Depression treatment in youth: effects on anxiety and dropout

Isobel M Wright

Thesis portfolio submitted in part fulfilment of the Doctorate in Clinical Psychology

Doctoral Programme in Clinical Psychology

University of East Anglia

Faculty of Medicine and Health Sciences

Submission Date: 4th March 2019

Word count: 22856

Acknowledgements

I would firstly like to thank Professor Richard Meiser-Stedman for his thoughtful and supportive supervision, enthusiasm and generosity with his time. I have greatly appreciated his guidance and encouragement, prior to and during training. I was privileged to be allowed access to the IMPACT trial dataset, I am indebted to the study team and all clinicians, researchers and participants involved in the trial; particular thanks to Sharon Neufeld, Professor Ian Goodyer and Dr Paul Wilkinson from the Department of Psychiatry, University of Cambridge. I would like to express my appreciation for my fellow trainees and my family for their support throughout this process. Finally, to C, thank you for your patience, humour and constant support.

Abstract

Background: Depression is a prevalent and disabling condition in youth. Concurrent anxiety symptoms are common. Several psychological treatments have demonstrated effectiveness at reducing depression in youth, but the acceptability of these treatments and impact on concurrent anxiety symptoms are not known.

Aims: To investigate dropout from youth depression treatments as a measure of acceptability. To investigate the trajectory of anxiety symptoms over the course of intervention aimed at depression using longitudinal data from a randomised controlled trial ('IMPACT', Goodyer et al., 2017).

Methods: A meta-analysis calculated dropout rates from randomised controlled trials investigating psychotherapy interventions for depression in youth. For the empirical study, growth mixture modelling was used to identify trajectories of anxiety symptoms in adolescents during depression intervention and follow-up.

Results: The meta-analysis included 37 studies (N=4343), and the overall estimate of dropout from active interventions was 14.6% (CI 12.0, 17.4); in general dropout was equally likely across intervention and control conditions, and interventions offering more sessions had fewer dropouts. From the 'IMPACT' trial dataset a 2-class piecewise model was identified. The smaller class (n=46) showed an improvement in anxiety symptoms during but not after treatment, the larger class (n=419) had no change in anxiety symptoms during or after treatment. When gender and baseline anxiety were controlled for, greater impairment in mood, self-esteem and increased suicidal thoughts were associated with membership to the non-improving class.

Conclusions: Depression interventions were acceptable, with little dropout. Anxiety symptoms may not be responsive to depression treatment in youth. Offering more

sessions and assessment of non-target symptoms for potential intervention may be beneficial.

Table of Contents

List of Tables

List of Figures

Chapter 1: Systematic Review

Prepared for submission to the Journal of Affective Disorders

See Appendix A for Instructions for authors

UEA word count (all content except references and appendices): 5428

Journal word count (excluding abstract, highlights, tables, references and appendices): 3052

For ease of reference, Tables and Figures are presented alongside the text.

Dropout from psychological treatments for depression in young people: a systematic review and meta-analyses.

Isobel Wright[a] and Dr Richard Meiser-Stedman[a]

[a]Department of Clinical Psychology, University of East Anglia, Norwich, United Kingdom.

Correspondence regarding this article should be addressed to Dr Richard Meiser-Stedman, Department of Clinical Psychology, University of East Anglia, Norwich Research Park, Norwich, NR4 7TJ. Email r.meiser-stedman@uea.ac.uk. Tel: 01603 593601 Fax: 01603 593752.

Declarations of interest: none.

Abstract

Background

Depression is a prevalent and disabling condition in youth. Treatment efficacy has been demonstrated for several therapeutic modalities. Acceptability of treatments is also important to explore and was addressed by investigating treatment dropout using meta-analyses.

Methods

A systematic search was conducted using MEDLINE, CINAHL and PsycARTICLES databases. Peer-reviewed randomised controlled trials investigating psychotherapy treatment of depression in youth were included. Proportion meta-analyses were used to calculate estimated dropout rates; odds ratios assessed whether there was greater dropout from intervention or control arms and meta-regressions investigated associations between dropout, study and treatment characteristics.

Results

Thirty-seven studies were included (N=4343). Overall estimate of dropout from active interventions was 14.6%. Dropout was equally likely from intervention and control conditions, aside from trials of family/dyadic interventions (dropout more likely from control). Interventions offering more sessions had less dropout and there was less dropout from IPT than other interventions. There were no significant associations between dropout and study quality, treatment duration, CBT, family or individual versus other approaches.

Limitations

Given limited power, null findings should not be interpreted as confirmed absence of effects. Lack of consistent reporting decreased the factors which could be analysed.

Conclusions

Dropout from depression treatment in youth was similar across different types of intervention and control conditions. Future treatment trials should specify minimum treatment dose, define dropout and provide information about participants who dropout. This may inform treatment choice and modification of treatments.

Key words: depression, psychotherapy, youth, dropout, meta-analysis

Highlights

- Dropout from psychotherapy interventions for depression in youth was 14.6%.
- Overall dropout was equally likely from intervention and control conditions.
- Interventions offering more sessions had less dropout.
- Lack of detail reported regarding dropout limited the factors to be analysed.

Introduction

Depression is a prevalent and disabling condition for all ages, including youth. In 13-18 year olds the prevalence of depression has been estimated to be 5.6% (Costello, Erkanli, & Angold, 2006). The lifetime prevalence of depression with severe impairment by late adolescence has been estimated at 8.7% (Merikangas et al., 2010). Adolescent depression has been associated with poorer physical health, higher healthcare utilisation and increased work impairment due to physical health by age 20 (Miller, Constance, & Brennan, 2007) and significantly reduced years of schooling (Fletcher, 2010). Early-onset depression often continues into adulthood, has high comorbidity with other psychiatric disorders, is associated with poor psychosocial and academic outcomes and increased risk for bipolar disorder, substance abuse and suicide (Birmaher et al., 1996). In adults, depression has been identified as one of the ten leading diseases for global disease burden (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006). Suicide is one of the leading causes of death in youth globally (Blum & Nelson-Mmari, 2004).

Effectiveness for depression treatment in youth has been demonstrated for several therapy modalities. Interpersonal psychotherapy (IPT) and Cognitive Behavioural Therapy (CBT) have been found to be more effective than control conditions in meta-analyses (Arnberg & Ost, 2014; Pu et al., 2017; Zhou et al., 2015). A systematic review found preliminary evidence that computerised CBT is acceptable and effective for the treatment of depression in children and adolescents (Richardson, Stallard, & Velleman, 2010). Limited evidence supports the effectiveness of behavioural activation for depression in young people (Tindall et al., 2017). There is also some evidence that family approaches can be effective in treating depression in young people (Diamond, Russon, & Levy, 2016). Medication

is not a focus of the present review, but meta-analyses have found that combined treatment with CBT and antidepressants can be more effective than antidepressants alone in adolescents (Calati et al., 2011). However, in a large meta-analysis evaluating youth psychological therapy for internalizing and externalizing disorders, depression treatment was found to have the weakest mean effect size (Weisz et al., 2017). Alongside further treatment development it is necessary to determine which interventions are more acceptable.

Treatment effectiveness is not the only factor to consider; it is important to work out which interventions young people find acceptable and are able to engage in. This can be explored by investigating treatment dropout. Poor clinical outcomes, demoralisation of clinicians and overutilization of services have been associated with adults who have terminated therapeutic interventions early (Reis & Brown, 1999). Attrition decreases the cost-effectiveness of services (the financial burden from staff salaries and overhead costs from missed appointments) and contributes to waiting lists (Barrett, Chua, Crits-Christoph, Gibbons, & Thompson, 2008).

In order to inform choices about which treatments may balance both efficacy and retention it is necessary to know what the typical dropout rate for psychotherapeutic depression treatment is and which factors are associated with dropout. Meta-analyses investigating psychotherapy interventions for depression in adults have found average dropout rates from 17.5% to 19.2% (Cooper & Conklin, 2015; Swift & Greenberg, 2014). Longer treatment duration has been associated with higher rates of dropout in adults (Cooper & Conklin, 2015). Therapeutic modality also impacts retention. In one meta-analysis addressing adults, integrative approaches had significantly lower dropout rates than cognitive behavioural-analysis system of psychotherapy (CBASP), cognitive therapy, CBT, IPT, solution-focussed

and supportive psychotherapy. The same study found CBASP had significantly higher dropout than cognitive therapy and integrative approaches (Swift & Greenberg, 2014). One meta-analysis investigated dropout from antidepressant drug treatments in adolescents and found that medication only had highest dropout; CBT combined with drugs had lower nonadherence prevalence (Rohden et al., 2017). To the authors' knowledge there have been no dropout meta-analyses focussing specifically on psychotherapeutic treatment of depression in youth and no investigation of moderators.

The present review had three aims. The first was to conduct a systematic review and meta-analysis of randomised controlled trials on psychotherapeutic treatments for depression in youth and calculate a pooled estimate of dropout rate. The second aim was to determine whether any participant or intervention factors are related to dropout. The third aim was to explore reasons for dropout, if data on this were available.

Method

Details of the protocol for this systematic review were registered on PROSPERO (CRD42018092696).

Study selection

MEDLINE, CINAHL and PsycARTICLES databases were searched. No filters were applied. The following search terms were entered: depress* or Depression [MeSH] or Depressive Disorder [MeSH] AND child* OR young OR adolescen* OR youth OR pupil OR student or Child [MeSH] or Adolescent [MeSH] AND psychotherapy OR therapy OR cognitive therap* OR CBT OR psychodynamic OR bibliotherap* OR client-cent* OR intervention OR interpersonal OR family

therap* OR counsel* OR Psychotherapy [MeSH] AND RCT OR random* OR control* OR clinical trial OR randomised OR randomized or Randomized Controlled Trial [MeSH].

The inclusion criteria were:

- Peer-reviewed journal articles published in English;
- Randomised controlled trials investigating psychotherapy interventions with participants aged up to (and including) 18 years;
- Participants met criteria for diagnosis of depression or scored above a cut-off.

Studies investigating interventions which were universally delivered (e.g. to a whole school year group) were excluded, as it was not possible to determine dropout rates for participants who met criteria for depression prior to the intervention. Preventative intervention studies were excluded, as the focus of this review is treatment for existing depression. Inpatient interventions were not included. Interventions which were systemic changes (e.g. quality improvement/collaborative care) were not included, as these are not psychotherapy interventions. Transdiagnostic or interventions where depression was not the primary treatment target were also excluded. Studies which selected participants based on suicidality or self-harm only (without also meeting criteria/scoring above cut-off for depression) were not included.

Screening

Titles and abstracts were screened by the first author and irrelevant studies excluded. Full texts of relevant studies were sought, and inclusion criteria applied. In ambiguous cases the second author was consulted.

Data extraction

Data were extracted by the first author. The extracted data included information about methodology, participant characteristics, whether/how treatment completion and dropout were defined, intervention/s, number of participants who dropped out at different stages and their characteristics, reasons given for dropout. It was noted whether studies defined dropout *a priori*.

In the current review two definitions of 'dropout' are used: study rated treatment non-completion, or if this was unavailable, participants who had missing post-treatment assessment data. The former was preferred in order to capture dropout from treatment rather than research assessment. Withdrawal post randomisation was considered dropout. These two definitions were investigated separately in sub-group analyses.

Study quality was rated on a six-point scale. One point was given for each of the following: intent to treat analysis; presentation of a CONSORT diagram; definition of treatment completion; utilisation of a treatment manual; therapists trained in conducting the therapy; and treatment integrity checked (e.g. recording and rating of sessions, use of measures, covered in supervision). The latter three criteria were defined in a review of empirically supported therapies (Chambless & Hollon, 1998) and used in subsequent psychological treatment reviews (Cuijpers et al., 2014; Gersh et al., 2017). Self-directed interventions where clients were provided with standardised content (i.e. bibliotherapy or computerised treatment) were rated as meeting the latter three criteria; as the material received was inherently identical across participants. Where information about a criterion was not presented (e.g. no mention of treatment integrity/adherence checks) a score of 0 was given.

In order to test inter-rater reliability of quality rating, 8 studies (22% of those included) were randomly selected and co-rated by two collaborators using a coding guide that was specifically created for this review, with the six-point scale described above. Cohen's Kappa with all datapoints was 0.58, indicating moderate agreement (Landis & Koch, 1977).

Analysis

Proportion meta-analyses were carried out to calculate the estimated dropout rates using OpenMeta[Analyst] software (Wallace et al., 2012), which uses the metafor package in R (Viechtbauer, 2010). A random effects model was used in order to take account of the degree of heterogeneity between studies (Borenstein, Hedges, Higgins, & Rothstein, 2009). Studies were weighted based on sample size using the inverse variance. Heterogeneity was examined using Cochran's *Q* and I^2, which indicates how much variation across studies is due to heterogeneity rather than chance (Higgins & Thompson, 2002). Proportion meta-analyses were conducted for all arms and for sub-groups of intervention and control conditions.

