Always: *several times a day*
14. What happens if the strategies that help are not available?	- How long does this response go on for?	*List of behaviours* Example: if you do not give reassurance (duration in minutes)
15. How does the anxiety affect (X) day to day?	- What is the biggest impact it has? - How severely would you say this impacts (X)?	**<u>Q17/Q18</u>** (e.g. Peers/family relationships, In the home, outside of the home) **N/A (0)** **Mild:** Slight impact on relationships, home life, outside home life **(1)** **Moderate:** Clear interference, withdrawal from normal routine, conflicts with others **(2)** **Severe:** Marked interference, significantly affects relationships with others, totally or almost totally unable to maintain appropriate family relationship/ function at home/ outside of home) **(3)**
16. How does (X)'s anxiety affect you and your family? **(N.B. Only applicable when speaking to parent)**	- What is the biggest impact this has on you and your family? - How severely would you say this affects you? - Has the impact changed over time (i.e. improved/worsened) - Do you do anything to prevent/reduce the impact?	

18. How much control do you feel you have over X's anxiety and the impact it has on you? (Scale of 0-10)		0 = no control 10 = extreme amount of control
19. Does anyone else close to (X) share the same or similar emotions?		
20. Is there anything else you think is important to tell us?		

SECTION C
Useful prompt to be used when appropriate: 'can you tell me a little more about that?'

Opening Question	Prompts	Information
1. At what age did (X) begin showing these emotions?		
2. Did anything happen around the time that the anxiety began to develop?	- Were there any specific triggers or events? - Did it happen gradually over time or suddenly?	
3. When (X) feels like this, how do they behave?	- Do you see any physical changes in their body? - Do you see any changes in their face? - Do you see any changes in their speech pattern? - Do you see changes in how the X moves? - Do these behaviours occur in an order/sequence?	
4. What do you think (X) is thinking during this emotion? Why do you think that?	- What behaviours do (X) show/what does (X) say to make you think this? - Do you think they are feeling any other emotions?	

5. How severe would you say the anxiety shown during these events is?	- Are the symptoms very noticeable? - How distressed does (X) become? - Does (X) overcome the anxiety quickly or does it continue for a long period?	**N/A: (0)** **Mild:** only noticeable to family/people who know X very well, slightly distressing but no lasting impact, overcome fairly easily few physical symptoms **(1)** **Moderate:** often noticeably anxious to others (i.e. teachers/friends), moderately distressing, often takes time to overcome anxiety feelings, persistent physical symptoms, impacts well-being **(2)** **Severe:** always noticeable to others/strangers, severely distressing continues for long period, interferes with ability to function, severe physical symptoms, often or almost totally unable to overcome **(3)**
6. Is there a particular time of day when (X) is more likely to show this emotion?	- Are there times when it is better/worse?	
7. Is there anything (X) typically does himself/herself that helps reduce their anxiety?	- How often do they use these strategies? - Do they work? How well?	**List all strategies** *Code avoidance strategies and safety strategies separately* -Never

		-Sometimes: *several times a month* -Often: *several times a week* -Always: *several times a day*
8. Is there anything that you can do that helps reduce (X)'s difficult feeling?	- How often do you try using these techniques? - Do these strategies work? How often?	**List three most often used strategies** -Never -Sometimes: *several times a month* -Often: *several times a week* -Always: *several times a day*
9. What happens if the strategies that help are not available?	- How long does this response go on for?	*List of behaviours* Example: if you do not give reassurance (duration in minutes)
10. How does this affect (X) day to day?	- What is the biggest impact anxiety has on (X)? - How severely would you say this impacts (X)?	**<u>Q12/Q13</u>** (e.g. Peers/family relationships, In the home, outside of the home **N/A (0)** **Mild:** Slight impact on relationships, home life, outside home life **(1)** **Moderate:** Clear interference, withdrawal from normal routine, conflicts with others **(2)** **Severe:** Marked interference, substantial clinical significance, significantly affects
11. How does this affect you and your family? **(N.B. Only applicable when speaking to parent)**	- What is the biggest impact (X)'s anxiety has on you and your family? - How severely would you say this affects you? - Has the impact changed over time (i.e. improved/worsened) - Do you do anything to prevent/reduce this impact?	

		relationships with others/home functioning/outside of home functioning (i.e. refusal to leave house) **(3)**
12. How much control do you feel you have over the anxiety X experiences and the impact it has on you? (Scale of 0-10)		0 = no control 10 = extreme amount of control
13. Does anyone else close to (X) share the same or similar emotions?		
14. Is there anything else you think is important to tell us?		

SECTION D: Use Section D if **anxiety and depression** are both discussed in Section A.

Opening Question	**Sub Questions**
1. Do you think (X)'s anxiety and depression is related?	- Do they present together?
2. Which one came first?	- Did the anxious symptoms come before the depressive symptoms? - When did X first show depressive symptoms/low mood?

Appendix 29 Chapter four clinician interview schedule

Anxiety in Intellectual Disabilities: Clinical Bottom-up Interview – Prompt Sheet

Prompt Sheet SECTION A

Format of the interview: The interview is fluid, therefore clinicians should be encouraged to talk freely and the order and direction of the interview may vary between participants. During the interview, questions which are not deemed relevant may be omitted by the researcher and extra prompts may be added if the researcher considers that further information is necessary. All questions asked should be kept within the guidelines given although the interview will be guided by the participants and the order of questions may be changed to best suit the direction of the interview. Participants will not be subjected to leading questions.

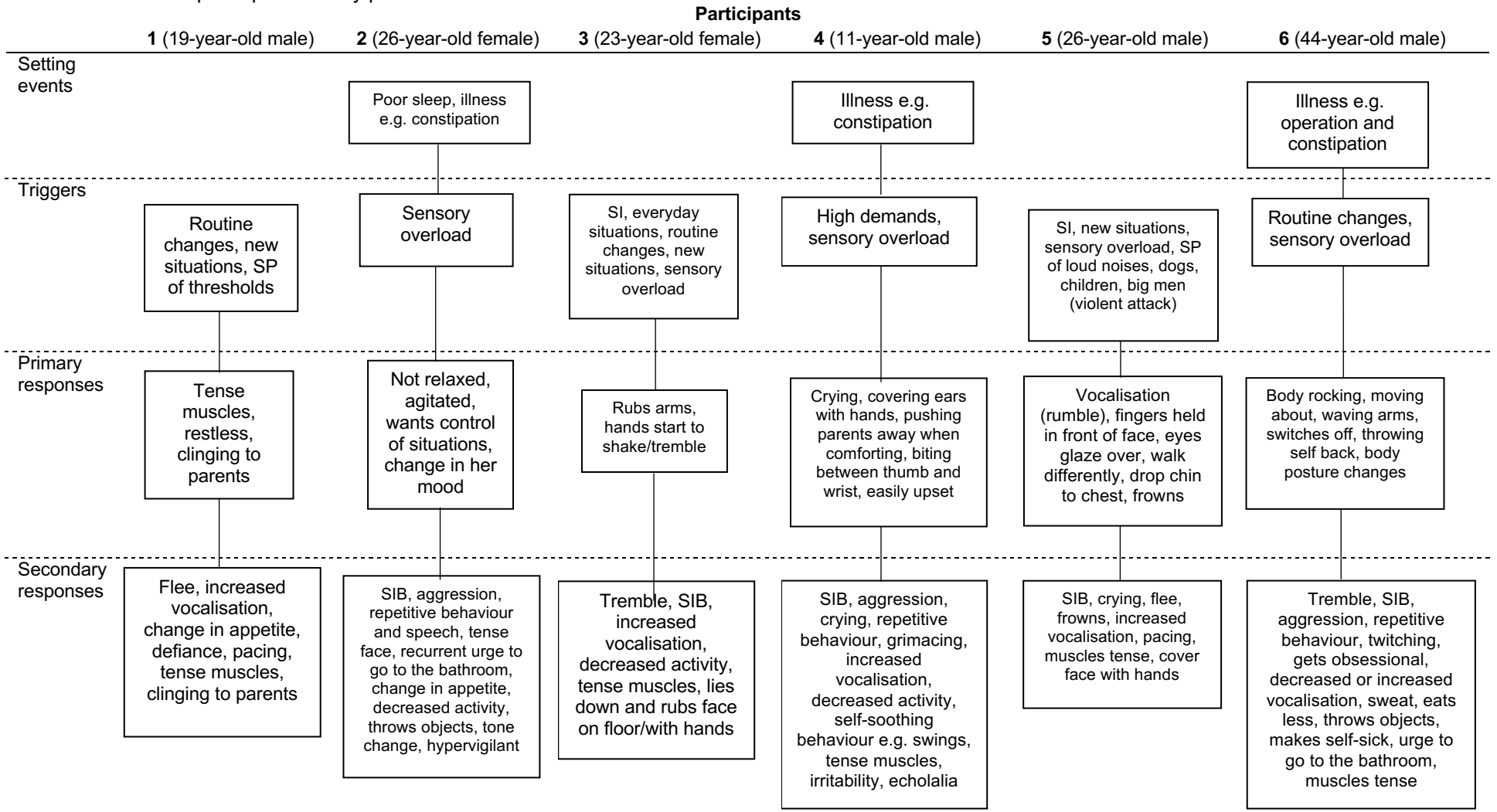
Useful prompt to be used when appropriate: 'can you tell me a little more about that?'

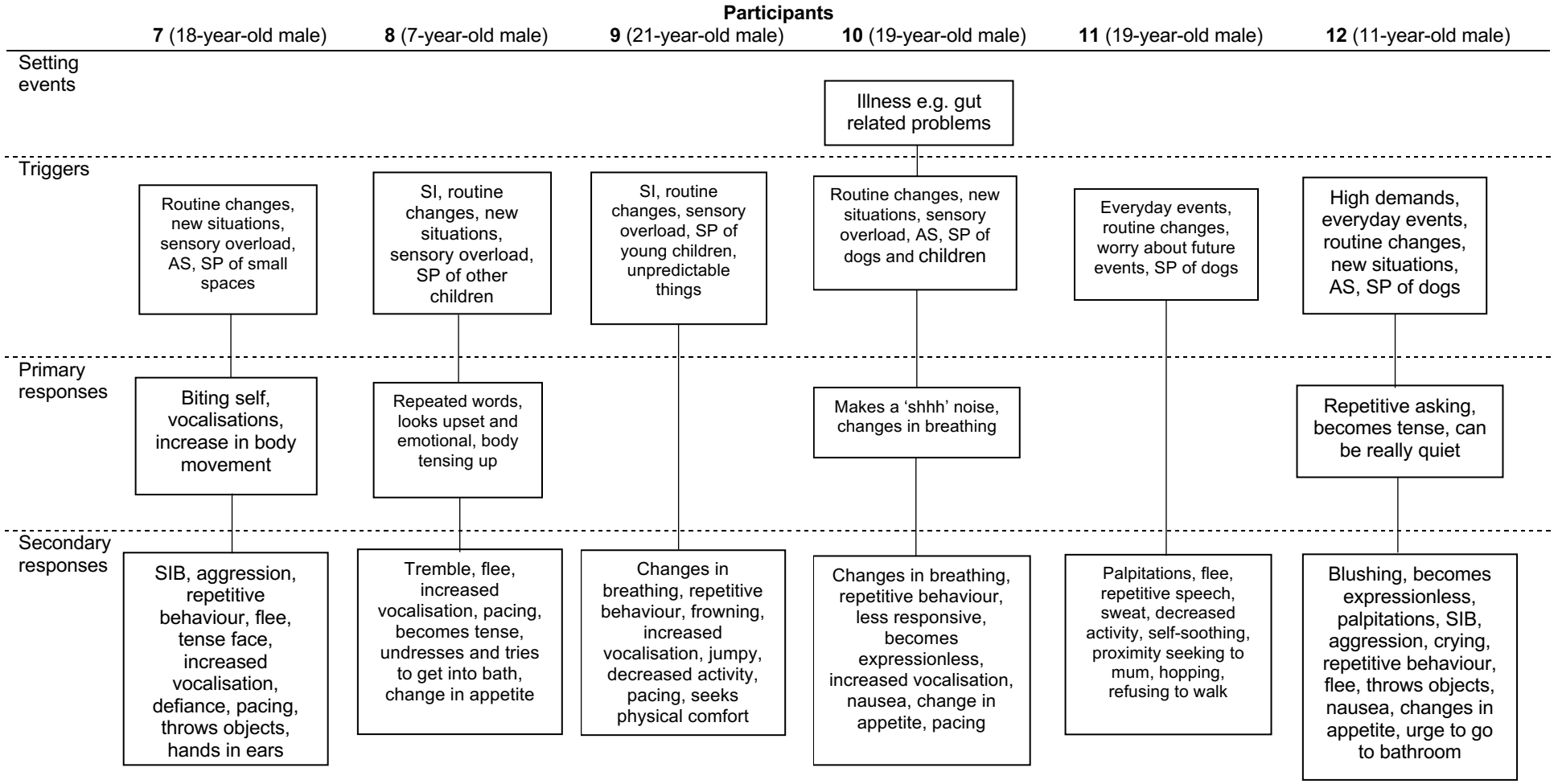
Opening Question	- Prompts
1. When you are assessing anxiety, are there specific things you look for in minimally verbal people?	- Do you see any physical changes in their bodies? - Do you see changes in how people move? - Do you see any changes in their faces? - Do you see any changes in their speech patterns? - Do the behaviours occur in an order/sequence? - Do the behaviours differ between events/bursts? Are the same behaviours always shown?
2. When you are assessing anxiety in minimally verbal people, how do you differentiate this from other diagnoses, such as pain or autism spectrum disorder?	- Do you see any physical changes in their bodies? - Do you see changes in how the person moves? - Do you see any changes in their faces? - Do you see any changes in their speech patterns? - Do these behaviours occur in an order/sequence? - Do the behaviours differ between events/bursts? Are the same behaviours always shown?
3. Do you ever think anxiety is diagnosed incorrectly, or	- Are there particular behaviours that are shown that cause confusion?

overlooked? What leads to this?	
4. Do you ever think pain is diagnosed incorrectly, or overlooked? What leads to this?	- Are there particular behaviours that are shown that cause confusion?