Odds ratios were used to assess whether there was a higher proportion of dropout from intervention or control arms. Sub-group analyses of therapeutic modalities (CBT, family approaches, IPT) versus different control conditions (any, active control, wait list or treatment as usual) were carried out.

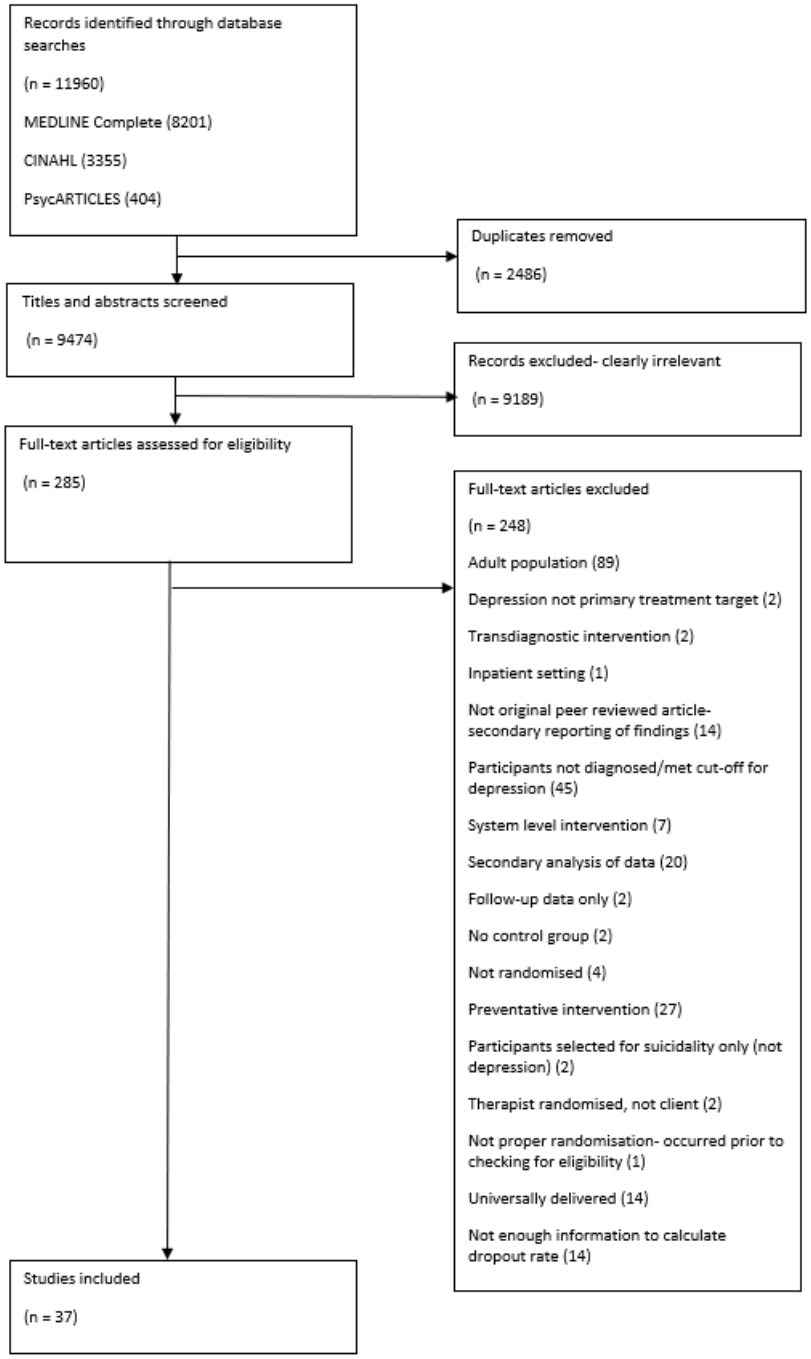
Meta-regressions were conducted to investigate whether there was a relationship between dropout and study quality, number of sessions and treatment duration. Dropout was compared between types of intervention; CBT, family and IPT modalities were separately grouped together and compared to all other active

treatment arms. Interventions delivered individually (across modalities) were compared to all other methods of delivery. Studies were only included in the meta-regressions if they reported the relevant variable.

For all analyses results for studies that defined dropout were also reported separately; overall results included studies where dropout was not defined specifically and instead inferred from missing post-treatment assessment data.

Results

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.



Thirty-seven eligible studies were identified (see Figure 1). A summary of these is presented in Table 1. There were a total of 4343 participants, with an approximate mean age of 14.2 years, approximately 37% male (1 study gave median

ages for treatment arms; 1 did not collect ages, just school year; 6 studies were included in the calculations but only reported demographics for completers; 2 studies did not report sex). Studies were mostly conducted in the USA (48.6%) and UK (21.6%). Sample sizes ranged from 20 to 470. Duration of interventions ranged from 4 to 39 weeks.

Table 1. Description of included studies.

Study No.	Study	Country	Total participants	% Male	Mean age (years)	Treatments	Number of sessions	Duration of treatment (weeks)	Dropout, all arms (%)	
									Study-defined	Post-treatment assessment missing
1	(Ackerson, Scogin, McKendree-Smith, & Lyman, 1998)	USA	30	36.4[a]	15.9[a]	Immediate/delayed cognitive bibliotherapy	-	4	26.7	
2	(Brent et al., 1997)	USA	107	24.3	15.6	CBT/Systemic Behaviour Family Therapy/Nondirective supportive treatment	12-16	12-16	27.1	
3	(Brent et al., 2008)	USA	334	30.3	15.9	Venlafaxine/Venlafaxine + CBT/ SSRI/ SSRI + CBT	12	12	30.5	

Study No.	Study	Country	Total participants	% Male	Mean age (years)	Treatments	Number of sessions	Duration of treatment (weeks)	Dropout, all arms (%)	
									Study-defined	Post-treatment assessment missing
4	(Clarke, Rohde, Lewinsohn, Hops, & Seeley, 1999)	USA	123	29.2[a]	16.2[a]	Group CBT/ Group CBT + parent group / Wait list	16	8	13.8	
5	(Clarke et al., 2016)	USA	212	31.6	14.6	TAU + CBT / TAU	14	12		12.3
6	(Clarke et al., 2005)	USA	152	22.4	15.3	Brief CBT + TAU SSRIs / TAU SSRIs	9	12		19.7
7	(Diamond, Reis, Diamond, Siqueland, & Isaacs, 2002)	USA	32	22.0	14.9	Attachment Based Family Therapy / Wait List	12	12		3.1

Study No.	Study	Country	Total participants	% Male	Mean age (years)	Treatments	Number of sessions	Duration of treatment (weeks)	Dropout, all arms (%)	
									Study-defined	Post-treatment assessment missing
8	(Fristad et al., 2016)	USA	72	57.0	11.6	Omega 3 / Psychoeducation + Placebo / Psychoeducation + Omega 3 / Placebo	12	12		25.0
9	(Gaete et al., 2016)	Chile	342	49.7	15.9	Group CBT / Control (no intervention)	8	8		18.4
10	(Goodyer et al., 2008)	UK	208	26.0	14.0	SSRI / SSRI + CBT	12	12	9.1	
11	(Goodyer et al., 2017)	UK	470	25.2	15.0	Brief Psychological Intervention / CBT / Short Term Psychoanalytical Psychotherapy	12-28	20-30	9.6	
12	(Iftene, Predescu, Stefan, & David, 2015)	Romania	88	44.3	15.3	Rational Emotive CBT Group / Medication / Rational Emotive CBT Group + Medication	16	16	15.9	

Study No.	Study	Country	Total participants	% Male	Mean age (years)	Treatments	Number of sessions	Duration of treatment (weeks)	Dropout, all arms (%)	
									Study-defined	Post-treatment assessment missing
13	(Israel & Diamond, 2013)	Norway	20	45.0	15.6	Attachment Based Family Therapy / TAU	-	12		30.0
14	(Luby, Barch, Whalen, Tillman, & Freedland, 2018)	USA	229	65.1	5.2	Parent-Child Interaction Therapy / Wait List	20	18		16.6
15	(Luby, Lenze, & Tillman, 2012)	USA	54	62.8[a]	4.4[a]	Parent-Child Interaction Therapy / Psychoeducation	12-14	12		46.3
16	(March et al., 2004)	USA	439	45.6	14.6	Fluoxetine + CBT / Fluoxetine / CBT / Placebo	15	12		18.2
17	(McCauley et al., 2016)	USA	60	36.0	14.9	Behavioural Activation / Clinic Standard Care	14	-	11.7	
18	(Melvin et al., 2006)	Australia	73	34.3	15.3	CBT / Sertraline / CBT + Sertraline	12	12	15.1	

Study No.	Study	Country	Total participants	% Male	Mean age (years)	Treatments	Number of sessions	Duration of treatment (weeks)	Dropout, all arms (%)	
									Study-defined	Post-treatment assessment missing
19	(Merry et al., 2012)	New Zealand	187	34.2	15.6	Computerised CBT (SPARX) / TAU	7	9		9.1
20	(Mufson, Weissman, Moreau, & Garfinkel, 1999)	USA	48	27.1	15.8	Interpersonal psychotherapy for depressed adolescents / Clinical monitoring	12	12	33.3	
21	(Mufson et al., 2004)	USA	64	16.0	15.1	Interpersonal psychotherapy for depressed adolescents / TAU school clinic	12	12-16	10.9	
22	(Nelson, Barnard, & Cain, 2003)	USA	38	71.4[a]	10.3[a]	CBT via videoconferencing / CBT face to face	8	8	26.3	

Study No.	Study	Country	Total participants	% Male	Mean age (years)	Treatments	Number of sessions	Duration of treatment (weeks)	Dropout, all arms (%)	
									Study-defined	Post-treatment assessment missing
23	(O'Shea, Spence, & Donovan, 2015)	Australia	39	15.4	15.3	Group Interpersonal Psychotherapy / Individual Interpersonal Psychotherapy	12	12		10.3
24	(Poole et al., 2018)	Australia	64	26.6	15.2	Multi-family Group intervention (BEST MOOD) / Supportive parenting programme	8	8		20.3
25	(Reynolds & Coats, 1986)	USA	30	36.7	15.7	CBT Group / Relaxation Training Group	10	5		20.0
26	(Rickhi et al., 2015)	Canada	31	29.0	15.3	Online spirituality/compassion programme (LEAP) / Wait List	8	8	16.1	

Study No.	Study	Country	Total participants	% Male	Mean age (years)	Treatments	Number of sessions	Duration of treatment (weeks)	Dropout, all arms (%)	
									Study-defined	Post-treatment assessment missing
27	(Rosselló, Bernal, & Rivera-Medina, 2012)	USA	112	44.6	14.5	Individual CBT / Group CBT / Individual Interpersonal Psychotherapy / Group Interpersonal Psychotherapy	12	12	5.4	
28	(Smith et al., 2015)	UK	112	-	-	Computerised CBT (Stressbusters) / Wait List	-	8		1.8
29	(Stallard, Richardson, Velleman, & Attwood, 2011)	UK	20	66.6[a]	-	Computerised CBT (Think Feel Do) / Wait List	6	6	25.0	
30	(Stasiak, Hatcher, Frampton, & Merry, 2014)	New Zealand	34	58.8	15.2	Computerised CBT (The Journey) / Computerised Psychoeducation	7	10	11.8	

Study No.	Study	Country	Total participants	% Male	Mean age (years)	Treatments	Number of sessions	Duration of treatment (weeks)	Dropout, all arms (%)	
									Study-defined	Post-treatment assessment missing
31	(Tang, Jou, Ko, Huang, & Yen, 2009)	Taiwan	73	-	15.3	Interpersonal psychotherapy for depressed youth with suicidal risk / Psychoeducation and supportive counselling	12	6	4.1	
32	(Tompson, Sugar, Langer, & Asarnow, 2017)	USA	134	44.0	10.8	Family focussed treatment for childhood depression / Individual supportive psychotherapy	15	22		13.4
33	(Topooco et al., 2018)	Sweden	70	5.7	17.0	Online CBT including chat sessions / Online attention control including messaging	16	8		5.7
34	(Trowell et al., 2007)	UK, Greece, Helsinki	72	62.0	11.7	Individual Psychodynamic Psychotherapy / Family Therapy	8-30	39		4.2

Study No.	Study	Country	Total participants	% Male	Mean age (years)	Treatments	Number of sessions	Duration of treatment (weeks)	Dropout, all arms (%)	
									Study-defined	Post-treatment assessment missing
35	(Wilkinson & Goodyer, 2008)	UK	26	30.4[a]	15.3[a]	SSRI + Psychoed as usual + CBT / SSRI + Psychoed as usual	10-15	28		11.5
36	(Wood, Harrington, & Moore, 1996)	UK	53	31.2[a]	14.2[a]	CBT / Relaxation Training	5-8	9	9.4	
37	(Wright et al., 2017)	UK	91	34.1	15.4	Computerised CBT (Stressbusters) / Attention control (self-help websites)	8	8	30.8	

[a]Demographic information reported for completers only

CBT=Cognitive Behavioural Therapy; SSRI= selective serotonin reuptake inhibitor; TAU= treatment as usual

Study quality

Of the 37 included studies, 36 specified that a treatment manual was used and that therapists had been trained in treatment delivery. Treatment integrity was checked (e.g. by use of recordings or checklists) in 32 studies. Intent to treat analysis was implemented in 26 studies, CONSORT diagrams were presented by 24 studies. Treatment completion was specifically defined in 9 studies. An overall study quality score was calculated (summing these 6 indicators), the average across included studies was 4.4. See Appendix B for details of scores for each study.

Proportion meta-analyses

A proportion meta-analysis yielded a pooled estimate of 15.2% dropout across all arms (i.e. psychological therapy arms and control arms) of included studies (k=88, 95% CI 13.0, 17.5), with significant heterogeneity (Q = 299.400, df = 87, p <.001, I^2= 70.9). The forest plot (Figure 2) shows dropout rates with 95% confidence intervals. I^2 statistics indicated that approximately 71% of the total variance was attributable to variability in true effects (Borenstein et al., 2009). A separate proportion meta-analysis was conducted including only studies that defined dropout, with similar results; pooled estimate of 15.9% dropout across all arms (k=47, 95% CI 12.9, 19.4), with significant heterogeneity (Q = 171.784, df = 46, p <.001, I^2= 73.2).

Further proportion meta-analyses were carried out to explore dropout rates in sub-groups of intervention types (see Table 2). Across all studies dropout generally ranged from 12.5% to 20.8%, IPT was an outlier with an estimate of 4.3%. Estimated dropout rates for study-defined dropout were generally within 3% of the estimates for all studies. The exceptions to this were CBT plus medication (20.8%

for all studies; 24.2% for defined dropout studies) and computerised CBT (13.1% for all studies; 26.0% for defined dropout studies).

Figure 2. Forest plot of dropout rate for all arms of included trials.

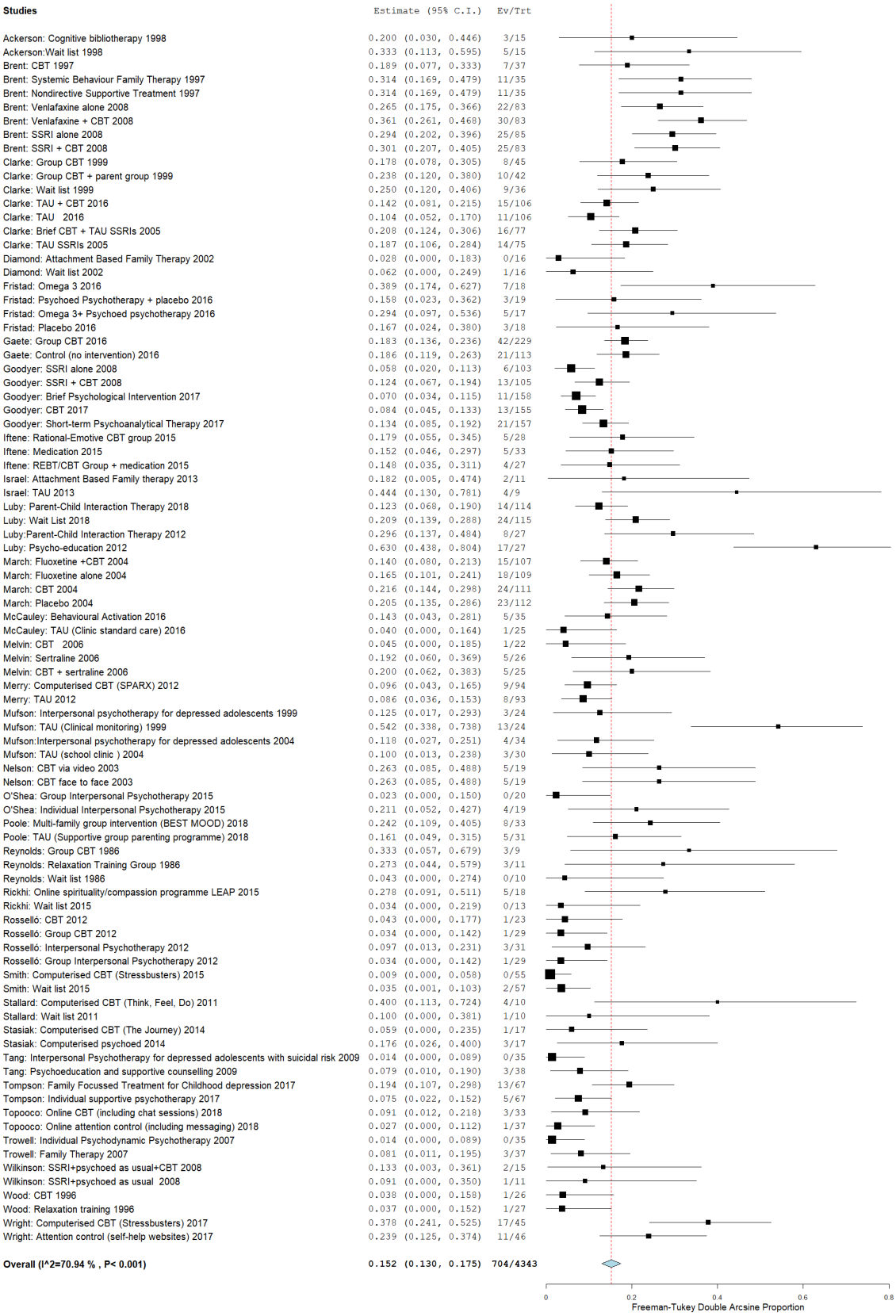


Table 2. Proportion meta-analyses comparing intervention types.

	All studies						Defined dropout					
	N	k	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2	N	k	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2
All arms	4343	88	0.152	0.130, 0.175	Q = 299.400, df = 87, p <.001	70.9	2057	47	0.159	0.126, 0.194	Q = 171.784, df = 46, p <.001	73.222
Any active psychotherapy	2504	51	0.146	0.120, 0.174	Q = 149.552, df = 50, p <.001	66.6	1253	29	0.156	0.117, 0.199	Q = 93.922, df = 28, p <.001	70.188
Active psychotherapy (no medication)	1965	42	0.125	0.098, 0.153	Q = 183.033, df = 41, p <.001	77.6	930	24	0.139	0.100, 0.183	Q = 62.189, df = 23, p <.001	63.016
Active psychotherapy (with medication)	539	9	0.208	0.146, 0.276	Q = 23.691, df = 8, p = .003	66.2	323	5	0.226	0.130, 0.338	Q = 18.082, df = 4, p = .001	77.878
Individual psychotherapy	1419	26	0.145	0.110, 0.182	Q = 76.272, df = 25, p <.001	67.2	913	17	0.139	0.094, 0.191	Q = 59.624, df = 16, p <.001	73.165
Group psychotherapy	458	9	0.133	0.081, 0.195	Q = 17.088, df = 8, p = .029	53.2	200	6	0.129	0.066, 0.208	Q = 10.361, df = 5, p = .066	51.741

	All studies						Defined dropout					
	N	k	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2	N	k	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2
Family/dyadic approaches	307	7	0.163	0.096, 0.241	Q = 14.069, df = 6, p = .029	57.4	-	1	-	-	-	-
Supportive intervention (active control- includes psychoed and relaxation training)	463	10	0.159	0.073, 0.267	Q = 61.403, df = 9, p <.001	85.3	321	6	0.135	0.058, 0.235	Q = 20.634, df = 5, p <.001	75.769
IPT (Individual or group)	227	8	0.043	0.011, 0.074	Q = 11.213, df = 7, p = .130	37.6	153	5	0.068	0.026, 0.123	Q = 4.930, df = 4, p = .295	18.9
Any CBT	1691	30	0.157	0.122, 0.196	Q = 100.759, df = 29, p <.001	71.2	855	20	0.172	0.121, 0.229	Q = 69.406, df = 19, p <.001	72.6
CBT alone	518	9	0.130	0.080, 0.188	Q = 20.067, df = 8, p = .010	60.1	301	7	0.111	0.054, 0.182	Q = 12.823, df = 6, p = 0.046	53.2
CBT + medication	495	7	0.208	0.138, 0.288	Q = 22.405, df = 6, p = .001	73.2	296	4	0.242	0.130, 0.374	Q = 17.018, df = 3, p <.001	82.4
Group CBT	382	6	0.168	0.111, 0.232	Q = 8.025, df = 5, p = .155	37.7	144	4	0.153	0.073, 0.252	Q = 6.408, df = 3, p = .093	53.2
Computerised CBT	254	6	0.131	0.031, 0.276	Q = 34.708, df = 5, p <.001	85.6	72	3	0.260	0.063, 0.518	Q = 7.777, df = 2, p = .020	74.3

	All studies						Defined dropout					
	N	k	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2	N	k	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2
Wait list	272	8	0.123	0.052, 0.214	Q = 19.526, df = 7, p = .007	64.2	74	4	0.179	0.067, 0.324	Q = 5.178, df = 3, p = .159	42.1
Treatment as Usual	287	6	0.167	0.062, 0.304	Q = 29.351, df = 5, p <.001	83.0	79	3	0.192	0.002, 0.527	Q = 19.760, df = 2, p <.001	89.9

Between groups comparisons (Odds ratios)

The relative likelihoods of dropout between different types of intervention and control conditions were assessed using odds ratios, shown in Table 3. The only significant finding was greater dropout for wait list or treatment as usual as compared to family/dyadic interventions (all studies) (OR = 0.485, 95% CI 0.250, 0.940 p = .032) with no significant heterogeneity between studies (Q = 0.422, df = 2, p = .810).

Table 3. Odds ratios comparing intervention and control conditions.

		All studies						Defined dropout					
		N	k (arms)	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2	N	k	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2
Any active psychotherapy intervention	Any control	2117	41	1.025	0.836, 1.257	*Q* = 50.875, *df* = 40, *p* = .116	21.4	1092	23	1.084	0.799, 1.470	*Q* = 30.698, *df* = 22, *p* = .102	28.3
	Any active control	687	13	1.137	0.720, 1.795	*Q* = 20.003, *df* = 12, *p* = .067	40.0	514	8	1.159	0.731, 1.838	*Q* = 8.791, *df* = 7, *p* = .268	20.4
	Wait List / TAU	570	14	0.799	0.485, 1.317	*Q* = 21.383, *df* = 13, *p* = .066	39.2	164	7	0.824	0.349, 1.949	*Q* = 12.803, *df* = 6, *p* = .046	53.1
Any CBT	Any control	1493	26	1.101	0.903, 1.343	*Q* = 17.313, *df* = 25, *p* = .870	0.0	769	16	1.130	0.860, 1.484	*Q* = 13.860, *df* = 15, *p* = .536	0
	Any active control	331	7	1.158	0.713, 1.881	*Q* = 5.672, *df* = 6, *p* = .461	0.0	283	5	1.053	0.589, 1.879	*Q* = 4.666, *df* = 4, *p* = .323	14.3

		All studies						Defined dropout					
		N	k (arms)	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2	N	k	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2
	Wait List / TAU	327	7	1.096	0.607, 1.980	*Q* = 7.389, *df* = 6, *p* = .286	18.8	61	3	0.894	0.282, 2.835	*Q* = 3.112, *df* = 2, *p* = .211	35.7
	Medication alone	584	10	1.164	0.859, 1.577	*Q* = 5.978, *df* = 9, *p* = .742	0.0	389	7	1.264	0.873, 1.830	*Q* = 4.911, *df* = 6, *p* = .555	0
	CBT + Medication	159	3	1.104	0.414, 2.948	*Q* = 3.356, *df* = 2, *p* = .187	40.4	52	2	0.597	0.099, 3.616	*Q* = 1.929, *df* = 1, *p* = .165	48.2
CBT + Medication	Medication alone	525	8	1.202	0.877, 1.647	*Q* = 3.539, *df* = 7, *p* = .831	0.0	330	5	1.342	0.908, 1.982	*Q* = 2.194, *df* = 4, *p* = .700	0
Any Family/Dyadic intervention	Any control	269	6	0.671	0.306, 1.474	*Q* = 12.042, *df* = 5, *p* = .034	58.5	-	1	-	-	-	-

		All studies						Defined dropout					
		N	k (arms)	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2	N	k	Estimate	95% CI	Heterogeneity stats (Q, df, sign)	I^2
	Any active control	129	3	0.912	0.233, 3.567	Q = 9.587, df = 2, p = .008	79.1	-	1	-	-	-	-
	Wait List / TAU	140	3	0.485*	0.250, 0.940	Q = 0.422, df = 2, p = .810	0.0	-	0	-	-	-	-
Any IPT	Any control	92	3	0.304	0.058, 1.598	Q = 4.675, df = 2, p = .097	57.2	92	3	0.304	0.058, 1.598	Q = 4.675, df = 2, p = .097	57.2
	Any active control	-	1	-	-	-	-	-	1	-	-	-	-
	Wait List / TAU	54	2	0.372	0.039, 3.528	Q = 4.381, df = 1, p = .036	77.2	54	2	0.372	0.039, 3.528	Q = 4.381, df = 1, p = .036	77.2

*p<.05

Meta-regressions

A series of meta-regression analyses investigated associations between predictor variables and dropout rate. Results are reported in Table 4 and demonstrate that there were significant associations between the maximum number of sessions and dropout (greater number of sessions was associated with less dropout) and for less dropout from IPT than other interventions. However, when considering only studies that defined dropout the only significant finding was for less dropout from IPT than other interventions. There were no significant associations between dropout and study quality, treatment duration, CBT, family or individual versus other approaches.