Appendix 30 Chapter four individual participant anxiety presentations

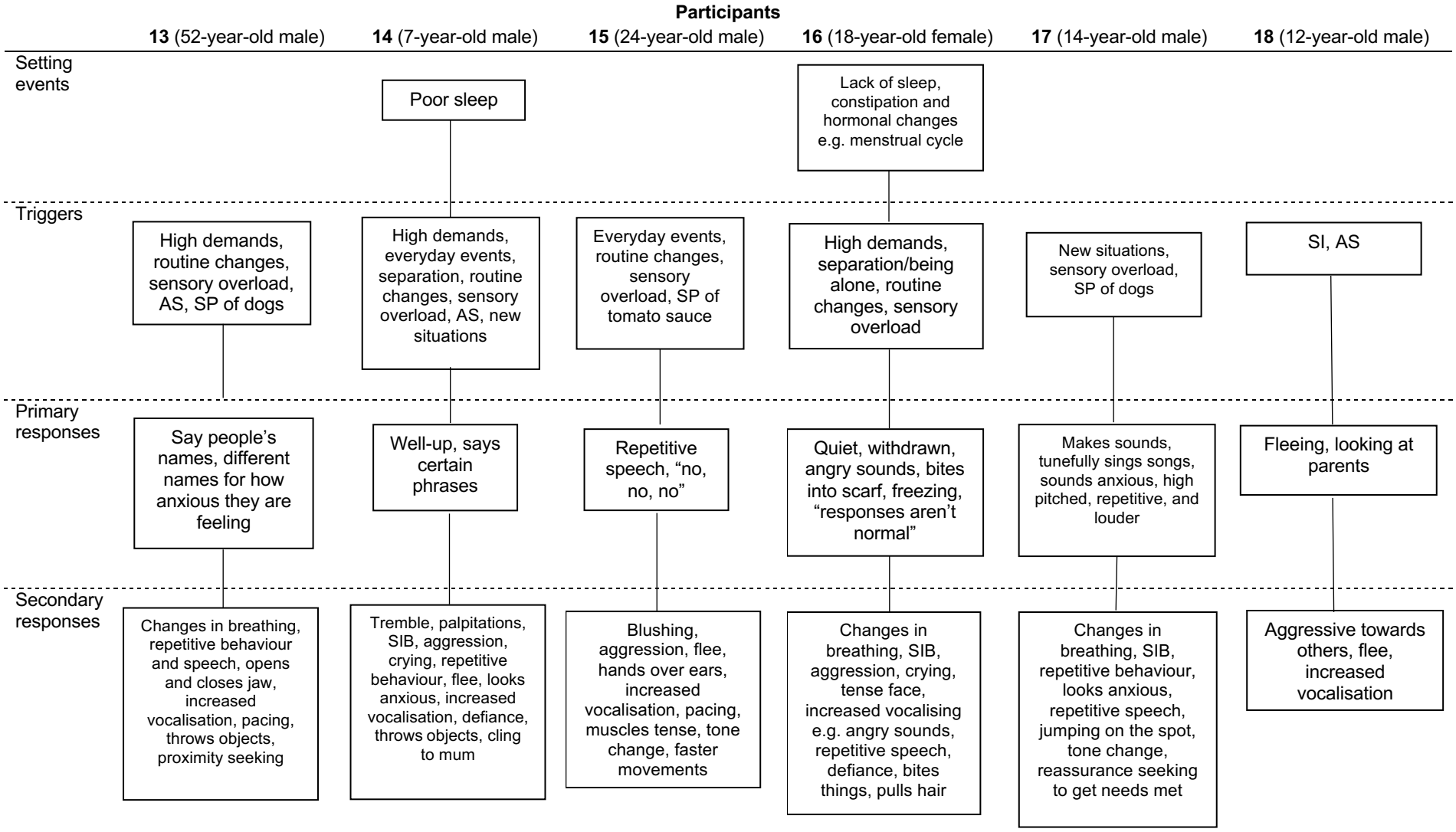
Table 23 Individual participant anxiety presentations



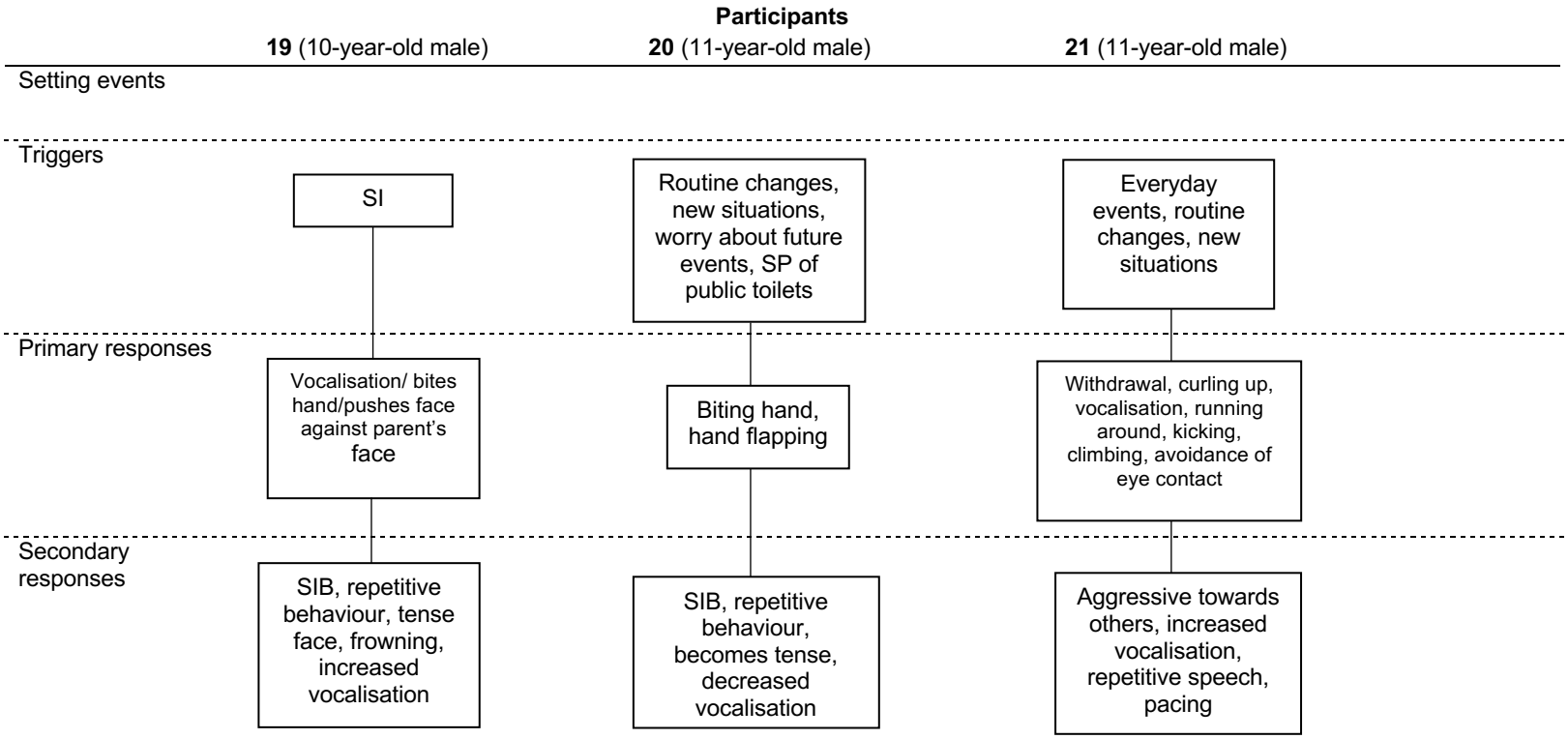


AS: aversive setting (school, beach, shops), SP: specific phobia, SI: social interactions, SIB: self-injurious behaviour; SI: social interactions, SP: specific phobia

Appendix Thirty. *Individual participant anxiety presentations*



AS: aversive setting (dentist, hospital), SP: specific phobia, SIB: self-injurious behaviour



SI: social interactions, SIB: self-injurious behaviour, SP: specific phobia

NHS
Health Research Authority

West Midlands - Coventry & Warwickshire Research Ethics Committee
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Appendix 31 Chapter five ethical approval

25 June 2019

Miss Georgina Theresa Edwards
Aston University
Aston Triangle
Birmingham
B4 7ET

Dear Miss Edwards

Study title:	**Person and environmental characteristics associated with anxiety in minimally verbal individuals with intellectual disability (and autism)**
REC reference:	**19/WM/0154**
Protocol number:	**276-2019-GE**
IRAS project ID:	**257157**

Thank you for your letter of 19/06/2019. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 06 June 2019

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Letters of invitation to participant [AppendixA_Invite_29.11.18_V1TrackChanges]	V1	29 November 2018
Letters of invitation to participant [AppendixA_Invite_06.06.19_V2]	V2	06 June 2019
Non-validated questionnaire [AppendixU_ParentDailyDiary_18.12.18_V1TrackChanges]	V1	18 December 2018
Non-validated questionnaire [AppendixU_ParentDailyDiary_06.06.19_V2]	V2	06 June 2019
Other [ProtocolTrackChanges]	V1	05 December 2018
Other [Protocol]	V2	06 June 2019

IRAS ID: 240250301

Other [REC response following meeting]	N/A	13 June 2019
Participant information sheet (PIS)	V1	30 November 2018
[AppendixC_Info_30.11.18_V1TrackChanges]		
Participant information sheet (PIS) [AppendixC_Info_06.06.19_V2]	V2	06 June 2019

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [AppendixL_Advert_30.11.18_V1]	V1	30 November 2018
Covering letter on headed paper [Cover letter REC submission]		
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Sponsor Insurance]		02 July 2018
GP/consultant information sheets or letters [AppendixO_PersonLD_GPLetter_30.11.18_V1]	V1	30 November 2018
GP/consultant information sheets or letters [AppendixZh_GPLetterParentDistress_30.11.18_V1]	V1	30 November 2018
GP/consultant information sheets or letters [AppendixZi_PersonLD_GPLetterFollowup_30.11.18_V1]	V1	30 November 2018
Interview schedules or topic guides for participants [AppendixS_VABS]		
Letter from sponsor [Letter from sponsor]		04 April 2019
Letters of invitation to participant [AppendixM_SchoolParentInvite_31.01.19_V1]	V1	31 January 2019
Letters of invitation to participant [AppendixN_InviteSchool_08.01.19_V1]	V1	08 January 2019
Letters of invitation to participant [AppendixB_EoI_29.11.18_V1]	V1	29 November 2018
Letters of invitation to participant [AppendixA_Invite_29.11.18_V1TrackChanges]	V1	29 November 2018
Letters of invitation to participant [AppendixA_Invite_06.06.19_V2]	V2	06 June 2019
Non-validated questionnaire [AppendixQ_BackgroundQ_04.12.18_V1]	V1	04 December 2018
Non-validated questionnaire [AppendixT_ClientServiceInventory_25.01.19_V1]	V1	25 January 2019
Non-validated questionnaire [AppendixZ_CIASP-ID_08.01.19_V1]	V1	08 January 2019
Non-validated questionnaire [AppendixZa_HealthQ_14.01.19_V1]	V1	14 January 2019
Non-validated questionnaire [AppendixZb_GDQ_11.01.19_V1]	V1	11 January 2019
Non-validated questionnaire [AppendixZe_AnxietyTriggers_12.02.19_V1]	V1	12 February 2019
Non-validated questionnaire [AppendixZj_FeedbackReportTemplate_30.11.18_V1]	V1	30 November 2018
Non-validated questionnaire [AppendixP_PreVisit Risk Assessment_30.11.18_V1]	V1	30 November 2018
Non-validated questionnaire [AppendixU_ParentDailyDiary_18.12.18_V1TrackChanges]	V1	18 December 2018

Non-validated questionnaire [AppendixU_ParentDailyDiary_06.06.19_V2]	V2	06 June 2019
Other [ProtocolTrackChanges]	V1	05 December 2018
Other [Protocol]	V2	06 June 2019
Other [REC response following meeting]	N/A	13 June 2019
Participant consent form [AppendixD_Consent_Under16_Able_30.11.18_V1]	V1	30 November 2018
Participant consent form [AppendixE_Consent_Over16_NotAble_30.11.18_V1]	V1	30 November 2018
Participant consent form [AppendixF_Consent_Under16_NotAble_30.11.18_V1]	V1	30 November 2018
Participant consent form [AppendixG_Consent_Over16_Able_03.12.18_V1]	V1	03 December 2018
Participant consent form [AppendixH_Consent_Over16_ParentCarer_03.12.18_V1]	V1	03 December 2018
Participant consent form [AppendixK_CapacityProtocol_30.11.18_V1]	V1	30 November 2018
Participant consent form [AppendixZg_ImageVideoReleaseConsent_30.11.18_V1]	V1	30 November 2018
Participant information sheet (PIS) [AppendixJ_SymbolInfoSheet _30.11.18_V1]	V1	30 November 2018
Participant information sheet (PIS) [AppendixI_Consultee_Information_03.12.18_V1]	V1	03 December 2018
Participant information sheet (PIS) [AppendixC_Info_30.11.18_V1TrackChanges]	V1	30 November 2018
Participant information sheet (PIS) [AppendixC_Info_06.06.19_V2]	V2	06 June 2019
REC Application Form [REC_Form_12042019]		12 April 2019
Summary CV for Chief Investigator (CI) [CV_JWaite]	V1	31 January 2019
Summary CV for student [CV_GEdwards]	V1	31 January 2019
Summary CV for supervisor (student research) [CV_JWaite]	V1	31 January 2019
Summary, synopsis or diagram (flowchart) of protocol in non technical language [FlowChart_11.04.19_V1]	V1	11 April 2019
Validated questionnaire [AppendixR_WessexQ]		
Validated questionnaire [AppendixV_SCQ]		
Validated questionnaire [AppendixW_ADAMS]		
Validated questionnaire [AppendixX_MIPQ]		
Validated questionnaire [AppendixY_DASH-II]		
Validated questionnaire [AppendixZc_RBQ2]		
Validated questionnaire [AppendixZd_SensoryProfile]		
Validated questionnaire [AppendixZf_RULESQ]		

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

19/WM/0154 **Please quote this number on all correspondence**

IRAS ID: 240250303

Yours sincerely

[signature removed]

Tadeusz Jones REC Manager

E-mail: NRESCommittee.WestMidlands-CoventryandWarwick@nhs.net

Copy to: *Miss Georgina Theresa Edwards*

Aston University

Appendix 32 Chapter five information sheet

Person and environmental characteristics associated with anxiety in minimally verbal individuals with intellectual disability (and autism)
(Anxiety in autism and intellectual disability)
Participant Information Sheet

Invitation

If you have questions or would like a verbal explanation of this study, contact Joanne Tarver on 0121 204 4386 or j.tarver@aston.ac.uk or Georgina Edwards on edwardg4@aston.ac.uk

We would like to invite you to take part in a research study.