Table 4. Meta-regressions investigating predictor variables and dropout rate.

	All studies				Defined dropout			
	k	Coefficient	95% CI	*p*	k	Coefficient	95% CI	*p*
Study quality	51	-0.004	-0.038, 0.029	.796	29	-0.011	-0.054, 0.032	.625
Max sessions	48	-0.007	-0.014, -0.000	.048	28	-0.005	-0.016, 0.006	.406
Treatment duration	50	-0.005	-0.009, 0.000	.057	28	-0.005	-0.013, 0.004	.275
CBT vs other[a]	51	0.036	-0.040, 0.111	.355	29	0.058	-0.050, 0.166	.293
Family approach vs other[a]	51	0.027	-0.082, 0.135	.631	29	0.186	-0.088, 0.460	.183
IPT vs other[a]	51	-0.119	-0.227, -0.010	.032	29	-0.157	-0.285, -0.028	.017
Individual) vs other[a]	51	-0.020	-0.094, 0.055	.599	29	-0.064	-0.170, 0.041	.234

[a]Treatment of interest = 1, control = 0

Reasons for dropout

It was not possible to analyse reasons for dropout as few studies reported these. Examples of reasons given are shown in Table 5.

Table 5. Reasons given for dropout.

Reason	Studies
Non-compliance with treatment	(Brent et al., 1997; Brent et al., 2008; Mufson et al., 1999)
Moving away	(Brent et al., 1997)
Not liking therapy/therapist	(Brent et al., 1997; Melvin et al., 2006)
Believing that the problem was physical health	(Brent et al., 1997)
Serious/adverse event from medication	(Brent et al., 2008; Fristad et al., 2016; Goodyer et al., 2008; Melvin et al., 2006)
Withdrawal of consent	(Brent et al., 2008; March et al., 2004; Wright et al., 2017)
Worsening depression	(Brent et al., 2008; Goodyer et al., 2008; Wright et al., 2017)
Other mental health condition requiring treatment	(Brent et al., 2008)
Insufficient attendance	(Clarke et al., 1999; Goodyer et al., 2017)
Starting external therapy	(Fristad et al., 2016; Goodyer et al., 2017; Stallard et al., 2011)
Time burden	(Fristad et al., 2016)
Protocol violation	(Goodyer et al., 2008)
Improvement in symptoms	(Goodyer et al., 2017; Melvin et al., 2006)
Clinical decision by therapist	(Goodyer et al., 2017; Merry et al., 2012;Mufson et al., 1999)
Withdrawn by parent	(Goodyer et al., 2017)
Transport problems	(Goodyer et al., 2017)

Discussion

The overall dropout rate for active psychotherapy interventions for depression in youth was found to be 14.6% (95% CI 12.0, 17.4) for the randomised controlled trials included here, with significant heterogeneity. This is similar to average dropout rates from adult depression treatment studies, which have been estimated at 17.5% to 19.2% (Cooper & Conklin, 2015; Swift & Greenberg, 2014). It is slightly less than the 23% dropout prevalence found from randomised clinical trials of antidepressant drug treatment in adolescents (Rohden et al., 2017). In the current review dropout generally ranged from 12% to 20% when therapeutic modalities were analysed separately, but IPT was an outlier to this with a lower dropout rate of 4.3% (95% CI 1.1, 7.4) and little heterogeneity, albeit with a smaller sample. Studies which identified how many participants had dropped out (rather than this being inferred from missing post-treatment data) were also analysed separately, with generally similar results. An exception to this was computerised CBT, dropout was 13.1% for all studies and 26.0% for defined dropout. Dropout from wait list and treatment as usual control conditions did not differ substantially from treatment or active control conditions.

Odds ratios were used to look for differences in relative likelihood of dropout between different interventions and control conditions, none were found aside from there was greater dropout for wait list or treatment as usual as compared to family/dyadic interventions (all studies) (OR = 0.485, 95% CI 0.250, 0.940 p = .032) with no significant heterogeneity. Meta-regressions found that interventions offering more sessions had less dropout and there was less dropout from IPT than other interventions. There were no significant associations between dropout and study quality, treatment duration, CBT, family or individual versus other approaches.

It was not possible to analyse the effect of depression severity or therapist experience on dropout, as several different measures of depression were used between studies and therapist experience was not consistently reported. It was also not possible to analyse reasons for dropout as few studies reported these.

Increased reporting of factors related to dropout would enhance understanding of treatment acceptability. It would help for the timeframe of dropout to be reported (e.g. before starting, before halfway through or after halfway through sessions) to elucidate whether there may be an aspect of the treatment that participants find difficult. Although quality checks indicated that the included studies met most of the chosen criteria, a minority reported the minimum number of sessions for treatment completion. Specification of the minimum number of sessions required would help with determination of dropout. Future studies may consider administration of outcome measures at each session, to track change and provide end of treatment scores for those who dropout prematurely (as suggested by Swift & Greenberg, 2012). More detailed reporting of the characteristics of participants who dropout (e.g. gender, age, baseline scores) would assist future reviews to assess whether certain interventions are more/less acceptable for different presentations. Wider reporting of reasons given for dropout would be useful and potentially inform decisions about which interventions to offer to whom.

The main clinical implication of results presented here is that psychological therapies for depression in youth seem to be broadly acceptable, with minimal dropout. Dropout was less likely when more intervention sessions were offered. It could be that participants may have felt more hopeful or validated by the offer of more sessions and engaged more, or there was more time for consolidation of new ideas, or that a stronger therapeutic alliance was built up with more contact time.

Individual choice and preferences should be considered when deciding on treatment options, particularly as dropout rates were similar across different types of intervention. It has been suggested that depression treatment for adolescents involving psychotherapy is more acceptable (less dropout) than medication alone (Rohden et al., 2017).

The current review has several limitations. As just 37 studies met the inclusion criteria, power was limited. Therefore, null findings should not be interpreted as definitive absence of effects. It would be beneficial for future research to build on this analysis as future treatment trials are published, including analysis of additional factors, for example therapist experience, reasons for dropout, stage of treatment at which dropout occurred and characteristics of participants who dropout if these variables are available.

In conclusion, an overall estimate of dropout from active interventions was 14.6%, largely comparable results were found when considering different therapeutic modalities and forms of intervention. There was greater dropout from wait list/treatment as usual than family/dyadic interventions, no other differences in the relative likelihoods of dropout between active interventions and control conditions were found. There were significant associations between the maximum number of sessions and dropout (greater number of sessions was associated with less dropout) and for less dropout from IPT than other interventions. There were no significant associations between dropout and study quality, treatment duration, CBT, family or individual versus other approaches. Future studies should provide detailed information about minimum treatment dose, how dropout is defined and information about participants who dropout to further understanding, inform which treatments

are offered and allow modification of treatments to help reduce attrition and optimise effectiveness of psychotherapy treatments for depression in young people.

Chapter 1 References

Ackerson, J., Scogin, F., McKendree-Smith, N., & Lyman, R. D. (1998). Cognitive bibliotherapy for mild and moderate adolescent depressive symptomatology. *Journal Of Consulting And Clinical Psychology*, *66*(4), 685–690.

Arnberg, A., & Ost, L.-G. (2014). CBT for children with depressive symptoms: a meta-analysis. *Cognitive Behaviour Therapy*, *43*(4), 275–288.

Barrett, M. S., Chua, W., Crits-Christoph, P., Gibbons, M. B., & Thompson, D. (2008). Early withdrawal from mental health treatment: implications for psychotherapy practice. *Psychotherapy Theory, Research, Practice, Training*, *45*(2), 247–267.

Birmaher, B., Ryan, N. D., Williamson, D. E., Brent, D. A., Kaufman, J., Dahl, R. E., … Nelson, B. (1996). Childhood and adolescent depression: a review of the past 10 years. Part I. *Journal Of The American Academy Of Child And Adolescent Psychiatry*, *35*(11), 1427–1439.

Blum, R. W., & Nelson-Mmari, K. (2004). The Health of Young People in a Global Context, 402–418. https://doi.org/10.1016/j.jadohealth.2003.10.007

Borenstein, M., Hedges, L. V., Higgins, J. P. ., & Rothstein, H. R. (2009). *Introduction to meta-analysis.* West Sussex, UK: John Wiley And Sons.

Brent, D. A., Holder, D., Kolko, D., Birmaher, B., Baugher, M., Roth, C., … Johnson, B. A. (1997). A clinical psychotherapy trial for adolescent depression comparing cognitive, family, and supportive therapy. *Archives Of General Psychiatry*, *54*(9), 877–885.

Brent, D., Emslie, G., Clarke, G., Wagner, K. D., Asarnow, J. R., Keller, M., …

Zelazny, J. (2008). Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRI-resistant depression: the TORDIA randomized controlled trial. *JAMA*, *299*(8), 901–913.

Calati, R., Pedrini, L., Alighieri, S., Alvarez, M. I., Desideri, L., Durante, D., … De Girolamo, G. (2011). Is cognitive behavioural therapy an effective complement to antidepressants in adolescents? A meta-analysis. *Acta Neuropsychiatrica*, *23*(6), 263–271.

Chambless, D. L., & Hollon, S. D. (1998). Defining Empirically Supported Therapies. *Journal Of Consulting And Clinical Psychology*, *66*(1), 7–18.

Clarke, G., DeBar, L. L., Pearson, J. A., Dickerson, J. F., Lynch, F. L., Gullion, C. M., & Leo, M. C. (2016). Cognitive Behavioral Therapy in Primary Care for Youth Declining Antidepressants: A Randomized Trial. *Pediatrics*, *137*(5).

Clarke, G., Debar, L., Lynch, F., Powell, J., Gale, J., O'Connor, E., … Hertert, S. (2005). A randomized effectiveness trial of brief cognitive-behavioral therapy for depressed adolescents receiving antidepressant medication. *Journal Of The American Academy Of Child And Adolescent Psychiatry*, *44*(9), 888–898.

Clarke, G. N., Rohde, P., Lewinsohn, P. M., Hops, H., & Seeley, J. R. (1999). Cognitive-behavioral treatment of adolescent depression: efficacy of acute group treatment and booster sessions. *Journal Of The American Academy Of Child And Adolescent Psychiatry*, *38*(3), 272–279.

Cooper, A. A., & Conklin, L. R. (2015). Dropout from individual psychotherapy for major depression : A meta-analysis of randomized clinical trials. *Clinical Psychology Review*, *40*, 57–65.

Costello, E. J., Erkanli, A., & Angold, A. (2006). Is there an epidemic of child or adolescent depression ? *Journal Of Child Psychology And Psychiatry*, *12*(47), 1263–1271.

Cuijpers, P., Sijbrandij, M., Koole, S., Huibers, M., Berking, M., & Andersson, G. (2014). Clinical Psychology Review Psychological treatment of generalized anxiety disorder : A meta-analysis. *Clinical Psychology Review*, *34*(2), 130–140.

Diamond, G., Russon, J., & Levy, S. (2016). Attachment-Based Family Therapy: A Review of the Empirical Support. *Family Process*, *55*(3), 595–610.

Diamond, G. S., Reis, B. F., Diamond, G. M., Siqueland, L., & Isaacs, L. (2002). Attachment-based family therapy for depressed adolescents: a treatment development study. *Journal Of The American Academy Of Child And Adolescent Psychiatry*, *41*(10), 1190–1196.

Fletcher, J. M. (2010). Adolescent depression and educational attainment: results using sibling fixed effects. *Health Economics*, *19*, 855–871. https://doi.org/10.1002/hec

Fristad, M. A., Vesco, A. T., Young, A. S., Healy, K. Z., Nader, E. S., Gardner, W., … Arnold, L. E. (2016). Pilot Randomized Controlled Trial of Omega-3 and Individual-Family Psychoeducational Psychotherapy for Children and Adolescents With Depression. *Journal Of Clinical Child And Adolescent Psychology: The Official Journal For The Society Of Clinical Child And Adolescent Psychology, American Psychological Association, Division 53*, 1–14.

Gaete, J., Martinez, V., Fritsch, R., Rojas, G., Montgomery, A. A., & Araya, R.

(2016). Indicated school-based intervention to improve depressive symptoms among at risk Chilean adolescents: a randomized controlled trial. *BMC Psychiatry*, *16*, 276.

Gersh, E., Hallford, D. J., Rice, S. M., Kazantzis, N., Gersh, H., Gersh, B., & Mccarty, C. A. (2017). Systematic review and meta-analysis of dropout rates in individual psychotherapy for generalized anxiety disorder. *Journal of Anxiety Disorders*, *52*(August), 25–33.

Goodyer, I. M., Dubicka, B., Wilkinson, P., Kelvin, R., Roberts, C., Byford, S., … Harrington, R. (2008). A randomised controlled trial of cognitive behaviour therapy in adolescents with major depression treated by selective serotonin reuptake inhibitors. The ADAPT trial. *Health Technology Assessment (Winchester, England)*, *12*(14), iii.

Goodyer, I. M., Reynolds, S., Barrett, B., Byford, S., Dubicka, B., Hill, J., … Fonagy, P. (2017). Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superiori. *The Lancet. Psychiatry*, *4*(2), 109–119.

Higgins, J. P. T., & Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis, *1558*, 1539–1558. https://doi.org/10.1002/sim.1186

Iftene, F., Predescu, E., Stefan, S., & David, D. (2015). Rational-emotive and cognitive-behavior therapy (REBT/CBT) versus pharmacotherapy versus REBT/CBT plus pharmacotherapy in the treatment of major depressive disorder in youth; a randomized clinical trial. *Psychiatry Research*, *225*(3), 687–694.

Israel, P., & Diamond, G. S. (2013). Feasibility of Attachment Based Family Therapy for depressed clinic-referred Norwegian adolescents. *Clinical Child Psychology And Psychiatry*, *18*(3), 334–350.

Landis, J. R., & Koch, G. G. (1977). The Measurement of Observer Agreement for Categorical Data. *Biometrics*, *33*(1), 159–174.

Lopez, A. D., Mathers, C. D., Ezzati, M., Jamison, D. T., & Murray, C. J. L. (2006). Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet (London, England)*, *367*(9524), 1747–1757.

Luby, J. L., Barch, D. M., Whalen, D., Tillman, R., & Freedland, K. E. (2018). A Randomized Controlled Trial of Parent-Child Psychotherapy Targeting Emotion Development for Early Childhood Depression. *The American Journal Of Psychiatry*,

Luby, J., Lenze, S., & Tillman, R. (2012). A novel early intervention for preschool depression: findings from a pilot randomized controlled trial. *Journal Of Child Psychology And Psychiatry, And Allied Disciplines*, *53*(3), 313–322.

March, J., Silva, S., Petrycki, S., Curry, J., Wells, K., Fairbank, J., … Severe, J. (2004). Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. *JAMA*, *292*(7), 807–820.

McCauley, E., Gudmundsen, G., Schloredt, K., Martell, C., Rhew, I., Hubley, S., & Dimidjian, S. (2016). The Adolescent Behavioral Activation Program: Adapting Behavioral Activation as a Treatment for Depression in Adolescence. *Journal Of Clinical Child And Adolescent Psychology: The Official Journal For The*

Society Of Clinical Child And Adolescent Psychology, American Psychological Association, Division 53, *45*(3), 291–304.

Melvin, G. A., Tonge, B. J., King, N. J., Heyne, D., Gordon, M. S., & Klimkeit, E. (2006). A comparison of cognitive-behavioral therapy, sertraline, and their combination for adolescent depression. *Journal Of The American Academy Of Child And Adolescent Psychiatry*, *45*(10), 1151–1161.

Merikangas, K. R., He, J., Burstein, M., Swanson, S. A., Avenevoli, S., Cui, L., … Swendsen, J. (2010). Lifetime prevalence of mental disorders in US adolescents: results from the national comorbidity study- adolescent supplement (NCS-A). *Journal of the American Academy of Child and Adolescent Psychiatry*, *49*(10), 980–989.

Merry, S. N., Stasiak, K., Shepherd, M., Frampton, C., Fleming, T., & Lucassen, M. F. G. (2012). The effectiveness of SPARX, a computerised self help intervention for adolescents seeking help for depression: randomised controlled non-inferiority trial. *BMJ (Clinical Research Ed.)*, *344*, e2598–e2598.

Miller, D. K., Constance, H. L., & Brennan, P. A. (2007). Health outcomes related to early adolescent depression. *Journal of Adolescent Health*, *41*(3), 256–262.

Mufson, L., Dorta, K. P., Wickramaratne, P., Nomura, Y., Olfson, M., & Weissman, M. M. (2004). A randomized effectiveness trial of interpersonal psychotherapy for depressed adolescents. *Archives Of General Psychiatry*, *61*(6), 577–584.

Mufson, L., Weissman, M. M., Moreau, D., & Garfinkel, R. (1999). Efficacy of interpersonal psychotherapy for depressed adolescents. *Archives Of General Psychiatry*, *56*(6), 573–579.

Nelson, E.-L., Barnard, M., & Cain, S. (2003). Treating childhood depression over videoconferencing. *Telemedicine Journal And E-Health: The Official Journal Of The American Telemedicine Association*, *9*(1), 49–55.

O'Shea, G., Spence, S. H., & Donovan, C. L. (2015). Group versus individual interpersonal psychotherapy for depressed adolescents. *Behavioural And Cognitive Psychotherapy*, *43*(1), 1–19.

Poole, L. A., Knight, T., Toumbourou, J. W., Lubman, D. I., Bertino, M. D., & Lewis, A. J. (2018). A Randomized Controlled Trial of the Impact of a Family-Based Adolescent Depression Intervention on both Youth and Parent Mental Health Outcomes. *Journal Of Abnormal Child Psychology*, *46*(1), 169–181.

Pu, J., Zhou, X., Liu, L., Zhang, Y., Yang, L., Yuan, S., … Xie, P. (2017). Efficacy and acceptability of interpersonal psychotherapy for depression in adolescents: A meta-analysis of randomized controlled trials. *Psychiatry Research*, *253*, 226–232.

Reis, B. F., & Brown, L. G. (1999). Reducing psychotherapy dropouts: maximising perspective convergence in the psychotherapy dyad. *Psychotherapy*, *36*(2), 123–136.

Reynolds, W. M., & Coats, K. I. (1986). A comparison of cognitive-behavioral therapy and relaxation training for the treatment of depression in adolescents. *Journal of Consulting and Clinical Psychology*, *54*(5), 653–660.

Richardson, T., Stallard, P., & Velleman, S. (2010). Computerised cognitive behavioural therapy for the prevention and treatment of depression and anxiety in children and adolescents: a systematic review. *Clinical Child And Family Psychology Review*, *13*(3), 275–290.

Rickhi, B., Kania-Richmond, A., Moritz, S., Cohen, J., Paccagnan, P., Dennis, C., … Toews, J. (2015). Evaluation of a spirituality informed e-mental health tool as an intervention for major depressive disorder in adolescents and young adults - a randomized controlled pilot trial. *BMC Complementary And Alternative Medicine*, *15*, 450.

Rohden, A. I., Benchaya, M. C., Camargo, R. S., Moreira, T. de C., Barros, H. M. T., & Ferigolo, M. (2017). Dropout Prevalence and Associated Factors in Randomized Clinical Trials of Adolescents Treated for Depression: Systematic Review and Meta-analysis. *Clinical Therapeutics*, *39*(5), 971–992.e4.

Rosselló, J., Bernal, G., & Rivera-Medina, C. (2012). Individual and group CBT and IPT for Puerto Rican adolescents with depressive symptoms. *Journal of Latina/o Psychology*, *1*(S), 36–51.

Smith, P., Scott, R., Eshkevari, E., Jatta, F., Leigh, E., Harris, V., … Yule, W. (2015). Computerised CBT for depressed adolescents: Randomised controlled trial. *Behaviour Research And Therapy*, *73*, 104–110.

Stallard, P., Richardson, T., Velleman, S., & Attwood, M. (2011). Computerized CBT (Think, Feel, Do) for depression and anxiety in children and adolescents: outcomes and feedback from a pilot randomized controlled trial. *Behavioural And Cognitive Psychotherapy*, *39*(3), 273–284.

Stasiak, K., Hatcher, S., Frampton, C., & Merry, S. N. (2014). A pilot double blind randomized placebo controlled trial of a prototype computer-based cognitive behavioural therapy program for adolescents with symptoms of depression. *Behavioural And Cognitive Psychotherapy*, *42*(4), 385–401.

Swift, J. K., & Greenberg, R. P. (2012). Premature Discontinuation in Adult

Psychotherapy : A Meta-Analysis. *Journal Of Consulting And Clinical Psychology*, *80*(4), 547–559. https://doi.org/10.1037/a0028226

Swift, J. K., & Greenberg, R. P. (2014). A Treatment by Disorder Meta-Analysis of Dropout From Psychotherapy. *Journal of Psychotherapy Integration*, *24*(3), 193–207.

Tang, T.-C., Jou, S.-H., Ko, C.-H., Huang, S.-Y., & Yen, C.-F. (2009). Randomized study of school-based intensive interpersonal psychotherapy for depressed adolescents with suicidal risk and parasuicide behaviors. *Psychiatry And Clinical Neurosciences*, *63*(4), 463–470.

Tindall, L., Mikocka-Walus, A., McMillan, D., Wright, B., Hewitt, C., & Gascoyne, S. (2017). Is behavioural activation effective in the treatment of depression in young people? A systematic review and meta-analysis. *Psychology And Psychotherapy*, *90*(4), 770–796.

Tompson, M. C., Sugar, C. A., Langer, D. A., & Asarnow, J. R. (2017). A Randomized Clinical Trial Comparing Family-Focused Treatment and Individual Supportive Therapy for Depression in Childhood and Early Adolescence. *Journal Of The American Academy Of Child And Adolescent Psychiatry*, *56*(6), 515–523.

Topooco, N., Berg, M., Johansson, S., Liljethörn, L., Radvogin, E., Vlaescu, G., … Andersson, G. (2018). Chat- and internet-based cognitive-behavioural therapy in treatment of adolescent depression: randomised controlled trial. *Bjpsych Open*, *4*(4), 199–207.

Trowell, J., Joffe, I., Campbell, J., Clemente, C., Almqvist, F., Soininen, M., … Tsiantis, J. (2007). Childhood depression : a place for psychotherapy An

outcome study comparing individual psychodynamic psychotherapy and family therapy. *European Child & Adolescent Psychiatry*, (16), 157–167.

Viechtbauer, W. (2010). Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software*, *36*(3).

Wallace, B. C., Dahabreh, I. J., Trikalinos, T. A., Lau, J., Trow, P., & Schmid, C. H. (2012). End-Users : R as a Computational Back-End, *49*(5), 1–15.

Weisz, J. R., Kuppens, S., Ng, M. Y., Eckshtain, D., Ugueto, A. M., Vaughn-Coaxum, R., … Fordwood, S. R. (2017). What five decades of research tells us about the effects of youth psychological therapy: A multilevel meta-analysis and implications for science and practice. *The American Psychologist*, *72*(2), 79–117.

Wilkinson, P. O., & Goodyer, I. M. (2008). The effects of cognitive-behavioural therapy on mood-related ruminative response style in depressed adolescents. *Child And Adolescent Psychiatry And Mental Health*, *2*(1), 3.

Wood, A., Harrington, R., & Moore, A. (1996). Controlled trial of a brief cognitive-behavioural intervention in adolescent patients with depressive disorders. *Journal Of Child Psychology And Psychiatry, And Allied Disciplines*, *37*(6), 737–746.

Wright, B., Tindall, L., Littlewood, E., Allgar, V., Abeles, P., Trépel, D., & Ali, S. (2017). Computerised cognitive-behavioural therapy for depression in adolescents: feasibility results and 4-month outcomes of a UK randomised controlled trial. *BMJ Open*, *7*(1), e012834–e012834.

Zhou, X., Hetrick, S. E., Cuijpers, P., Qin, B., Barth, J., Whittington, C. J., … Xie, P.

(2015). Comparative efficacy and acceptability of psychotherapies for depression in children and adolescents: A systematic review and network meta-analysis. *World Psychiatry: Official Journal Of The World Psychiatric Association (WPA)*, *14*(2), 207–222.

Chapter 2: Bridging Chapter

The focus of the systematic review was to explore the acceptability of psychotherapeutic interventions for depression in youth by investigating rates of dropout. Only randomised controlled trials were included; these had been conducted for a range of therapeutic modalities including CBT, interpersonal psychotherapy, psychoanalytical psychotherapy, computerised interventions and family therapy approaches. A proportion meta-analysis yielded a pooled estimate of 14.6% dropout across all active interventions. Odds ratios were used to assess the relative likelihood of dropout between intervention and control conditions. The only significant finding was that dropout was more likely from wait list/treatment as usual than family/dyadic interventions. Meta-regressions showed that the only association between predictor variables and dropout rate was for less dropout when a greater number of intervention sessions was offered. It was not possible to analyse reasons for dropout, or to compare characteristics of participants who dropped out with those who did not as these factors were not widely reported. In summary, all depression interventions investigated seemed to be acceptable to young people, including control conditions and wait lists.