Before you decide if you would like to participate, take time to read the following information carefully and, if you wish, discuss it with others such as your family, friends or colleagues.

Please ask a member of the research team, whose contact details can be found at the end of this information sheet, if there is anything that is not clear or if you would like more information before you make your decision.

What is the purpose of the study?

We are inviting parents/carers of individuals with autism and/or intellectual disability who are minimally verbal to take part in a research study about anxiety experienced by the person they care for. This research study follows on from a recent interview and questionnaire study. We are now also inviting individuals with autism and/or intellectual disability to take part in a research assessment day. We hope that the study will help health care professionals working with individuals with autism and/or intellectual disability to understand the factors that influence anxiety.

The aim is to examine which person and environmental characteristics are common in individuals with autism and/or intellectual disability who are minimally verbal and experience anxiety.

Why have I been invited?

You are being invited to take part in this study because you recently took part in an interview/questionnaire study and indicated that you are happy for us to contact you for research purposes. Alternatively, we may have contacted you because you responded to an advert that was posted on a relevant website or because your child's school has agreed to support this research project with recruitment.

For this stage of the research, we are inviting individuals with autism and/or intellectual disability who are minimally verbal to take part. For the purposes of this study, we are defining “minimally verbal” as an individual who speaks no words or odd words only. We are inviting individuals who experience anxiety or have an anxiety disorder diagnosis and are between 4-55 years of age.

If you are unclear about any of the terms we have used above or you would like more information, please contact a member of the research team.

What will happen to me if I take part?

There is an interview to be completed with you prior to the assessment day that assesses the person you care for’s level of ability. This interview can be completed over the phone and it will give us some information about the person you care for before we meet them, face-to-face or online. During this phone call, we will also ask you about any input your child/the person you care for has had from health professionals during the past six months.

There are a number of tasks to be completed during the assessment day. The majority of tasks are for the person you care for to complete. We will ask you to complete some short questionnaires and take part in an interview about the person you care for. You can either complete the questionnaires on paper or online, via an online survey platform, Qualtrics. The interview you complete about the person you care for will be completed over the phone following the assessment day.

The research assessment day will take place at Aston University, your home or via an online video communication platform. You can decide where you would like it to take place. If you decide to come to Aston University, your travel and accommodation expenses will be reimbursed. Regardless of where the research assessment day takes place, you will receive a £15 online voucher for your participation in the study.

We will ask you to bring/have/scan a copy of a letter confirming the person you care for’s diagnosis, if possible, from a GP, paediatrician, geneticist or other professional. This will help us to confirm diagnosis on the direct assessment day. However, if you are unable to provide this letter, this will not preclude you from participating in the study.

The tasks we will ask the person you care for to complete will include an IQ assessment, a sensory assessment, an assessment of autism characteristics and an assessment of anxiety. If you decide to take part in the study via the online video communication platform, we are unable to complete the IQ assessment. The tasks we will ask the person you care for to complete will last between 45 minutes-1.5 hours. We will take regular breaks in between the tasks.

We will also ask parents/carers to complete a diary including ratings of anxiety during a two-week period prior to the direct assessment day for the person they care for.

With your permission, we will video record the tasks that we will ask the person you care for to complete during the assessment day, whether this is face-to-face or online. This is to allow us to be able to code some of the tasks after they have been completed. The video recordings will only be seen by members of the research team. Additionally, only researchers directly involved in this study will have access to your child's/person you care for's personal information, which will be stored on Aston's highly secure cloud storage.

Taking part in the assessment day will take you no longer than 1.5 hours.

We are collecting data for this stage of the research from participants from July 2020 until March 2021. After that, we will spend some time understanding the data and writing reports. This means that the study will be finished in June 2021. This study is part of a broader study of anxiety in people with autism and/or intellectual disability that is ongoing until 2021. You will be given the option for us to retain your details if you would like to be invited to take part in future research projects.

How will the video recordings made during the study be managed?

The video recordings will be destroyed as soon as the research team have analysed the information in them to answer the research question.

We will ensure that anything from the analysis of the videos that is included in the reporting of the study will be anonymous.

Do I have to take part?

No. It is up to you to decide whether or not you wish to take part.

If you do decide to participate, you will be asked to sign and date a consent form. You would still be free to withdraw from the study at any time without giving a reason.

Will my taking part in this study be kept confidential?

Yes. A code will be attached to all the data you provide to maintain confidentiality.

Your personal data (name and contact details) will only be used if the researchers need to contact you to arrange study visits or collect data by phone. Analysis of your data will be undertaken using coded data.

The data we collect will be stored in a secure document store (paper records) or electronically on a secure encrypted mobile device, password protected computer server or secure cloud storage device.

To ensure the quality of the research, Aston University may need to access your data to check that the data has been recorded accurately. If this is required, your personal data will be treated as confidential by the individuals accessing your data.

Will my GP be informed of my involvement in the study?

With your consent, the GP of your child/the person you care for will be notified of their participation in this study. A copy of the feedback report for your child will be shared with their GP at the end of this study.
If we become aware that your child/the person you care for may be experiencing an undiagnosed health difficulty, Professor Jackie Blissett will write to their GP to pass on this information.
We will only contact your GP if it becomes apparent that you are showing signs of distress or an undiagnosed health difficulty.

What happens if something is discovered during the study which requires further clinical investigation?

The investigations undertaken during this study are not intended to be diagnostic but occasionally we discover something unusual that we feel should be investigated. We call these incidental findings.

Should this occur we will write to your/the person you care for's GP who will be able to arrange further investigations for you.

What happens if I tell you something that concerns you about my health or welfare or that of the person I care for?

In the unlikely event of this happening, we will discuss with you how this should be addressed. If necessary, to protect you and the person you care for, we will report your concern to the appropriate person or bodies.

Any request for advice concerning the person with autism and/or intellectual disability will be passed on to Dr Joanne Tarver who will provide information about accessing local support.

What are the possible benefits of taking part?

You will receive an individualised feedback report summarising the results of the study. This study will help us find out more about the needs of people with autism and/or intellectual disability who may experience anxiety. You will also receive a £15 online voucher for your participation in this study.

What are the possible risks and burdens of taking part?

The tasks we will do on the assessment day are tasks which are commonly used in individuals with neurodevelopmental conditions and intellectual disability. However, some individuals can find some of the tasks difficult. We can take regular breaks to make the tasks easier for the person you care for.
As part of the questionnaires and interviews, we may ask about times where the person you care for has been distressed. Some parents may find this distressing.
Your decision to participate in this study will not impact your right to access services.
What will happen to the results of the study?

The results of this study may be published in scientific journals and/or presented at conferences. If the results of the study are published, your identity will remain

confidential. Research findings may also be published in newsletters of support groups and educational institutions. Data will also be included in student dissertations.
A lay summary of the results of the study will be available for participants when the study has been completed and the researchers will ask if you would like to receive a copy.
The anonymized results may be shared with the company providing funding for this study. The results of the study will also be used in Georgina Edwards' PhD thesis.

Expenses and payments
You will also receive a £15 online voucher for your participation in this study. Also, if you decide to come to Aston University for the research assessment day, your travel and accommodation expenses will be reimbursed.

Who is funding the research?

The study is being funded by: The Baily Thomas Charitable Fund and Autistica.

Who is organising this study and acting as data controller for the study?

Aston University is organising this study and acting as data controller for the study. You can find out more about how we use your information in Appendix A.
Who has reviewed the study?

This study was given a favorable ethical opinion by the Coventry and Warwickshire Research Ethics Committee (19/WM/0154).

What if I have a concern about my participation in the study?

If you have any concerns about your participation in this study, please speak to the research team and they will do their best to answer your questions. Contact details can be found at the end of this information sheet.

If the research team are unable to address your concerns or you wish to make a complaint about how the study is being conducted you should contact the Aston University Research Integrity Office at research_governance@aston.ac.uk or telephone 0121 204 3000.

Research Team
This research is being conducted by:

Joanne Tarver
Telephone: 0121 204 4386. Email: j.tarver@aston.ac.uk

Georgina Edwards (Doctoral Researcher)
Email: edwardg4@aston.ac.uk

Thank you for taking time to read this information sheet. If you have any questions regarding the study please don't hesitate to ask one of the research team.

Aston University takes its obligations under data and privacy law seriously and complies with the General Data Protection Regulation ("GDPR") and the Data Protection Act 2018 ("DPA").

Aston University is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study. Aston University will process your personal data in order to register you as a participant and to manage your participation in the study. It will process your personal data on the grounds that it is necessary for the performance of a task carried out in the public interest (GDPR Article 6(1)(e). Aston University may process special categories of data about you which includes details about your health. Aston University will process this data on the grounds that it is necessary for statistical or research purposes (GDPR Article 9(2)(j)). Aston University will keep identifiable information about you for 6 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

You can find out more about how we use your information at www.aston.ac.uk/dataprotection or by contacting our Data Protection Officer at dp_officer@aston.ac.uk.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

When you agree to take part in a research study, the information about you may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of research, and cannot be used to contact you.

Aston University

Appendix 33 Chapter five consent forms

Person and environmental characteristics associated with anxiety in minimally verbal individuals with intellectual disability (and autism)
Consent Form A: For children with autism and/or intellectual disabilities who are able to provide assent to participate in the study

Chief Investigator: Professor Jackie Blissett

Section 1 (Assent): Please complete this section if you are a person with autism and/or learning disability. If needed, your parent/carer or the researcher can read this form to you and you can let them know your answers.

	Please circle
Has somebody else explained the project to you?	YES/NO
Have you asked all of the questions you want?	YES/NO
Have you had your questions answered in a way you understand?	YES/NO
Do you understand it is OK to stop taking part at any time?	YES/NO
We will tell your GP you are taking part and show them your results. Is that OK?	YES/NO
Is it ok if we video record you?	YES/NO
The next question is optional: Are you happy for us to contact you again in the future?	YES/NO
Are you happy to take part?	YES/NO

Please write your name here:_____

Please write the date here:_____

Name of researcher taking assent: _____

Section 2 (Parent/carer consent): Please complete this section if you are a parent/carer/guardian of a person with autism and/or learning disability who has provided their assent/consent to participate in the study.

Please initial boxes

1.	I confirm that I have read and understand the Participant Information Sheet (Version 5, dated 27.08.20) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation and that of my child/person I care for is voluntary and that I am free to withdraw at any time, without giving any reason and without my or that of my child's/person I care for's legal rights being affected.	
3.	I agree to my personal data and that of my child/person I care for and data relating to me and that of my child/person I care for collected during the study being processed as described in the Participant Information Sheet.	
4.	I agree to my child/person I care for's GP being informed of their/my participation in the study.	
5.	I agree to the feedback report arising from this study being shared with my child/person I care for's GP.	
6.	I understand that if during the study I tell the research team something that causes them to have concerns in relation to my health and/or welfare or that of my child/person I care for they may need to breach my confidentiality.	
7.	I agree to study visits being video recorded (including if assessments are completed online).	
8.	I agree to my anonymised data being used by research teams for future research and by educational institutions such as my child/person I care for's school.	
9.	I agree to take part in this study.	
	The following statements are optional:	
1.	I agree to my personal data being processed for the purposes of inviting me to participate in future research projects. I understand that I may opt out of receiving these invitations at any time.	
2.	I agree to complete a short telephone interview about my child's/person I care for's ability.	
3.	I agree to be contacted about future research projects to consider whether I would like to take part.	

_____	_____	_____
Name of participant	Date	Signature

_____	_____	_____
Name of Person receiving consent.	Date	Signature

Aston University

Person and environmental characteristics associated with anxiety in minimally verbal individuals with intellectual disability (and autism)

<u>Consent Form C:</u> For a personal/nominated consultee of a person over the age of 16 who is not able to provide consent.

Chief Investigator: Professor Jackie Blissett

Before deciding whether to participate, please ensure you read the information on acting as a personal/nominated consultee in the attached document for the person you care for.

Please initial boxes

1.	I have been consulted about (name of participant) _____'s participation in the above research project. I confirm that I have read and understand the Participant Information Sheet (Version 5, dated 27.08.20) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I confirm that in my opinion he/she would have no objection to participating in the study.	
3.	I understand that my participation and the participation of the person for whom I am acting as a consultee is voluntary and that I am free to withdraw at any time, without giving any reason and without my legal rights being affected.	
4.	I agree to my/person for who I am acting as consultee's personal data and data relating to me and him/her collected during the study being processed as described in the Participant Information Sheet.	
5.	I agree to his/her GP being informed of their participation in the study.	
6.	I agree to the feedback report arising from this study being shared with the GP of the person for whom I am acting as a consultee.	
7.	I understand that if during the study I tell the research team something that causes them to have concerns in relation to my health and/or welfare, or, the health and/or welfare of the person for whom I am acting as consultee, they may need to breach my confidentiality.	
8.	I agree to study visits being video recorded (including if assessments are completed online).	
9.	I agree to my anonymised data being used by research teams for future research and by educational institutions such as the person for whom I am acting as a consultee for's school.	
10.	I agree to take part in this study.	
	The following statements are optional:	
1.	I agree to my personal data being processed for the purposes of inviting me to participate in future research projects. I understand that I may opt out of receiving these invitations at any time.	
2.	I agree to complete a short telephone interview about the ability of the person for whom I am acting as a consultee.	
3.	I agree to be contacted about future research projects to consider whether the person for whom I am acting as consultee would like to take part.	