To fully assess the clinical utility and impact of an intervention it is important to consider whether improvements occur across the range of presenting issues, not just those seen as primary. Comorbidity of mood and anxiety symptoms and disorders is common among young people presenting to National Health Service child and adolescent mental health services (NHS CAMHS) for treatment (Orchard, Pass, Marshall, & Reynolds, 2017). In order to evaluate and develop efficient and effective treatments it is important to thoroughly investigate data from treatment

trials, assessing change in symptoms over time. The IMPACT randomised controlled trial compared three treatment approaches for adolescent depression: CBT, short term psychoanalytical psychotherapy (STPP) and brief psychological intervention (BPI) (Goodyer et al., 2011). Participants were assessed at baseline then 6, 12, 36 (end of treatment), 52 and 86 weeks following this. Treatments were delivered by trained CAMHS clinicians over 20-30 weeks. All three interventions were clinically effective at treating depression symptoms and equally cost effective (Goodyer et al., 2017). Explorations of the pattern of change over time for depression symptoms in this large (N=465) trial dataset are underway. Permission was granted for access to the IMPACT trial dataset, to conduct secondary analyses of the data. This provided a valuable opportunity to explore the trajectory of anxiety symptoms in adolescents receiving psychological treatment for a primary diagnosis of depression. The aim of the empirical study was to characterise anxiety trajectories in this sample.

Chapter 2 References

Goodyer, I. M., Reynolds, S., Barrett, B., Byford, S., Dubicka, B., Hill, J., … Kelvin, R. (2017). Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre , pragmatic , observer-blind , randomised controlled superi. *The Lancet Psychiatry*, *4*(2), 109–119. https://doi.org/10.1016/S2215-0366(16)30378-9

Goodyer, I. M., Tsancheva, S., Byford, S., Dubicka, B., Hill, J., Kelvin, R., … Fonagy, P. (2011). Improving mood with psychoanalytic and cognitive therapies (IMPACT): a pragmatic effectiveness superiority trial to investigate whether specialised psychological treatment reduces the risk for relapse in adolescents with moderate to severe unipolar depres. *Trials*, *12*. https://doi.org/10.1186/1745-6215-12-175

Orchard, F., Pass, L., Marshall, T., & Reynolds, S. (2017). Clinical characteristics of adolescents referred for treatment of depressive disorders. *Child And Adolescent Mental Health*, *22*(2), 61–68. https://doi.org/10.1111/camh.12178

Chapter 3: Empirical Paper

Prepared for submission to the Journal of Clinical Child & Adolescent Psychology

See Appendix C for Instructions for authors

Journal wordcount (including references, footnotes, figures and tables): 9337

UEA wordcount (excluding references): 7084

For ease of reference, Tables and Figures are presented alongside the text.

The trajectory of adolescent anxiety symptoms over the course of psychological intervention aimed at depression

Isobel Wright[a], Sharon Neufeld[b], Richard Meiser-Stedman[a], Paul Wilkinson[b] & Ian Goodyer[b]

[a]The University of East Anglia, [b]University of Cambridge

Corresponding author: Isobel Wright, isobel.m.wright@uea.ac.uk

Abstract

The 'Improving mood with psychoanalytic and cognitive therapies' (IMPACT) randomised controlled trial (Goodyer et al., 2017) demonstrated that cognitive behaviour therapy, short-term psychoanalytic psychotherapy and brief psychosocial intervention were equally effective at reducing depression symptoms. It is important to know whether these interventions affect anxiety symptoms, which are frequently concurrent. IMPACT had an intent to treat population of n=465 11-17 year olds who met DSM-IV depression criteria. 40% also met criteria for anxiety disorder. 74.8% of the sample were female, 84.9% were white. Assessments took place at baseline then 6, 12, 36 (end of treatment), 52 and 86 weeks after this. Diagnoses, mood, anxiety, self-esteem, obsessional symptoms, rumination and suicidality were measured. SSRIs were prescribed if indicated. The aim of this study was to utilise the IMPACT dataset to examine anxiety trajectories. Growth mixture modelling indicated that a 2-class piecewise model was the best fit, with the first slope occurring during treatment and the second slope during the follow-up period. The smaller class (n=46) showed an improvement in anxiety symptoms during but not after treatment, whereas the larger class (n=419) exhibited no significant change in anxiety symptoms. After controlling for gender and baseline anxiety, greater impairment in mood and self-esteem, and increased suicidal thoughts were associated with membership to the non-improving class. Findings indicate that for most youth, co-occurring anxiety symptoms may not be responsive to these depression treatments. Depression interventions should be tailored to target comorbid anxiety symptoms and post-treatment assessments should identify residual anxiety symptoms for further intervention.

Introduction

Depression and anxiety are closely associated disorders and significant contributors to disease burden in youth worldwide (Erskine et al., 2015). Both can cause significant impairment in functioning and increase the risk of suicide (Gould et al., 1998). In one community sample young people with anxiety disorders had comorbid depression in 10-20% of cases, whereas 25 to 50% of youth with primary depression also met criteria for comorbid anxiety disorder (Axelson & Birmaher, 2001). Anxiety has been shown to predict depression at subsequent points in time, after controlling for baseline depression (Cole, Peeke, Martin, Truglio, & Seroczynski, 1998). Worryingly, the presence of anxiety or depression in adolescence is predictive of either disorder in future years (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Pine, Cohen, Gurley, Brook, & Ma, 1998).

Comorbid anxiety and depression is more persistent than either alone in adults (Merikangas et al., 2003) and shows a worse course trajectory than pure anxiety or depression (Penninx et al., 2011). In youth a similar pattern has been found, with higher risk of recurrence, longer duration, increased suicide attempts, greater impairment, less favourable response to treatment and greater utilisation of mental health services in comorbid anxiety and depression rather than either alone (Birmaher et al., 1996; Ezpeleta, Domenech, & Angold, 2006).

Several longitudinal studies have used growth mixture modelling or similar techniques to identify groups of individuals with similar trajectories of symptoms over time. Factors predicting group membership are then examined. In observational studies that have investigated depression in community samples, generally multiple trajectories have been found: one class with consistently low depression symptoms,

at least one class with increasing symptoms over time and at least one class with decreasing symptoms over time. The majority of youth do not develop depression symptoms, some initially high mid-childhood depression lessens over time and for others depression emerges in adolescence. Usually three classes have been found (Mezulis, Funasaki, & Hyde, 2011; Mezulis, Salk, Hyde, Priess-Groben, & Simonson, 2014). Studies that identified four classes found similar patterns, with an additional class. Ellis and colleagues (2017) found two classes with decreasing symptoms (one with initially high, one with moderately high); Wickrama and Wickrama (2010) found a class with chronically high symptoms. In these studies predictors of group membership fell into three categories: demographic (gender, pubertal timing), psychological (MDD diagnosis, negative affectivity, cognitive style, maternal cognitive style, rumination, temperament) and life event (total stress, maltreatment, quality of life) and risk taking behaviour.

Results from anxiety trajectory analyses are less similar across studies. In an investigation of at-risk children from preschool through to school age, 4 distinct trajectories were found: 2 stable groups (high and moderate) and 2 decreasing groups (high and low) (Kertz, Sylvester, Tillman, & Luby, 2017). Predictors of class were depression, social adversity, maternal depression and social functioning. In a community sample of mid to late adolescence, four Generalised Anxiety Disorder (GAD) trajectories were identified: low increasing (45%), moderate decreasing slightly (34%), high decreasing (11%) and very high decreasing rapidly (10%, Ohannessian, Milan, & Vannucci, 2017). For social anxiety a five class solution was found, the same as GAD but with an additional low stable trajectory. In summary, these studies suggest the following: in early childhood (around the transition to school) anxiety generally decreased, but remained stable at a moderate level for

some children and stable at a higher level for a small proportion of children (Kertz et al., 2017). This was an at-risk sample, recruited from a depression study and symptoms are likely to have been higher than in the general population. In a large school sample of mid-adolescents anxiety symptoms decreased or remained stable over time for the majority but increased for nearly half (Ohannessian et al., 2017).

Previous research has mainly focussed on the effectiveness of disorder-specific treatments on the conditions they target, or on multiple disorders when investigating transdiagnostic approaches. The primary psychotherapy for depression and anxiety is cognitive behavioural therapy (CBT), which has a substantial evidence base (Compton et al., 2004). The influence of comorbid diagnoses on treatment response and the effectiveness of interventions on non-target comorbid disorder symptoms has been variable. Anxiety treatment has been shown to be effective despite the presence of comorbid disorders in some studies (Flannery-Schroeder, Suveg, Safford, Kendall, & Webb, 2004; Kendall, Brady, & Verduin, 2001). However, depressive symptoms have been found to reduce the efficacy of an exposure-based treatment for phobic and anxiety disorders (Berman, Weems, Silverman, & Kurtines, 2000). Several studies have found that interventions aimed at anxiety have also reduced depression symptoms (Kendall et al., 1997; Kendall, Hudson, Gosch, Flannery-Schroeder, & Suveg, 2008; Kendall, Safford, Flannery-Schroeder, & Webb, 2004). In depression interventions, comorbid anxiety has been found to predict worse outcome in individual therapy (Curry et al., 2006; Vostanis, Feehan, & Grattan, 1998) and better outcome in group treatment (Rohde, Clarke, Lewinsohn, Seeley, & Kaufman, 2001).

CBT is not the only evidence-based treatment for anxiety and depression. Short term psychoanalytical psychotherapy (STPP) has also been shown to be

effective for depression in adults (Leichsenring, Rabung, & Leibing, 2004), and non-inferior to CBT (Connolly Gibbons et al., 2016). It is also effective for anxiety in adults (Leichsenring et al., 2009) and a range of disorders in adolescents, including anxiety and depression (Abbass, Rabung, Leichsenring, Refseth, & Midgley, 2013). In childhood, psychodynamic therapy aimed at depression was effective and reduced comorbidities, including anxiety (Trowell et al., 2007). Interestingly, interventions conceived as active control conditions have also shown significant reduction in depressive symptoms, such as support groups, bibliotherapy, expressive writing and journaling (Stice, Burton, Bearman, & Rohde, 2007). In a large meta-analysis looking at five decades of psychological therapy research in youth, efficacy was found to differ by target problem; largest treatment effects for anxiety, smallest for depression; moreover, treating multiple problems concurrently produced smaller effects than treating any single targeted problem (Weisz et al., 2017).

In the face of the above uncertainty and given high rates of comorbidity of depression and anxiety in youth, it is particularly important to clarify whether depression treatment has an impact on concurrent anxiety symptoms. For example, it would be helpful to elucidate whether some youth follow a consistent recovery trajectory or experience temporary respite during therapy but then have a resurgence in anxiety symptoms, or if some youth maintain a consistent level of anxiety throughout and after intervention. There are several elements of depression treatment that may also be useful for anxiety, for example behavioural activation and reductions in the use of avoidance. However, it has not yet been tested whether various depression treatments do indeed influence anxiety trajectories in young people.

The ‘Improving mood with psychoanalytic and cognitive therapies’ (IMPACT) randomized controlled trial provides an opportunity to investigate trajectories of anxiety symptoms over the course of three types of depression treatment and follow-up.

IMPACT was designed to compare CBT and STPP with a brief psychosocial intervention (BPI) in adolescents with depression (Goodyer et al., 2011). BPI included psychoeducation about depression, action-oriented, goal-focussed and interpersonal activities; self-understanding and cognition change were not components. The aim was to compare the effectiveness at reducing depression as well as cost-effectiveness of the two therapies compared with BPI. Contrary to hypothesis, no superiority effect was found for CBT or STPP over BPI in the reduction of depression symptoms 12 months after treatment, as all three interventions were clinically effective at treating depression symptoms and equally cost effective (Goodyer et al., 2017). A secondary hypothesis was made that participants receiving either CBT or STPP would be more likely to exhibit significantly lower anxiety symptoms 12 months post treatment. This was not supported, but in the raw data anxiety symptoms were significantly reduced for the psychological treatments combined versus the BPI at post-treatment. This important finding is consistent with literature that psychological treatment can reduce anxiety in patients with depression (Weisz, Mccarty, & Valeri, 2006). IMPACT’s assessments at 6, 12, 36 (just after end of treatment), 52 and 86 weeks after baseline allow ample investigation of the longitudinal patterns of anxiety symptoms during and after these depression treatments.

The aim of the current study was to use a data-driven approach to characterise anxiety trajectories over the course of three depression treatments in a youth sample.