_____	_____	_____
Name of participant	Date	Signature
_____	_____	_____
Name of consultee	Date	Signature
_____	_____	_____
Name of Person receiving consent.	Date	Signature

Aston University

Person and environmental characteristics associated with anxiety in minimally verbal individuals with intellectual disability (and autism)

Consent Form B: For parents/carers whose child is under the age of 16 and is not able to make an informed decision about participation in the study.

Chief Investigator: Professor Jackie Blissett

Please initial boxes

1.	I confirm that I have read and understand the Participant Information Sheet (Version 5, dated 27.08.20) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I confirm that my child is not able to understand all the information needed to decide about participating in this study, but that I have shared as much information as possible with my child about the study.	
3.	I understand that my participation and that of my child/person I care for is voluntary and that I am free to withdraw at any time without giving any reason and without my or that of my child's/person I care for's legal rights being affected.	
4.	I agree to my personal data and that of my child/person I care for and data relating to me collected during the study being processed as described in the Participant Information Sheet.	
5.	I agree to my child/person I care for's GP being informed of their/my participation in the study.	
6.	I agree to the feedback report arising from this study being shared with my child/person I care for's GP.	
7.	I understand that if during the study I tell the research team something that causes them to have concerns in relation to my heath and/or welfare or that of my child/person I care for they may need to breach my confidentiality.	
8.	I agree to study visits being video recorded (including if assessments are completed online).	
9.	I agree to my anonymised data being used by research teams for future research and by educational institutions such as my child/person I care for's school.	
10.	I agree to take part in this study.	
	The following statements are optional:	
1.	I agree to my personal data being processed for the purposes of inviting me to participate in future research projects. I understand that I may opt out of receiving these invitations at any time.	
2.	I agree to complete a short telephone interview about my child's/the person I care for's ability	
3.	I agree to be contacted about future research projects to consider whether I would like to take part.	

_____	_____	_____
Name of participant	Date	Signature

_____	_____	_____
Name of Person receiving consent.	Date	Signature

Person and environmental characteristics associated with anxiety in minimally verbal individuals with intellectual disability (and autism)

<u>Consent Form E:</u> For adults with autism and/or intellectual disability who are able to provide consent to participate in the study

Chief Investigator: Professor Jackie Blissett

Please initial boxes

1.	I confirm that I have read and understand the Participant Information Sheet (Version 5, dated 27.08.20) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my legal rights being affected.	
3.	I agree to my personal data and data relating to me collected during the study being processed as described in the Participant Information Sheet.	
4.	I agree to my GP being informed of my participation in the study.	
5.	I agree to the feedback report arising from this study being shared with my GP.	
6.	I understand that if during the study I tell the research team something that causes them to have concerns in relation to my health and/or welfare they may need to breach my confidentiality.	
7.	I agree to study visits being video recorded (including if assessments are completed online).	
8.	I agree to my anonymised data being used by research teams for future research.	
9.	I agree to take part in this study.	
The following statements are optional:		
1.	I agree to my personal data being processed for the purposes of inviting me to participate in future research projects. I understand that I may opt out of receiving these invitations at any time.	
2.	I agree to be contacted about future research projects to consider whether I would like to take part.	

_____	_____	_____
Name of participant	Date	Signature
_____	_____	_____
Name of Person receiving consent	Date	Signature

Person and environmental characteristics associated with anxiety in minimally verbal individuals with intellectual disability (and autism)

Consent Form D: For parents/carers of individuals over the age of 16 and able to make an informed decision about participation in the study

Chief Investigator: Professor Jackie Blissett

Please initial boxes

1.	I confirm that I have read and understand the Participant Information Sheet (Version 5, dated 27.08.20) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my legal rights being affected.	
3.	I agree to my personal data and data relating to me collected during the study being processed as described in the Participant Information Sheet.	
4.	I agree to the feedback report arising from this study being shared with the individual with autism and/or intellectual disability's GP.	
5.	I understand that if during the study I tell the research team something that causes them to have concerns in relation to my health and/or welfare or that of the individual with autism and/or intellectual disability they may need to breach my confidentiality.	
6.	I agree to study visits being video recorded (including if assessments are completed online).	
7.	I agree to my anonymised data being used by research teams for future research and by educational institutions such as the individual with autism and/or intellectual disability's school.	
8.	I agree to take part in this study.	
The following statements are optional:		
1.	I agree to my personal data being processed for the purposes of inviting me to participate in future research projects. I understand that I may opt out of receiving these invitations at any time.	
2.	I agree to completing a short telephone interview about the individual with autism and/or intellectual disability.	

3.	I agree to be contacted about future research projects to consider if I would like to take part.	

_____	_____	_____
Name of participant	Date	Signature
_____	_____	_____
Name of Person receiving consent.	Date	Signature

Appendix 34 Chapter five written Anx-DOS instructions

Written instructions for administration of the Anxiety Dimensional Observation Schedule (Anx-DOS)

1. Spider condition

Pick the toy spider and the remote control for the spider. If possible, keep the spider and the remote control out of sight of your child/ the person you care for, until you get their attention and say…

"Look, what I've got here, it's a soft fuzzy spider, go ahead and pet it, it won't bite, it's a nice spider"
(*repeat if child doesn't touch spider*)

Once child/adult goes to touch the spider, press one of the remote-control buttons to make the spider move. Then say the following:

"Oh, he jumped at you, but that's ok, go ahead and pet him again, he won't bite"

Encourage your child/the person you care for to touch the spider for a second time.

After you have allowed your child to explore the spider, you can show your child/the person you care for the remote control and indicate to them that you know it's really a toy, some prompts that you could say are below:

"It's just a toy, do you want to see how it works", "it's squidgy", "It's not real"
"We can make him jump by doing this"

2. Mystery jar

Next, you will present the mystery jar to your child/the person you care for and ask them to put their hand in the jar. For example…

"Can you put your hand in this jar for me?"
"Can you put your hand inside the jar?"

Try and encourage your child/the person you care for if they are a bit reluctant to put their
hand in the jar. Prompts could be used such as…

"Let's just try it once, can you put your hand inside the jar?"
"All the way in"
"I'd really like to see you put your hand in the  **jar, without looking"**

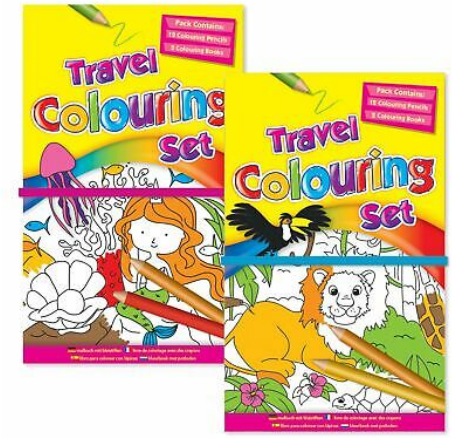
You could also model the behaviour by pretending to put your hand into jar too.

Once your child/the person you care for has put their hand in the jar, or you've tried a few times to encourage them to, you can show them that there's nothing in the jar.

3. **<u>Parental separation</u>**

You will be given some colouring books and materials to look at with your child and we ask for you to engage with your child and do some colouring with them for a few minutes. You could say the following to your child/the person you care for:

"Because you've done so well, now we get to play with some toys and do some colouring with me"



After a few minutes, please leave the room. After you have waited outside the room for a few minutes, please re-enter the room. You may want to indicate your return by saying…

"See, mummy/daddy didn't go anywhere"

Appendix 35 Chapter five risk assessment

Pre-Visit Risk Assessment

The following checklist should be used when arranging direct face to face research visits or assessments with participants. Prior to the research visit it is essential that the measure of adaptive functioning identified in the protocol (i.e. The Vineland Adaptive Behaviour Scales-II) has been administered to ensure that the researcher has an overview of the participant's developmental level. The following checklist should then be administered with the family over the telephone at the time of booking the research visit.

PART ONE

To be completed by the principal researcher conducting the assessment day:
DATE AND TIME OF THE VISIT:

VISIT LOCATION:

Q1) I have completed the Vineland Adaptive Behaviour Scale
Y/N
Q2) I have shared these details with all researchers conducting the direct assessments Y/N
Q3) I have shared the visit details with another researcher in the team who will contact me if I do not call within two hours of the end of the visit. That researcher will attempt to contact me, followed by the participant's family, my next of kin, and the police if necessary Y/N
The name of the researcher who will contact me is:
_____
Their contact numbers are:
mob:_____other:_____
My contact numbers are: mob:_____other:_
_____
My next of kin is: _____
No:_____
The ID number of the participant is:_____
mob:_____

THIS FORM SHOULD BE PHOTOCOPIED AND SHARED WITH ALL RESEARCHERS AND CONTACT PERSON PRIOR TO THE VISIT

PART TWO

To be completed with parent/carer/guardian:

Covid-19 specific questions

Q1) Have you or anyone you have been in personal contact with experienced any Covid-19 symptoms within the last week?

This includes: has confirmed or suspected coronavirus?
Is self-isolating?
Has a high temperature and/or a new, continuous cough?
Has experienced a sudden loss of smell and/or taste?

IF THE PERSON SAYS 'YES' TO ANY COVID-19 SYMPTOMS, DO NOT INVITE TO ATTEND A RESEARCH VISIT AT THIS TIME. CONSULT PUBLIC HEALTH ENGLAND TO CALCULATE THE TIME PERIOD THAT WOULD NEED TO PASS PRIOR TO RE-CONTACTING THAT FAMILY AND RE-ASSESSING THE SITUATION.

Q2) Are you or any member of your family or anyone that you are personally in contact with currently shielding?

Q3) Do you or any member of your family have a health condition that increases your/their risk of Covid-19? E.g. respiratory condition

Q4) Do you live, or have you travelled to an area within the last week that is undergoing a localised lockdown or has additional restrictions implemented?

Q5) Does your child/person you care for show any challenging behaviour? (e.g. self-injurious behaviour, aggressive behaviour, destruction of property)

Q6) If Yes, when is your child/person you care for most likely to show challenging behaviour?

Q6a) Are there any specific causes of behaviour that we need to be aware of because they may place the researcher or your child/person you care for at risk during the visit? (e.g. clothing, scents, phrases, actions).

Q7) How do you usually manage behaviour when it occurs?

Q8) Do you have any household pets that we should be aware of (if visiting participants house only)?

Q9) Is there parking close to your house (if visiting participants house only)?

Q10) Is there anything we should be aware of to ensure the visit goes well, or that may place the researcher at risk?

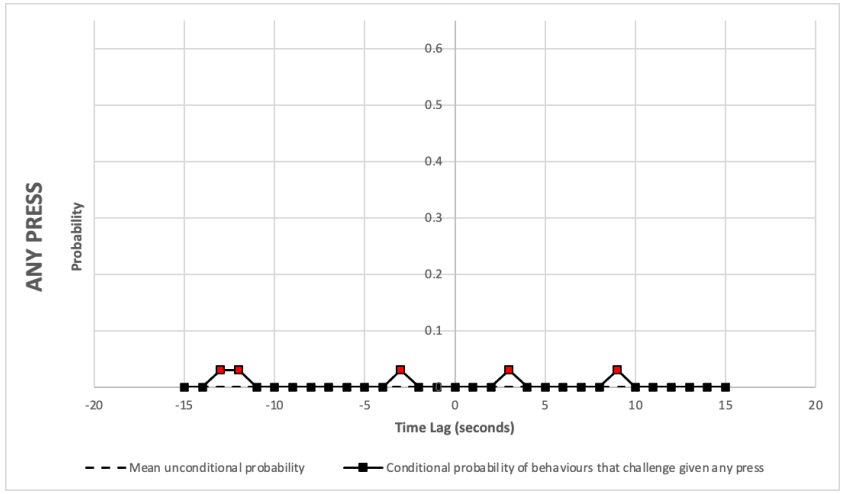
Q11) Will you be available throughout the entire assessment day? (note: parent/guardian/carer needs to be available for the visit to take place).

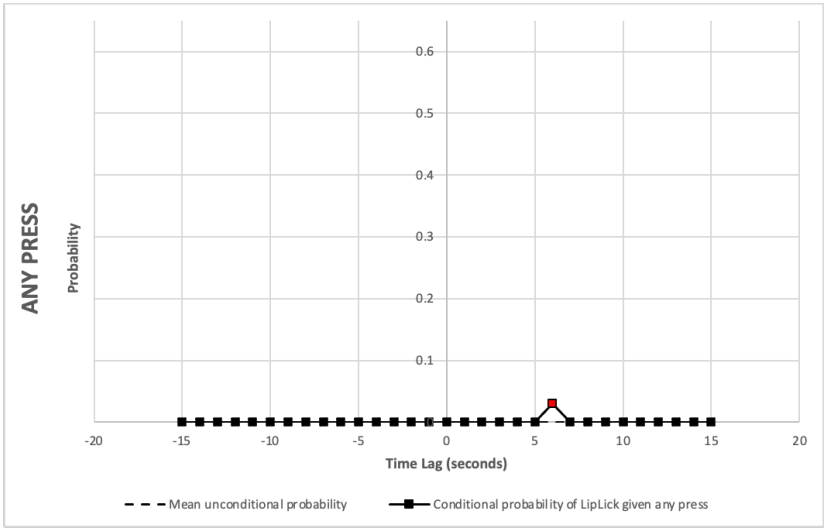
Q12) To ensure we get off to a good start, what are your child/person you care for's main likes/dislikes?

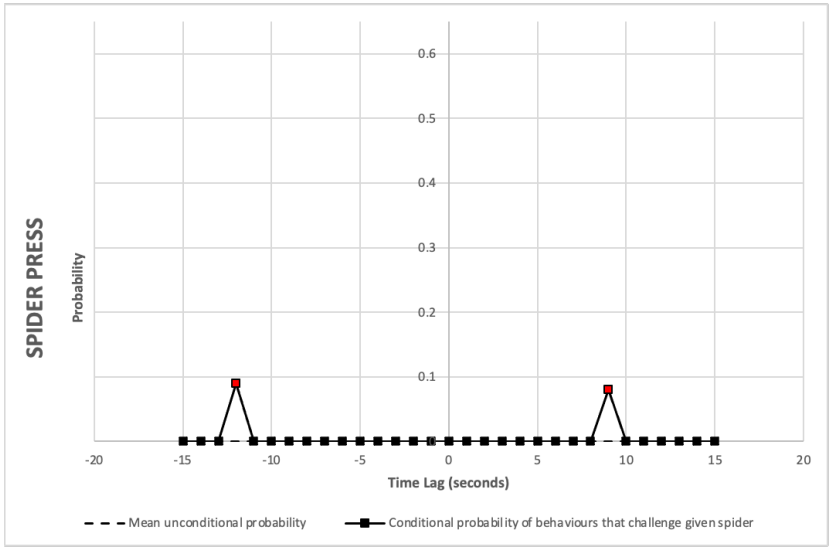
Q13) Does your child/person you care for have any allergies?

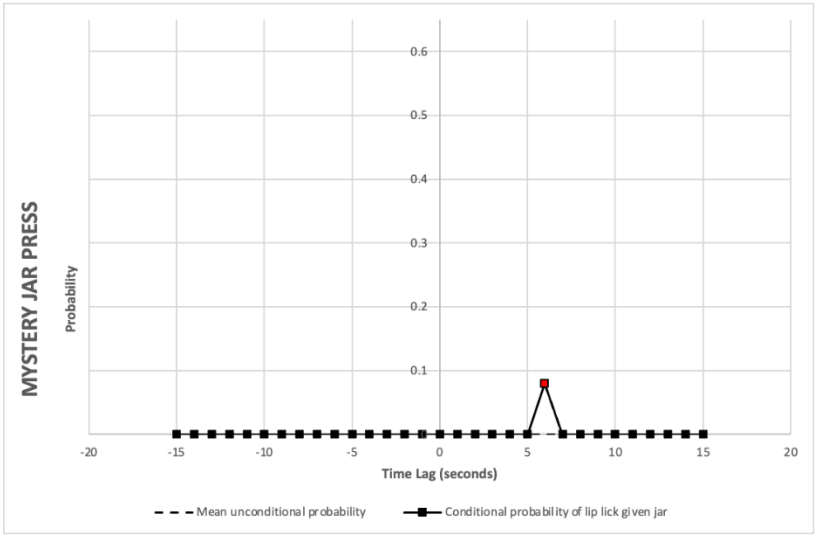
Appendix 36 Chapter five remaining analyses (significant)

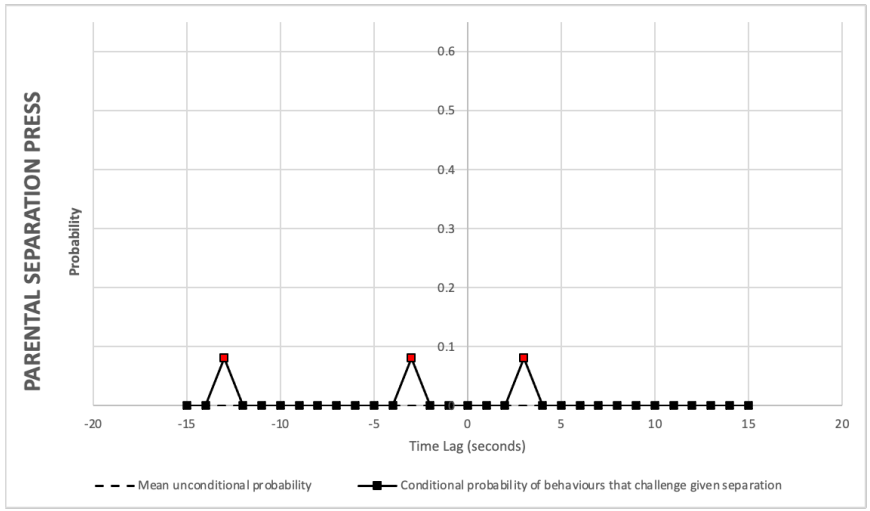
Appendices Figure 158 Significant findings for behaviours that challenge and lip lick across any press, spider press, mystery jar press and parental separation press. Analyses are only based on *n*=1 so need to be interpreted with caution.





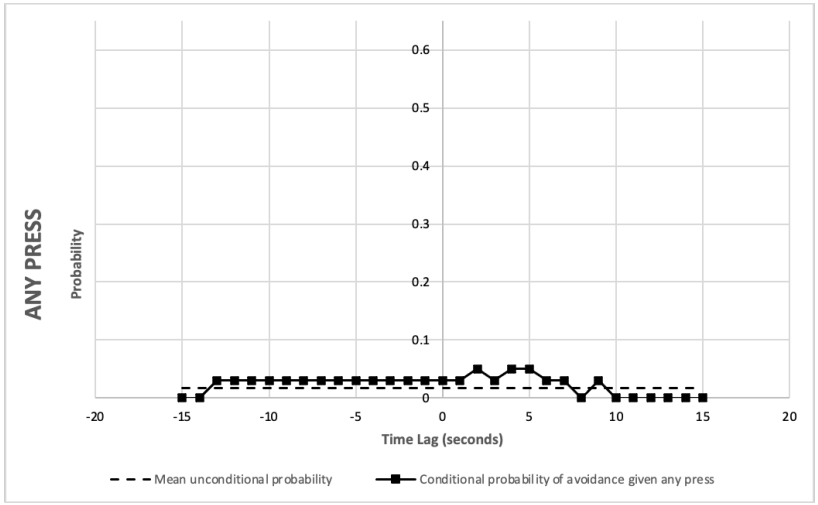

SPIDER PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of behaviours that challenge given spider

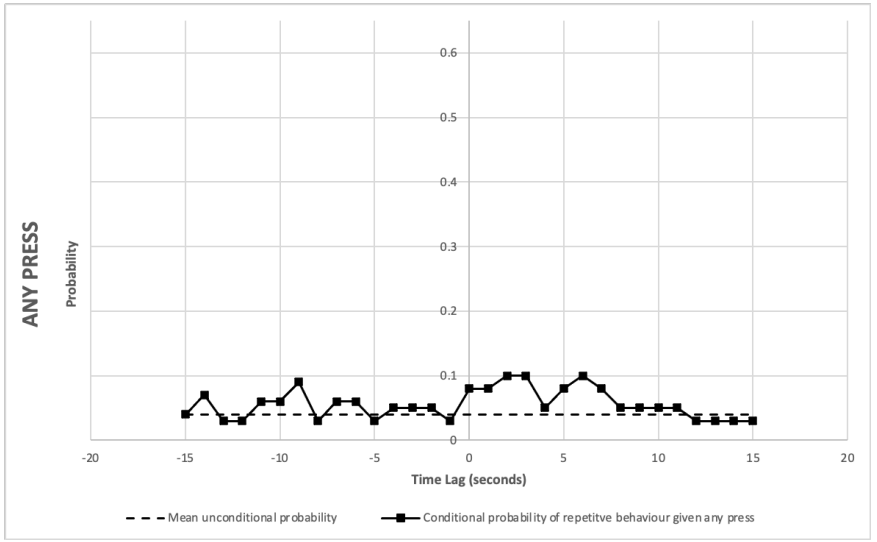

MYSTERY JAR PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of lip lick given jar

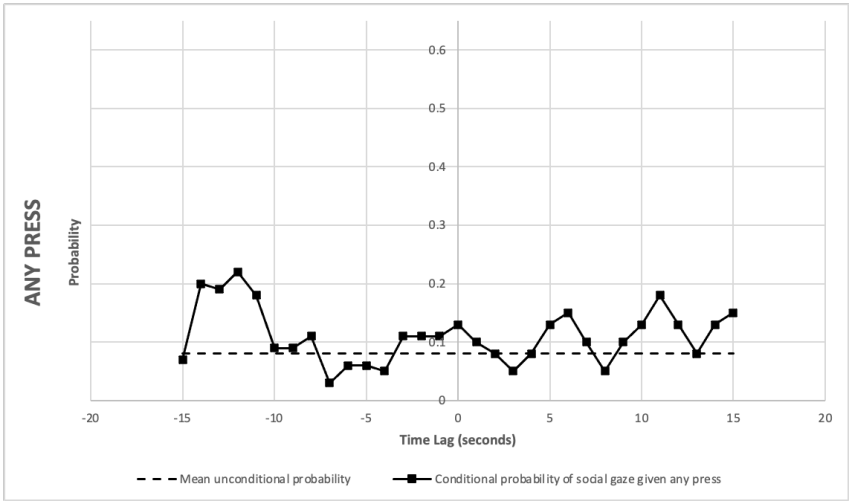

PARENTAL SEPARATION PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of behaviours that challenge given separation

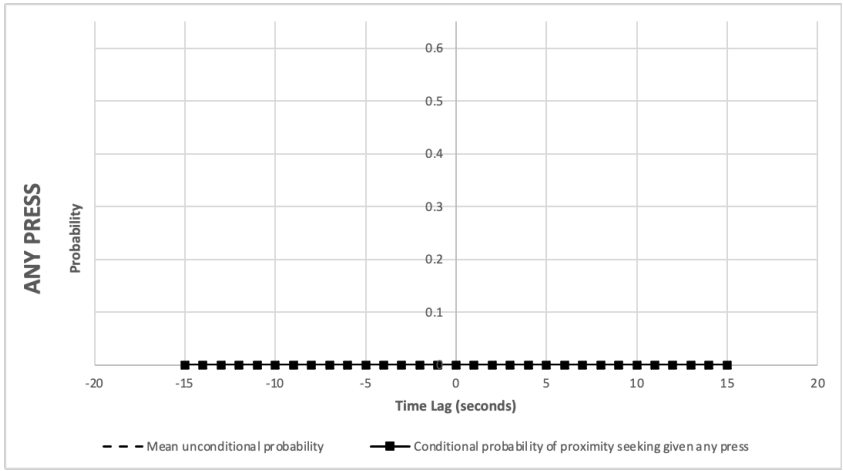
Appendix 37 Chapter five remaining analyses (non-significant)

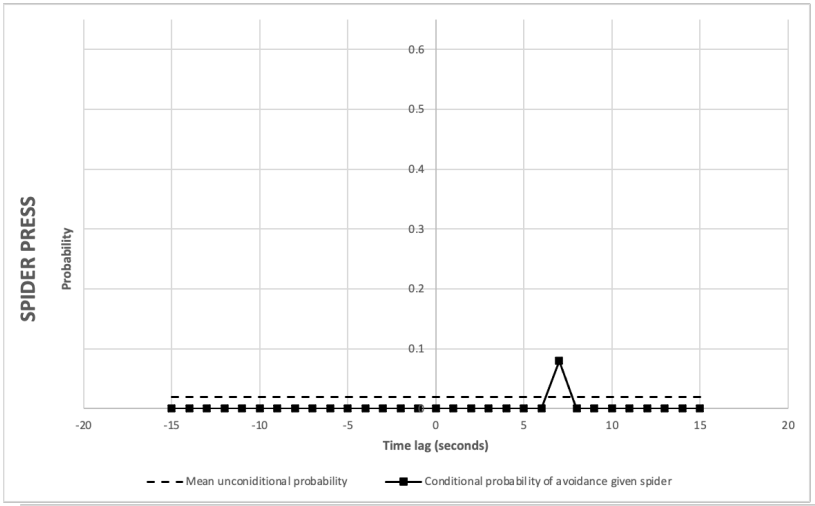
Appendices Figure 159 Remaining analyses which are non-significant exploring sequences of behaviours in relation to any press as well as individual presses