Methods

Sample

The 'Improving mood with psychoanalytic and cognitive therapies' (IMPACT) trial was a multicentre, pragmatic randomised controlled superiority trial comparing adolescent depression treatments (Goodyer et al., 2017). 465 11-17 year olds with a diagnosis of DSM-IV unipolar major depressive disorder were randomised and commenced treatment. Participants were recruited from 15 routine National Health Service child and adolescent mental health services (CAMHS) in East Anglia (largely rural), North London (urban) and the North West of England (urban/rural). 74.8% of the sample were female, 84.9% were white. Following baseline assessment participants were randomised to short-term psychoanalytical psychotherapy (STPP), cognitive behavioural therapy (CBT) or brief psychosocial intervention (BPI). STPP and CBT were planned to be delivered over 30 weeks, BPI over 20 weeks. The selective serotonin reuptake inhibitor (SSRI) fluoxetine was prescribed if clinically indicated.

The IMPACT trial received full ethical approval from Cambridgeshire 2 Research Ethics Committee (reference 09/H0308/137), including planned analysis of secondary outcomes; no additional ethical approvals or participant consent procedures were necessary.

Measures

*Diagnostic Measure***:** The Kiddie-Schedule for Affective Disorders and Schizophrenia Present and Lifetime (K-SADS-PL) is a diagnostic semi-structured interview measure (Kaufman et al., 1997). Symptoms are rated on a 3-point scale: 1=non-clinical, 2=subthreshold and 3=clinically relevant. DSM-IV criteria were used to ascertain current diagnoses. Participants and parents/guardians completed the interview and data were used from these collectively to inform diagnoses (symptom endorsement could be due to either respondent). Test-retest reliability has been found to be good to excellent and interrater agreement high (Kaufman et al., 1997). Thirty cases were randomly selected from the IMPACT dataset and the reliability of depression diagnosis was assessed. There was 100% agreement between two research assistants on diagnoses, 95% agreement on individual items (Goodyer et al., 2017).

Main outcome measure: The Revised Children's Manifest Anxiety Scale self-report questionnaire was used to measure current trait anxiety (Reynolds & Richmond, 1978). There are 28 items scored 0, 1, 2, endorsed items are summed to yield a total score. Similar to prior work (Muris, Merckelbach, Ollendick, King, & Bogie, 2002) RCMAS in the present sample had good internal consistency (Cronbach's alpha=0.93).

Covariates: The Mood and Feelings Questionnaire (MFQ; Costello & Angold, 1988) was used as a self-report measure of depression. MFQ has 33 items which relate to DSM-IV depressive symptoms over the past 2 weeks. Each ordinal item is scaled as for RCMAS; items are summed to give a total. MFQ in the present sample had high internal consistency (Cronbach's alpha=0.96), consistent with other

clinical samples, where it has also demonstrated moderate diagnostic accuracy (AUC=.82;Wood, Kroll, Moore, & Harrington, 1995).

The Rosenberg Self-esteem Scale (RSES; Rosenberg, 1965) is a 10-item self-report scale measuring global self-worth. Items are answered using a 4 point Likert scale from strongly agree to strongly disagree (scored 1-4). Five negatively worded items are reverse scored, then scores from all 10 items are summed to yield a total, with a higher score indicating higher self-esteem. In line with other work (Sharratt, Boduszek, Jones, & Gallagher, 2014) RSES had good internal consistency in this sample (Cronbach's alpha=0.91).

The Short Leyton Obsessional Inventory child version (LOI) is a self-report measure of obsessional symptoms. It has 11 ordinal items (scaled as for RCMAS) which are summed to yield a total score. High internal reliability and discrimination of OCD cases from non-cases irrespective of comorbid major depressive disorder has been previously demonstrated (Bamber, Tamplin, Park, Kyte, & Goodyer, 2002). Cronbach's alpha for this sample was 0.88.

The version of the Ruminative Responses Scale (RRS) used in IMPACT is a modification of the Response Styles Questionnaire (Nolen-Hoeksema & Morrow, 1991) with wording adjusted for adolescents (Park, Goodyer, & Teasdale, 2005). This modified version is also known as the Responses to Depression Questionnaire (Wilkinson & Goodyer, 2008). It is a self-report 39 item measure asking what participants typically think, feel or do when they experience low mood. Each item is scored from 0 to 3, summed to yield a total score. The original questionnaire has shown good discriminant validity and stability (Nolen-Hoeksema & Morrow, 1991); predictive validity for future and current depressive disorder has been shown for the

adolescent version (Goodyer, Herbert, Tamplin, & Altham, 2000). Cronbach's alpha for this sample was 0.91.

The Behaviour Checklist is an 11-item self-report measure of antisocial behaviour based on DSM-IV criteria for conduct disorder (Goodyer et al., 2017), with response scale as for RCMAS. Cronbach's alpha was 0.78.

The Columbia Suicide Severity Rating Scale (CSSRS) is a clinician rated measure consisting of three subscales: ideation (5 items scored 0/1), intensity (5 items scored 0-5, choices worded separately for each item) and behaviour (5 items scored 0/1). It has been shown to have good internal validity and consistency in clinical and research settings (Posner et al., 2011). Cronbach's alpha for the 5 suicidal ideation questions was 0.91. A single item of this scale was also used as a binary measure of non-suicidal self-injury (NSSI).

Deprivation was measured using Index of Multiple Deprivation, calculated for each participant using their postcode (Noble et al., 2008).

Whether SSRIs were currently prescribed was recorded at each assessment (0/1).

Data analytic plan

Missing data

Little's Missing Completely at Random (MCAR) test (Little, 1988) was run to assess whether data were missing completely at random (in a way that cannot be predicted by observed or unobserved data) or at random (in a way that can be predicted by observed data and therefore controlled for). Little's MCAR test

indicated that data were not missing completely at random $\chi^2 = 2505.07$ $p<.0001$. This supports the notion that data is missing at random. Multiple imputation is an appropriate way of dealing with this type of missingness and takes into account auxiliary variables when estimating the values of missing data (White, Royston, & Wood, 2011).

Whilst the amount of missing data on the RCMAS was moderate (from 0-34%) it was necessary to impute based on missing categorical diagnostic (K-SADS-PL) data (up to 52%, see Table 14, Appendix D). Chained equations were used to perform 54 imputations, greater than the highest percentage of missing data (White et al., 2011).

There was not enough raw data available (see Table 14, Appendix D) to accurately impute data for agoraphobia, specific phobia or panic disorder separately. As these diagnoses have symptomatic similarities and have previously been grouped together in factor analysis studies (e.g. Kessler et al., 2012) they were amalgamated into one variable. Obsessive Compulsive Disorder was excluded from the present study, as it is no longer classified as an anxiety disorder in DSM-5.

Statistical Analysis

Mixed models were run using STATA (StataCorp, 2017) to examine the patterns of diagnoses over the course of treatment and follow-up assessments. Main, linear and quadratic effects of time (exact time from baseline to assessment) were explored as well as interactions of time with age and gender. Main effects of gender, age, treatment arm and interactions between treatment arm, age and gender were also examined.

Mplus (Muthén & Muthén, 2017) was used to perform growth mixture modelling (GMM) to identify clusters of individuals with similar patterns of anxiety scores (on the RCMAS) across the assessment points of the treatment trial. Modelling was carried out using estimations of the imputed data.

Linear, quadratic and piecewise models were explored. Irrespective of fit statistics, quadratic models were not pursued where the quadratic term was non-significant. To allow for differing trajectories during and post treatment the piecewise models specified that the first slope started at baseline, included the 6 week and 12 week assessment points, finishing at the 36 week (end of intervention) assessment. The second slope started at the 36 week point and included the follow-up assessments, at 52 and 86 weeks. Variability in exact time of completing the assessments was accounted for by using the mean exact time in days rather than the planned assessment times.

The final model was selected based on several criteria. Firstly, the sample-size adjusted Bayesian Information Criterion (ssBIC) was consulted, as it performs better under realistic conditions than BIC and Akaike Information Criterion (AIC; Kim, 2014). As ICs do not always perform as well in the presence of missing data (Kim, 2014), it was deemed most appropriate to perform GMM on the imputed dataset. Additionally, to obtain the most parsimonious model, the Vuong-Lo-Mendell-Rubin (VLMR) Likelihood Ratio Test (LRT) and Lo-Mendell-Rubin adjusted LRT indicated whether higher order models added significant information. Finally, lower log likelihood values were preferred as well as higher model entropy. Starting with a single class for each model additional classes were added until model fit criteria indicated a poorer fit or that a lower order model was more parsimonious.

Linear, quadratic and piecewise models were explored. Quadratic models were presented if the quadratic term was significant, otherwise the linear model was presented. The piecewise models specified that the first slope started at baseline and included the 6 and 12 week assessment points. The second slope started just after end of treatment (36 weeks) and included the follow-up assessments, at 52 and 86 weeks. Variability in exact time of participants completing the assessments was accounted for by using number of days since baseline (group mean per assessment) rather than planned assessment times. Participants' probability of belonging to each of the latent classes was evaluated, and participants were assigned to the class with the highest probability.

Finally, logistic regressions were performed on the imputed RCMAS data to explore whether baseline variables predicted class membership.

Results

Anxiety Disorders

The prevalence of anxiety disorders across all timepoints in the raw data are shown in Table 6. Rates of PTSD were not equivalent across treatment arms at baseline, being higher in STPP than BPI (OR=2.34 (95% CI 1.04, 7.53), p=.041), but equivalent across the other groups (CBT vs. BPI p=.10; CBT vs. STPP p=.66). Rates of all other anxiety diagnoses were balanced across treatment arms at baseline (ps > 0.1). The most common disorder was GAD. See Table 15, Appendix D for raw RCMAS scores over time.

Table 6: Anxiety diagnoses across time, raw data.

K-SADS Diagnosis	Baseline % (n)	6 weeks % (n)	12 weeks % (n)	36 weeks % (n)	52 weeks % (n)	86 weeks % (n)
Separation	4.4 (20)	3.1 (9)	3 (9)	1.06 (3)	1.12 (3)	1.05 (3)
GAD	24.0 (99)	13.96 (37)	11.51 (32)	7.95 (21)	3.6 (9)	4.46 (12)
PTSD	8.27 (32)	2.76 (7)	1.09 (3)	1.57 (4)	2.52 (6)	0.76 (2)
Social phobia	13.15 (61)	11.42 (33)	10.89 (33)	7.89 (22)	6.37 (17)	5.94 (17)
Agoraphobia/ Specific phobia/ Panic	11.14 (41)	9.58 (23)	9.92 (24)	7.63 (19)	6.84 (16)	3.49 (9)
Any anxiety diagnosis	39.6 (107)	24.4 (48)	23.0 (47)	17.4 (37)	14.7 (28)	10.6 (24)

Missing data

Missing data in RCMAS total scores ranged from 1 missing case at baseline to a maximum of 33% missing at the 52-week follow-up (Table 7). As illustrated in Table 7 there were many predictors of missing RCMAS scores across the timepoints. The presence of such predictors indicates that the difference between missing and observed values can be explained by these auxiliary variables, supporting the hypothesis that data is missing at random and appropriate for multiple imputation. All of these auxiliary variables were included in the imputation model to increase accuracy of the imputations.

Table 7: Predictors of RCMAS missingness.