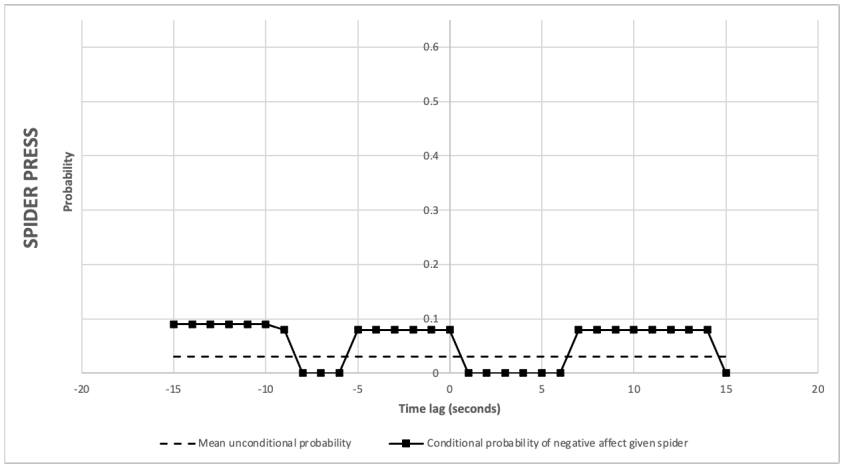


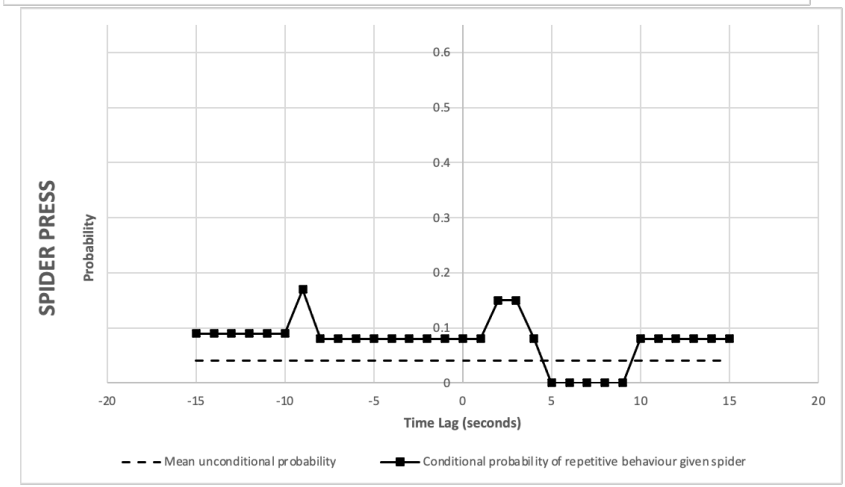


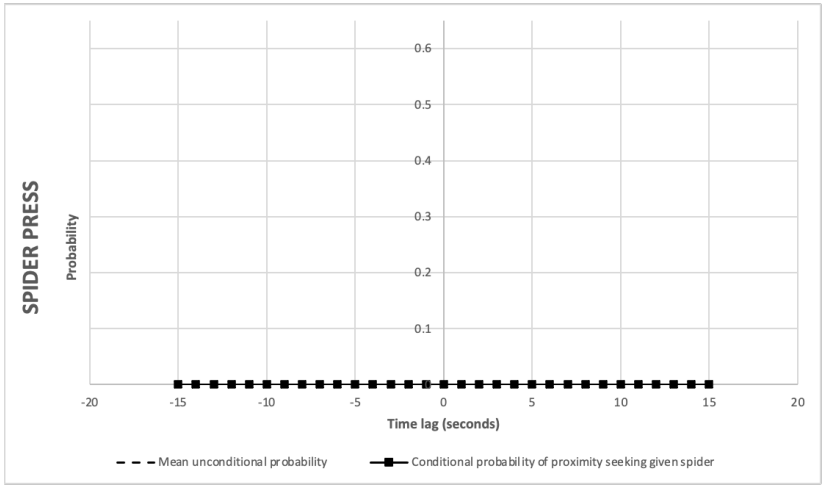


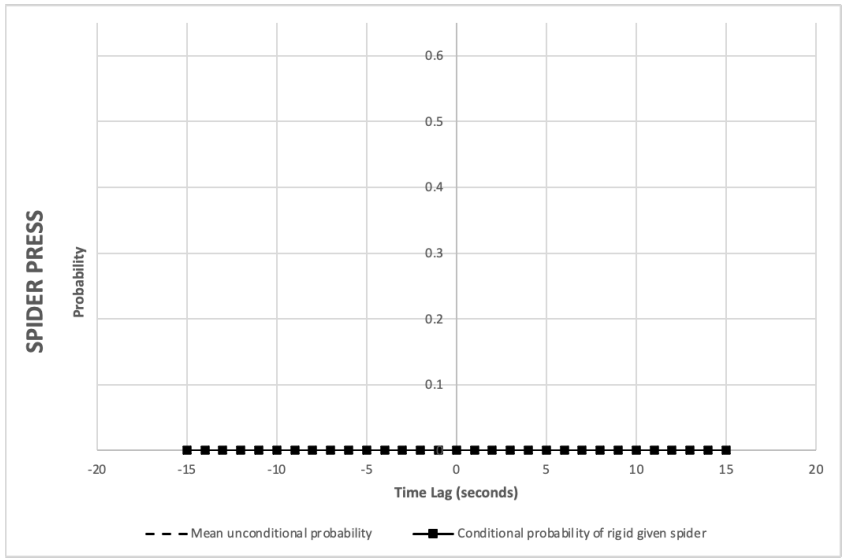


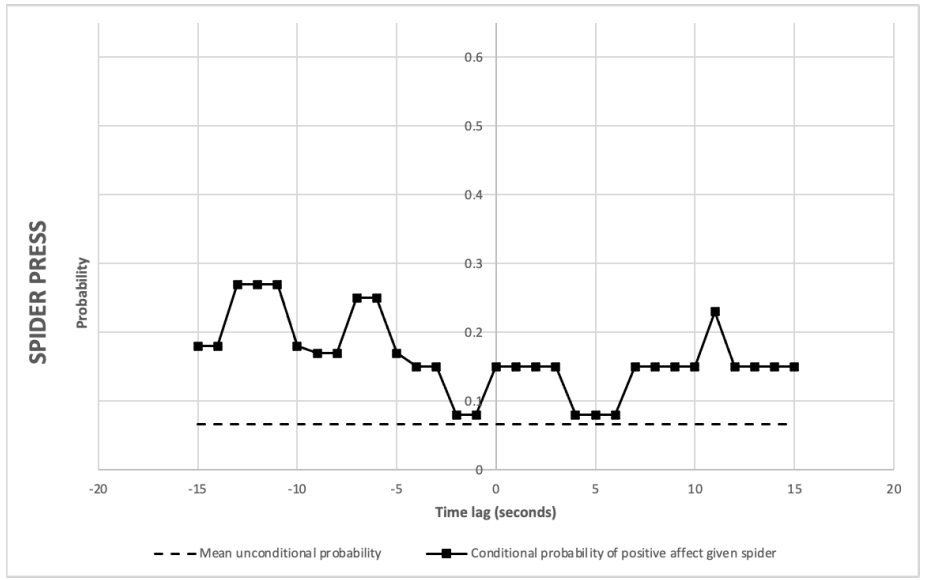

SPIDER PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20 -15 -10 -5 0 5 10 15 20
Time lag (seconds)
Mean unconiditional probability
Conditional probability of avoidance given spider

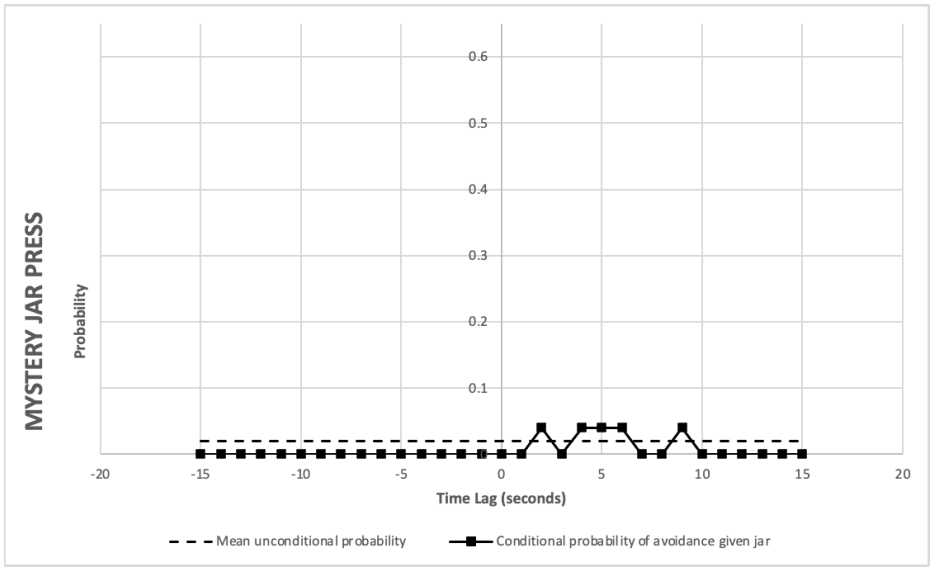

SPIDER PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
0
-20 -15 -10 -5 0 5 10 15 20
Time lag (seconds)
Mean unconditional probability
Conditional probability of negative affect given spider

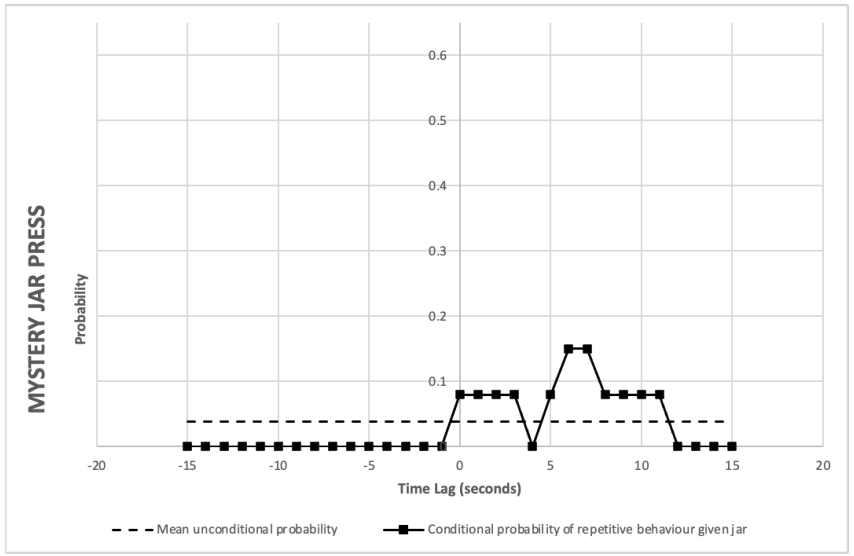

SPIDER PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
0
-20 -15 -10 -5 0 5 10 15 20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of repetitive behaviour given spider

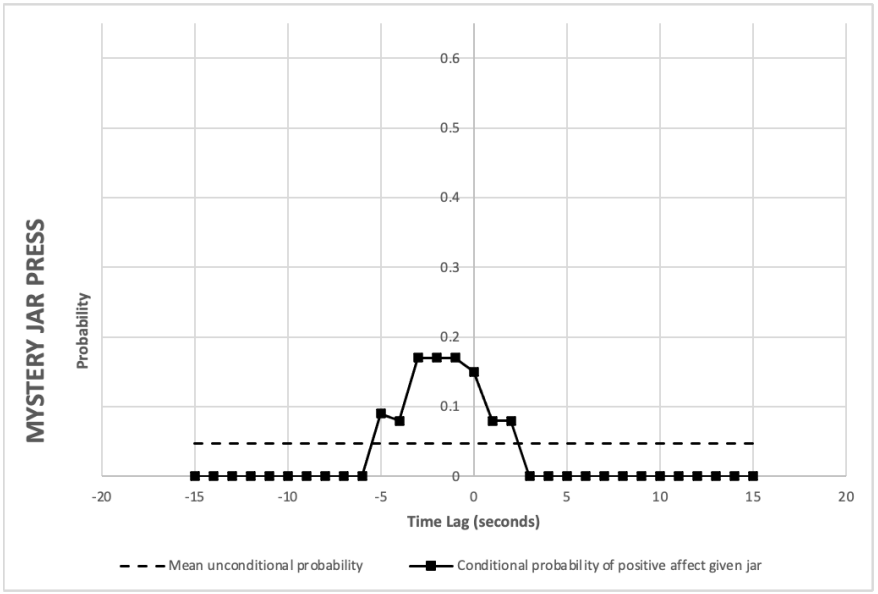

SPIDER PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20 -15 -10 -5 0 5 10 15 20
Time lag (seconds)
Mean unconditional probability
Conditional probability of proximity seeking given spider

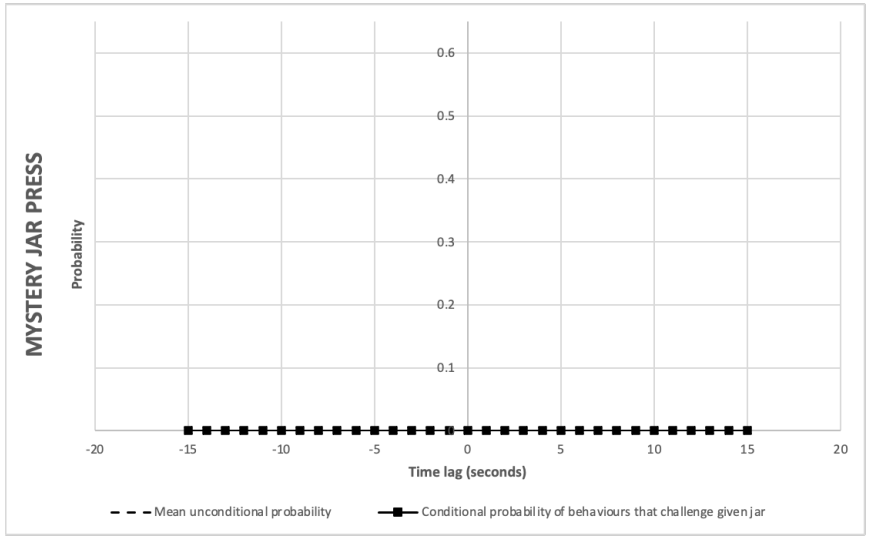

SPIDER PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20 -15 -10 -5 0 5 10 15 20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of rigid given spider

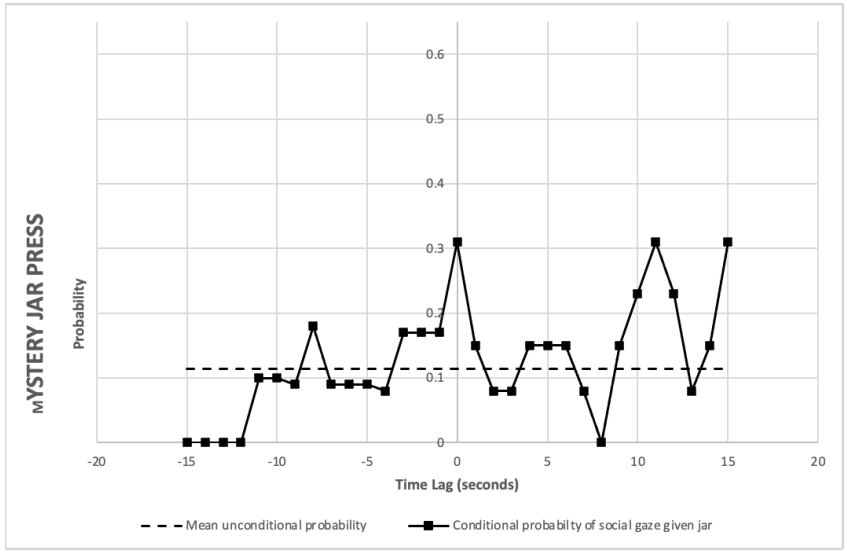

SPIDER PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0
-20 -15 -10 -5 0 5 10 15 20
Time lag (seconds)
Mean unconditional probability
Conditional probability of positive affect given spider

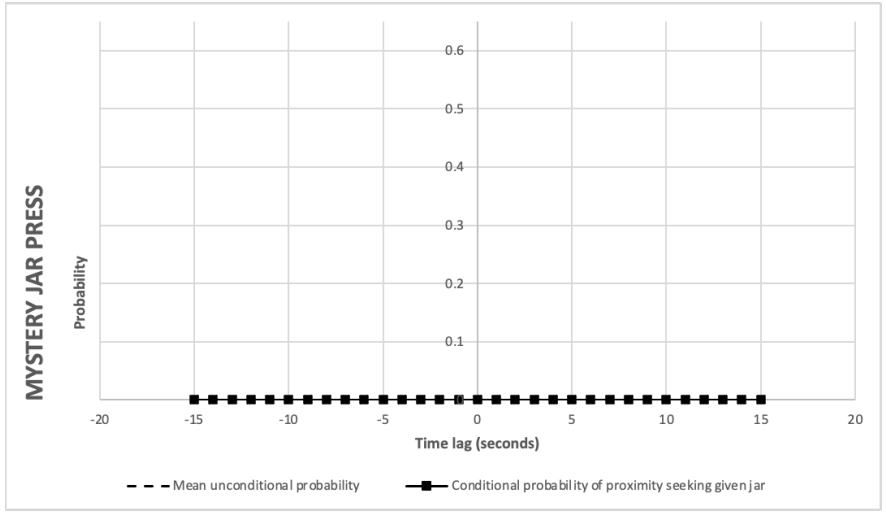

MYSTERY JAR PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20 -15 -10 -5 0 5 10 15 20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of avoidance given jar

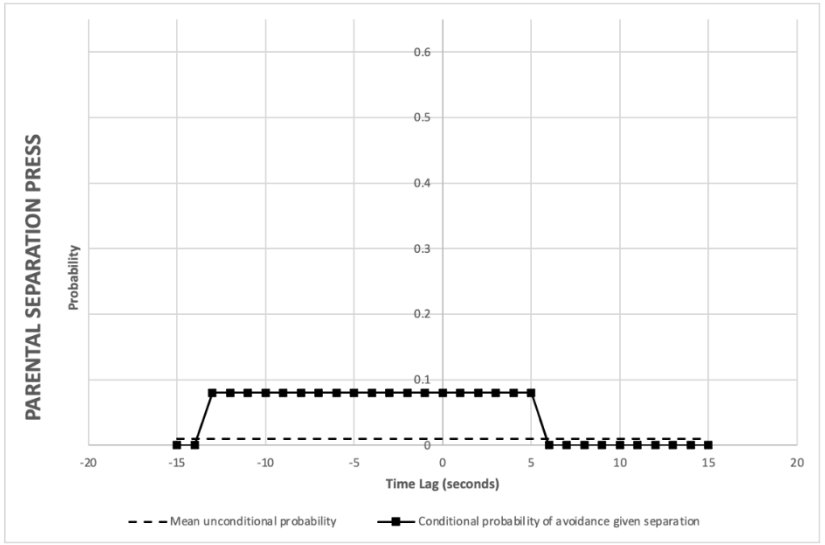

MYSTERY JAR PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20 -15 -10 -5 0 5 10 15 20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of repetitive behaviour given jar

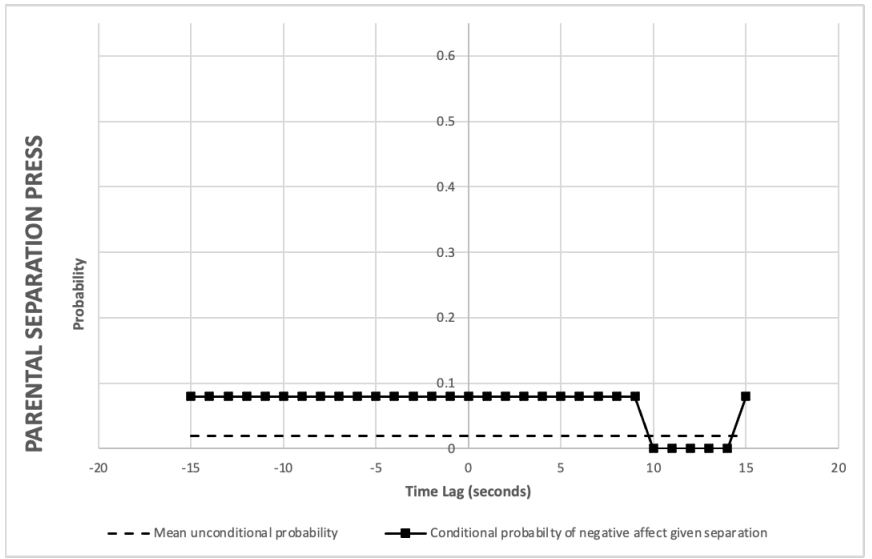

MYSTERY JAR PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
0
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of positive affect given jar

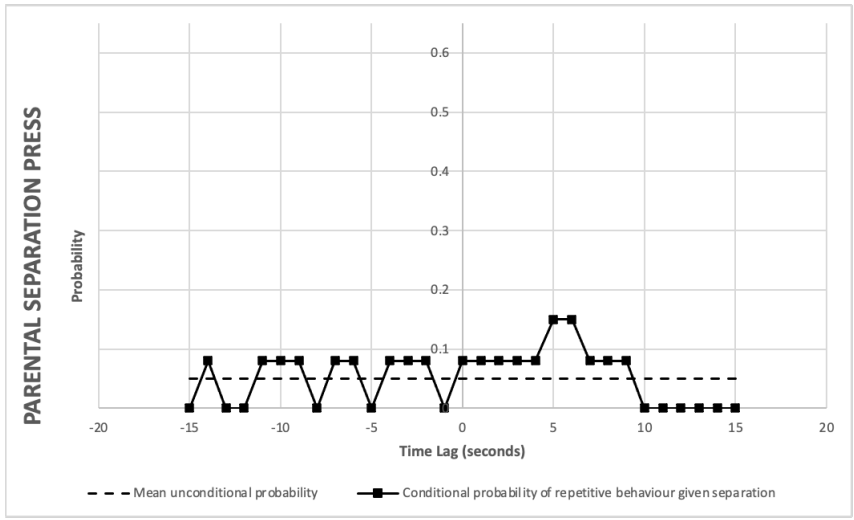

MYSTERY JAR PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20
-15
-10
-5
0
5
10
15
20
Time lag (seconds)
Mean unconditional probability
Conditional probability of behaviours that challenge given jar

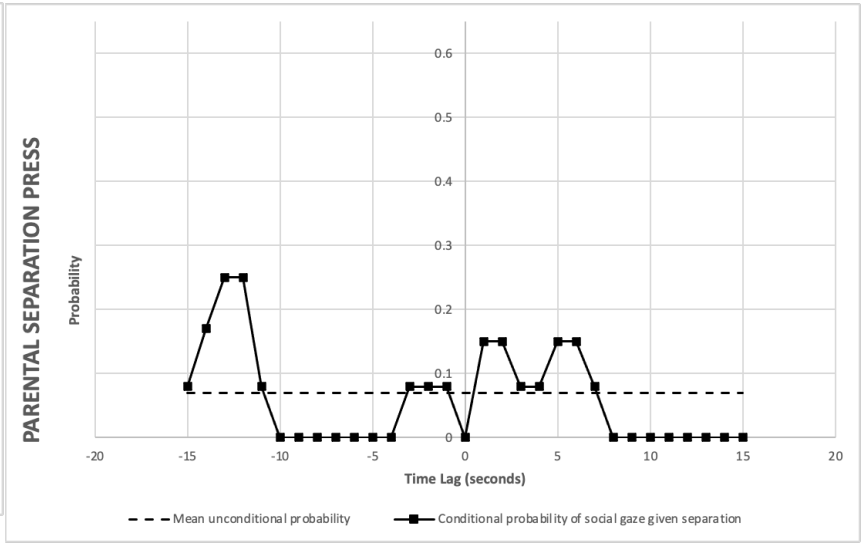

MYSTERY JAR PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
0
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probabilty of social gaze given jar

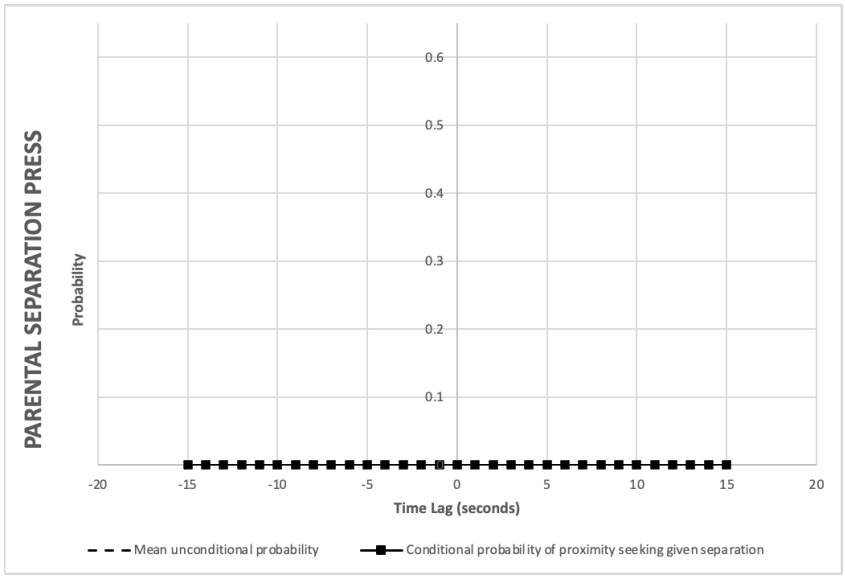

MYSTERY JAR PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20
-15
-10
-5
0
5
10
15
20
Time lag (seconds)
Mean unconditional probability
Conditional probability of proximity seeking given jar

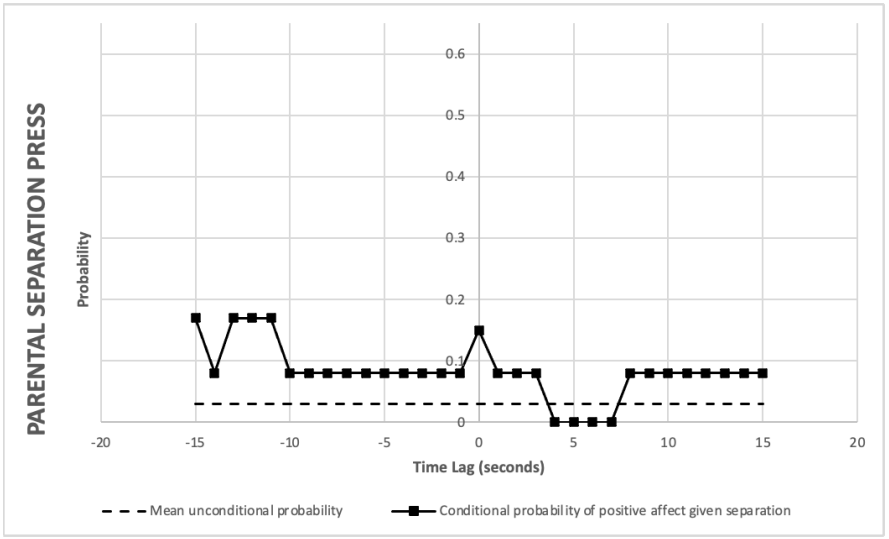

PARENTAL SEPARATION PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
0
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of avoidance given separation


PARENTAL SEPARATION PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
0
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of negative affect given separation


PARENTAL SEPARATION PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of repetitive behaviour given separation


PARENTAL SEPARATION PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
0
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of social gaze given separation


PARENTAL SEPARATION PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0.1
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of proximity seeking given separation

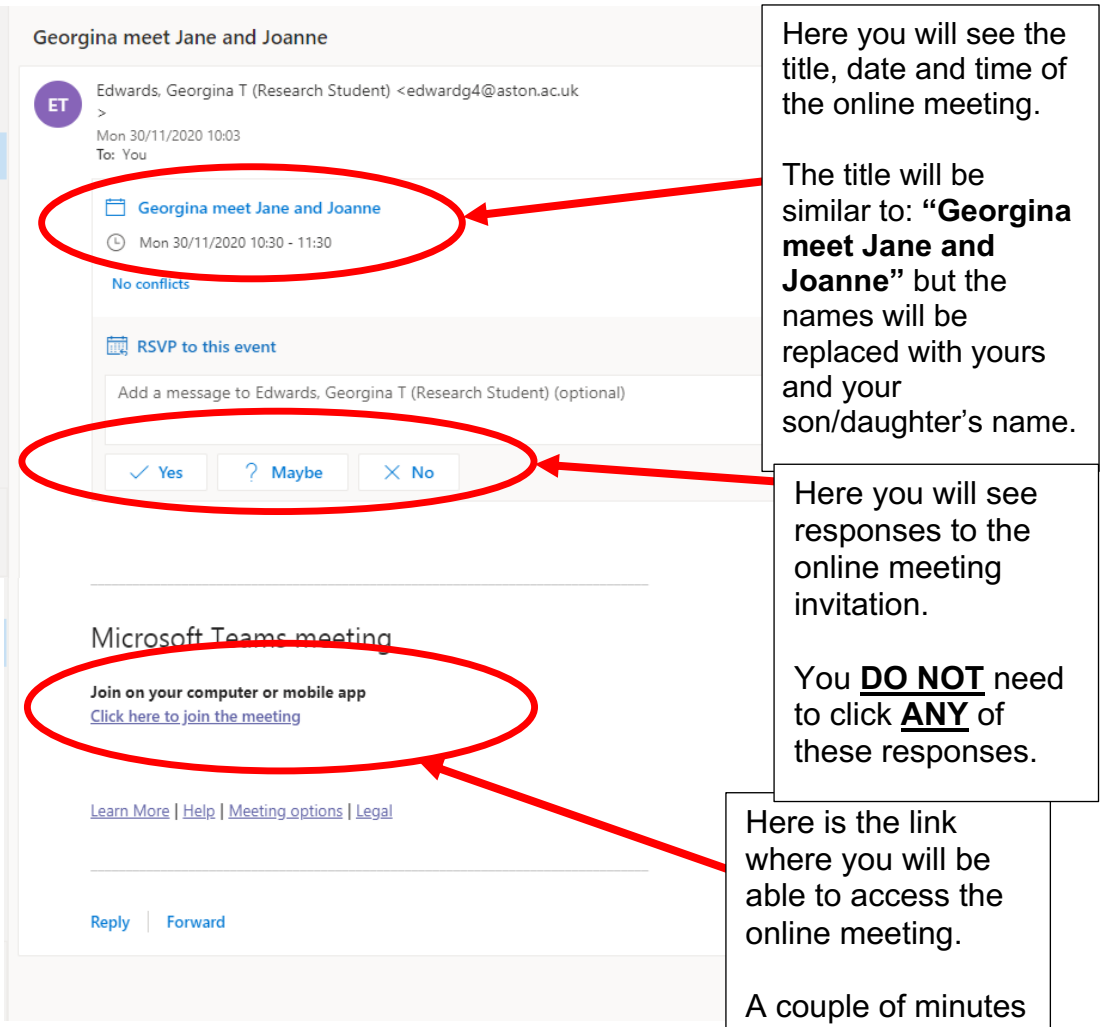

PARENTAL SEPARATION PRESS
Probability
0.6
0.5
0.4
0.3
0.2
0
-20
-15
-10
-5
0
5
10
15
20
Time Lag (seconds)
Mean unconditional probability
Conditional probability of positive affect given separation

Appendix 38 Chapter five Microsoft teams step-by-step instructions

Using Microsoft Teams to join our online meeting

Thank you for agreeing to participate in our research study. Here is a step-by-step guide to help you use Microsoft Teams to join our online meeting where we will complete our online assessments.

1. You will be sent an email from Georgina Edwards (edwardg4@aston.ac.uk) prior to the arranged online meeting. For example, if your arranged online meeting is on a Saturday or Sunday, Georgina will send you an email on the Friday at approximately 5pm. The email you will be sent will look like the image below:



Here you will see the title, date and time of the online meeting.

The title will be similar to: **"Georgina meet Jane and Joanne"** but the names will be replaced with yours and your son/daughter's name.

Here you will see responses to the online meeting invitation.

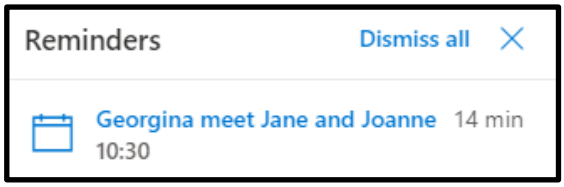
You **DO NOT** need to click **ANY** of these responses.

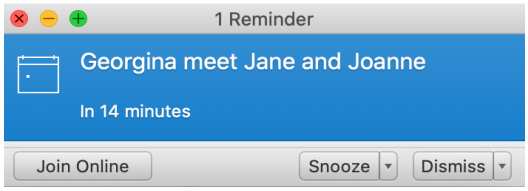
Here is the link where you will be able to access the online meeting.

A couple of minutes before the start of your arranged online meeting, please click on the link **"Click here to join the meeting"** and the link should direct you to the meeting page.

2. A couple of minutes before the arranged online meeting, if you are logged into your email account, you should also see a reminder pop up, that indicates to you that the online meeting is about to start.

   The reminder will look like one of the images below and the reminder may appear in the top or bottom right-hand corner of your screen.





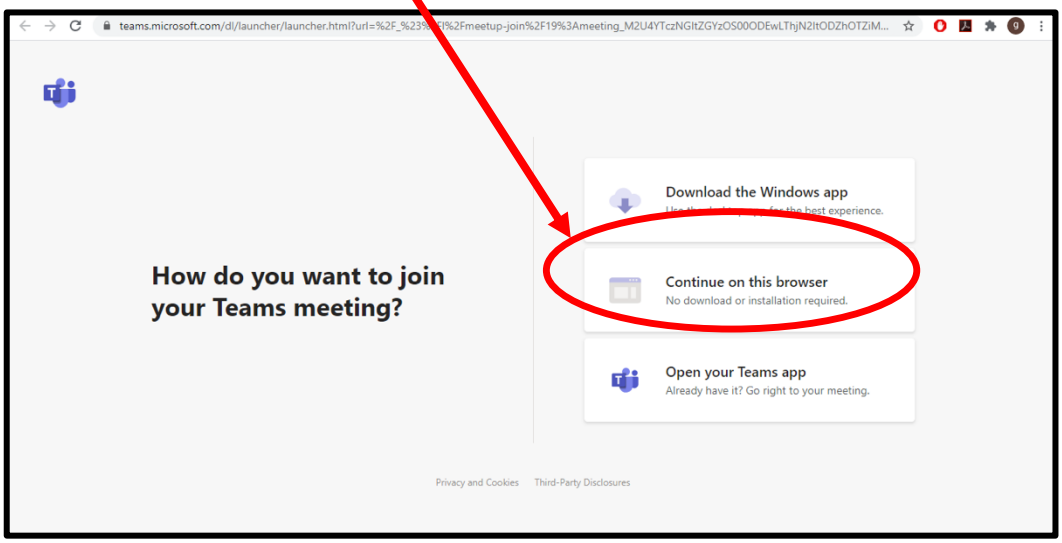
   If you see this reminder, you can also click on the title of the reminder **"Georgina meet Jane and Joanne"** or the button **"Join Online"**.

3. After clicking on the link/button, you should be presented with the following page.

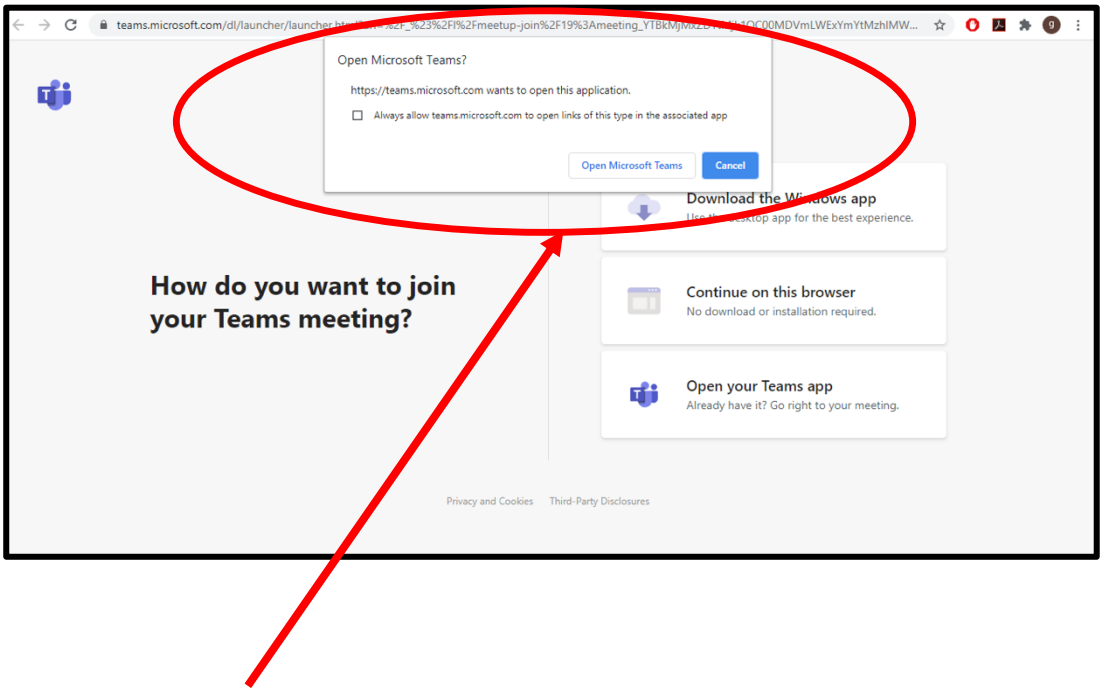
You should be presented with the three options below: 1. Download the Windows app. 2. Continue on this browser. 3. Open your Teams app.

You can click on option 1 if you would like to download the Microsoft Teams app or option 2 to continue to access Microsoft Teams without having to download anything.

Option 2 is the **quickest** option.

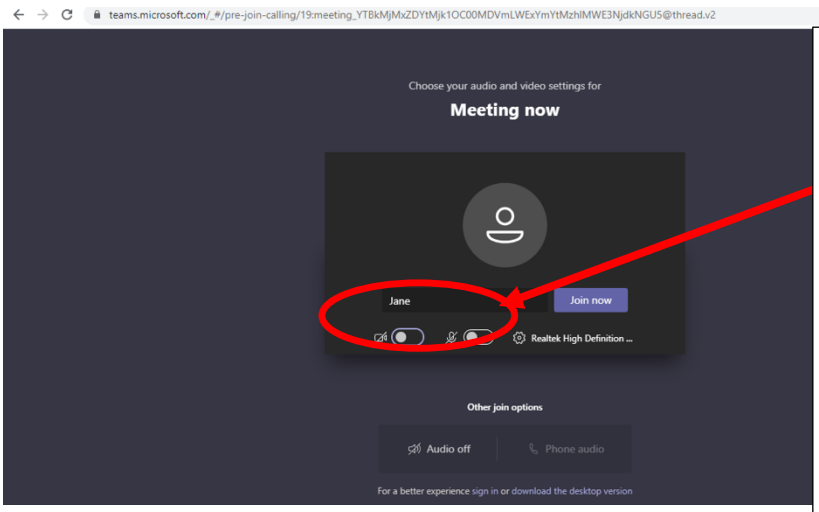


If you already have the Microsoft Teams app downloaded on your device that you are using, you may see a pop up notification, as seen below:



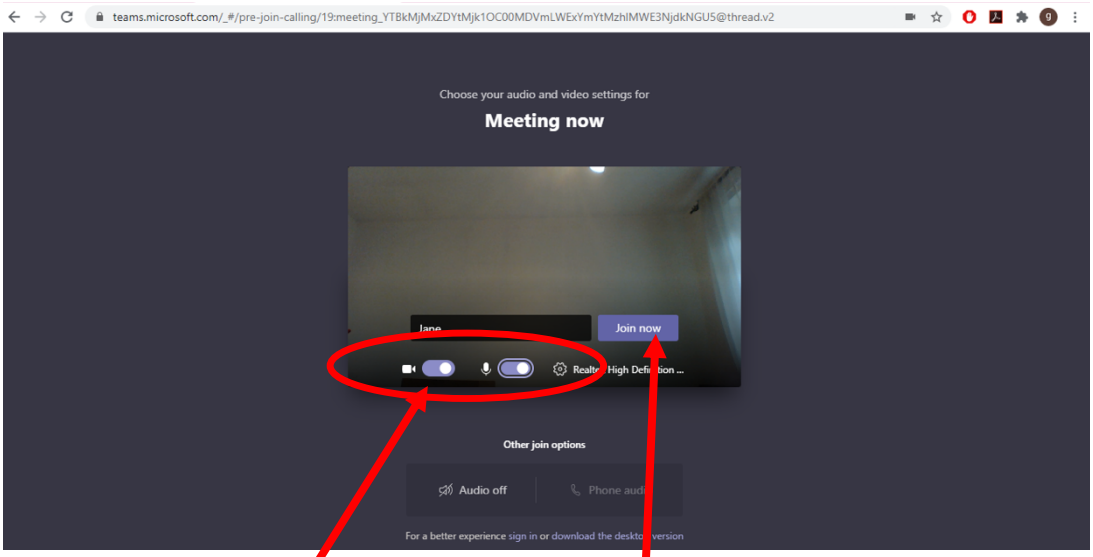
If you see this notification, you can click **'Open Microsoft Teams'** and it should open the app that is already downloaded on your device.

4. Once selecting the appropriate link for your device, you should see the following screen:



Here are two buttons that control your video/camera and your microphone.

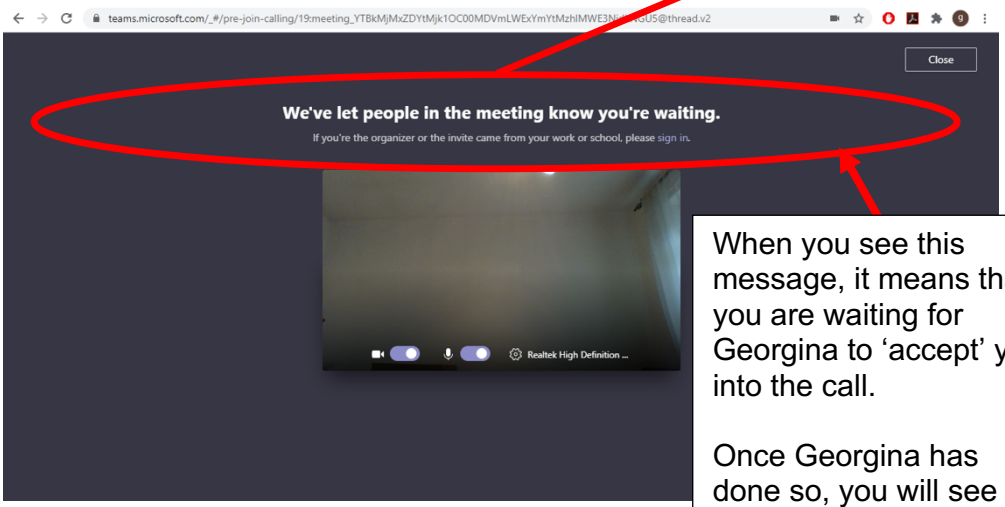
When the white dot is on the left of the button and it looks like this, this means that your video/camera and microphone are **OFF.**



If you click on each button, the white dot will move to the right and the buttons will turn purple, at this point, your camera and microphone should then turn on.

Once you have done this, you can then press the button **'Join now'**.

After clicking on the 'Join now' button, you should then see this screen



When you see this message, it means that you are waiting for Georgina to 'accept' you into the call.

Once Georgina has done so, you will see Georgina and she should be able to see you and the online assessments can start.