Predictor	RCMAS Assessment 5 Missing (n=134, 29%)			RCMAS Assessment 4 Missing (n=153, 33%)			RCMAS Assessment 3 Missing (n=152, 33%)			RCMAS Assessment 2 Missing (n=142, 31%)		
	Assessment*	r/rho	*p*	Assessment	r/rho	*p*	Assessment	r/rho	*p*	Assessment	r/rho	*p*
Background variables												
Age	-	-	-	0	-0.10	0.0345	-	-	-	-	-	-
Gender (1=male)	-	-	-	-	-	-	-	-	-	-	-	-
Ethnicity(1=non-white)	-	-	-	-	-	-	-	-	-	-	-	-
Deprivation	-	-	-	-	-	-	-	-	-	-	-	-
Region	0	-0.10	0.032	0	-0.12	0.0091	-	-	-	-	-	-
Treatment												
Treatment arm	-	-	-	-	-	-	-	-	-	-	-	-
Time to start treatment	-	-	-	-	-	-	-	-	-	-	-	-
Adherence to treatment	0	-0.18	0.0001	0	-0.17	0.0002	0	0.17	0.0002	0	-0.23	0.0001
Days since baseline	0	0.10	0.0316	1	0.11	0.0695	-	-	-	-	-	-
SSRI use	3	-0.12	0.45	-	-	-	1	-0.12	0.34	-	-	-
K-SADS Diagnoses												
MDD	0	-0.19	0.31	1	0.15	0.16	-	-	-	-	-	-
GAD	1	-0.17	0.28	1	-0.22	0.20	1	-0.17	0.28	1	-0.18	0.35
Social phobia	0	0.15	0.13	1	-0.42	0.0088	0	0.11	0.24	1	-0.33	0.09
PTSD	4	0.46	0.06	0	0.15	0.24	1	0.11	0.64	-	-	-
Agoraphobia/Specific/Panic	1	0.17	0.28	1	0.19	0.20	0	-0.11	0.48	0	-0.26	0.05
Separation anxiety	0	0.20	0.13	0	0.20	0.14	0	0.15	0.33	0	0.18	0.21
Behaviour disorder	0	0.26	0.0106	0	0.24	0.0198	0	0.36	0.0003	0	0.20	0.06
Other comorbidities	4	0.41	0.20	1	-0.16	1.00	-	-	-	0	-0.11	0.51
Questionnaire scores												
Baseline RCMAS	-	-	-	-	-	-	-	-	-	-	-	-

MFQ	2	0.15	0.0063	2	0.12	0.0301	-	-	-	-	-	-
RSES	2	-0.21	0.0001	2	-0.10	0.08	-	-	-	-	-	-
LOI	2	0.12	0.0355	3	0.11	0.06	1	0.11	0.05	-	-	-
RRS	2	0.12	0.043	-	-	-	-	-	-	-	-	-
BC	2	0.13	0.022	2	0.14	0.012	2	0.16	0.0053	0	0.10	0.028
NSSI	3	0.13	0.016	-	-	-	-	-	-	-	-	-
CSSRS	4	0.10	0.10	0	0.10	0.044	-	-	-	-	-	-

*Earliest assessment at which variable is predictive of RCMAS missingness, 0=baseline, 1=6 weeks, 2=12 weeks, 3=36 weeks, 4=52 weeks, 5=86 weeks

Mixed models

As shown in Table 8 GAD, PTSD, social phobia and the amalgamated agoraphobia/specific phobia/panic disorder group diagnoses all declined linearly over the study (i.e. diagnostic criteria were less likely to be met as time progressed). However, GAD and PTSD increased quadratically following this linear decline in diagnosis. A main effect of age was found for separation anxiety and GAD, with opposite patterns: separation anxiety being more likely in younger children and GAD more likely in older children. A main effect of gender was found for PTSD, with diagnosis being more likely in females than males. There were no significant interactions of time (linear or quadratic) with age or gender for any diagnoses. The above linear and quadratic effects were maintained following control for age and gender.

Table 8: Mixed models of diagnoses over time.

	Separation anxiety		GAD		PTSD		Social phobia		Agoraphobia/Specific phobia/Panic	
Main effects	Coefficient (95% CI)	*p* value	Coefficient (95% CI)	*p* value	Coefficient (95% CI)	*p* value	Coefficient (95% CI)	*p* value	Coefficient (95% CI)	*p* value
Time (linear)	[a]		-2.9×10^{-3} (-3.8×10^{-3}, -1.97×10^{-3})	*<.0001	-1.6×10^{-3} (-2.9×10^{-3}, -2.6×10^{-4})	*0.019	-1.5×10^{-3} (-2.4×10^{-3}, -6.6×10^{-4})	*0.001	-1.8×10^{-3} (-2.8×10^{-3}, -7.8×10^{-4})	*0.001
Time^2 (quadratic)	[a]		6.2×10^{-6} (2.8×10^{-6}, 9.7×10^{-6})	*<.0001	5.4×10^{-6} (8.6×10^{-7}, 9.9×10^{-6})	*0.020	2.1×10^{-6} (-1.8×10^{-6}, 5.9×10^{-6})	0.287	4.8×10^{-7} (-4.2×10^{-6}, 5.1×10^{-6})	0.84
Age	-0.25 (-0.45, -0.05)	*0.017	0.14 (0.013, 0.27)	*0.031	-0.036 (-0.20, 0.13)	0.676	0.093 (-0.051, 0.24)	0.206	0.16 (-0.0049, 0.33)	0.057
Gender	-0.44 (-1.24, 0.35)	0.274	-0.41 (-0.83, 0.017)	0.06	-0.91 (-1.71, -0.12)	*0.025	-0.37 (-0.87, 0.12)	0.139	-0.45 (-1.00, 0.096)	0.106
Interactions with age										
Time (linear)	[a]		1.4×10^{-4} (-5.3×10^{-4}, 8.2×10^{-4})	0.674	-5.4×10^{-4} (-1.4×10^{-3}, 3.6×10^{-4})	0.236	-1.2×10^{-4} (-7.3×10^{-4}, 5.0×10^{-4})	0.707	1.4×10^{-4} (-5.7×10^{-4}, 8.5×10^{-4})	0.699
Time^2 (quadratic)	[a]		2.5×10^{-7} (-6.2×10^{-7}, 1.1×10^{-6})	0.572	-4.4×10^{-7} (-1.5×10^{-6}, 6.3×10^{-7})	0.419	2.3×10^{-8} (-8.7×10^{-7}, 9.2×10^{-7})	0.96	3.6×10^{-7} (-7.9×10^{-7}, 1.5×10^{-6})	0.541
Gender	0.21 (-0.26, 0.67)	0.379	-0.013 (-0.28, 0.25)	0.925	0.054 (-0.39, 0.50)	0.809	0.19 (-0.14, 0.52)	0.27	0.072 (-0.29, 0.43)	0.698
Interactions with gender										
Time (linear)	[a]		-1.4×10^{-3} (-4.0×10^{-3},1.1×10^{-3})	0.268	1.3×10^{-3} (-2.9×10^{-3}, 5.5×10^{-3})	0.547	1.1×10^{-4} (-1.9×10^{-3}, 2.1×10^{-3})	0.912	-3.2×10^{-5} (-2.4×10^{-3}, 2.3×10^{-3})	0.979
Time^2 (quadratic)	[a]		-1.2×10^{-6} (-4.4×10^{-6}, 2.1×10^{-6})	0.485	1.5×10^{-6} (-0.3×10^{-6}, 6.1×10^{-6})	0.51	1.8×10^{-7} (-2.6×10^{-6}, 3.0×10^{-6})	0.901	-1.9×10^{-7} (-3.8×10^{-6}, 3.4×10^{-6})	0.918
Main effects with age and gender as control										
Time^2 (quadratic)	[a]		6.3×10^{-6} (2.8×10^{-6}, 9.8×10^{-6})	*<.0001	5.4×10^{-6} (8.6×10^{-7}, 9.9×10^{-6})	*0.020	2.1×10^{-6} (-1.7×10^{-6}, 6.0×10^{-6})	0.28	5.2×10^{-7} (-4.1×10^{-6}, 5.2×10^{-6})	0.828

[a]Model did not converge

Growth mixture models

Table 9 shows fit statistics for the various growth mixture models compared. All models were run on imputed data first with STARTS = 200 40, which was increased as necessary until the best log likelihood was replicated at least 12 times (Asparouhov & Muthén, 2012). In order to obtain the VLMR and LMR fit statistics, the mean intercept and slope values from the imputed data were used with one of the imputations (Muthén & Muthén, 2017). LRT STARTS 0 0 100 20 was used initially and increased if necessary until the best log likelihood was replicated (Asparouhov & Muthén, 2012).

Table 9: Fit statistics of growth mixture models.

Latent classes	Starts	LRT starts	AIC	BIC (sample size adjusted)	VLMR	VLMR *p*	LMR adjusted	LMR *p*	Loglikelihood	Entropy	Class Ns
Linear 1	200 40	*	15114.695	15130.187	*	*	*	*	-7541.347	*	465
Linear 2	200 40	0 0 100 20	15044.796	15063.193	-7541.347	0.0033	71.992	0.0042	-7503.398	0.907	30, 435
Linear 3	200 40	0 0 800 160	15003.394	15024.696	-7503.398	0.0207	44.962	0.0248	-7479.697	0.712	311, 27, 127
Linear 4	400 80	0 0 1600 320	14992.139	15016.345	-7479.697	0.0359	16.367	0.0410	-7471.069	0.724	11, 49, 294, 111
Quadratic 4	200 40	0 0 1200 240	14879.103	14910.088	-7429.196	0.1504	41.595	0.1602	-7407.552	0.692	80, 295, 62, 28
Piecewise 1	200 40	*	15016.947	15036.313	*	*	*	*	-7488.474	*	465
Piecewise 2	200 40	0 0 100 20	14939.363	14962.602	-7488.474	0.0113	82.237	0.0132	-7445.681	0.834	46, 419
Piecewise 3	12800 2560	0 0 1600 320	14910.741	14937.853	-7453.034	0.0809	49.320	0.0881	-7427.371	0.707	43, 289, 133

*N/A for single class model

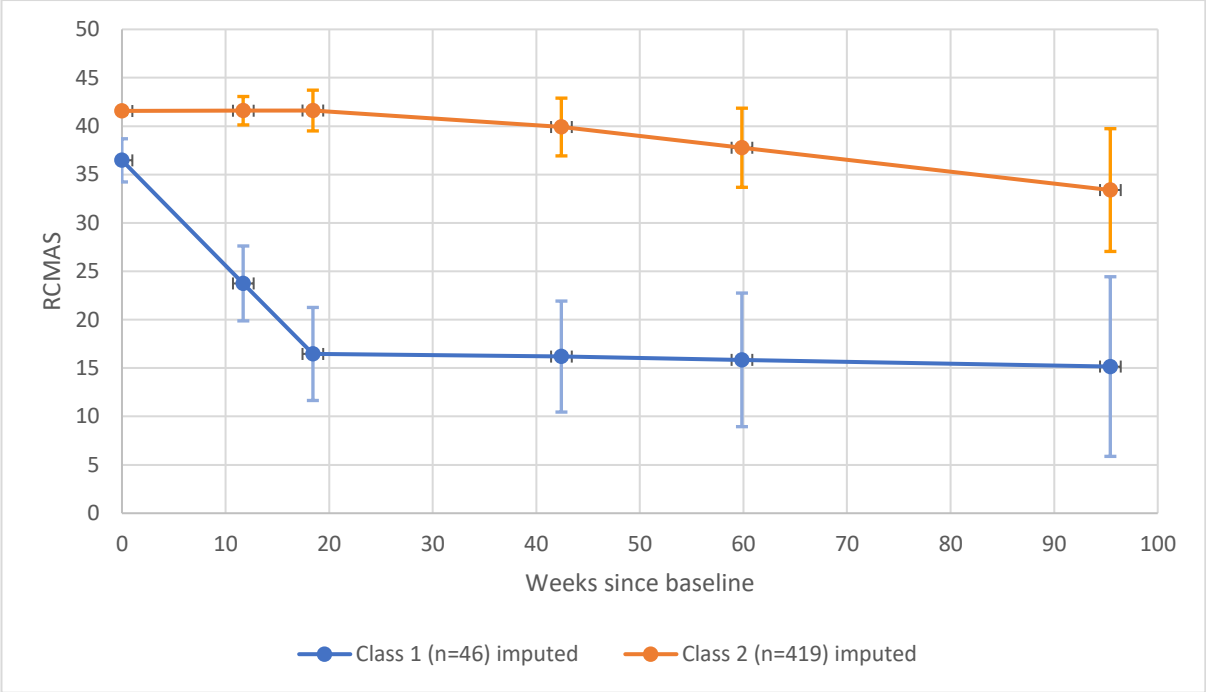
All 1, 2 and 3 class quadratic models all had a non-significant quadratic term, so these models were not pursued. The 4 class quadratic model was also rejected as it had non-significant VLMR and LMR, indicating that the addition of a fourth class (compared to three) was not warranted. The 3 class piecewise model was rejected for the same reason. The 2 class piecewise model was selected for further analysis, as from the remaining models it had the lowest ssBIC and loglikelihood. For this model the average probability of membership to class 1 was 0.91 and 0.96 for class 2.

Details of the model are shown in Table 10 and the trajectories of latent classes are graphed in Figure 3. Class 1, representing 10% of the sample, had a significant positive intercept and only the first slope was significant, indicating significant changes in anxiety symptoms during but not after treatment. Class 2, 90% of the sample also had a significant positive intercept but neither slope was significant, indicating that anxiety symptoms remained stable over time for this group.

Table 10: Estimates from growth mixture models of anxiety symptoms.

	Estimate	*SE*	Estimate / *SE*	Two-tailed *p*
Class 1: N=46				
Intercept	36.464	2.232	16.338	<.0001
Slope 1	-15.509	1.997	-7.765	<.0001
Slope 2	-0.278	0.956	-0.291	.771
Class 2: N=419				
Intercept	41.563	0.351	118.550	<.0001
Slope 1	0.039	1.361	0.029	.977
Slope 2	-1.756	0.905	-1.940	.052

Figure 3. Symptom trajectories for RCMAS.



In order to visualise the effect of multiple imputation on the data, these class trajectories were depicted with single class trajectory (imputed), single class trajectory (Full Information Maximum Likelihood); mean RCMAS scores (raw) and mean raw RCMAS scores for each class (using the latent classes derived from imputed data), see Figure 4.

Figure 4. Total RCMAS scores from baseline to 95 weeks under different modelling conditions.

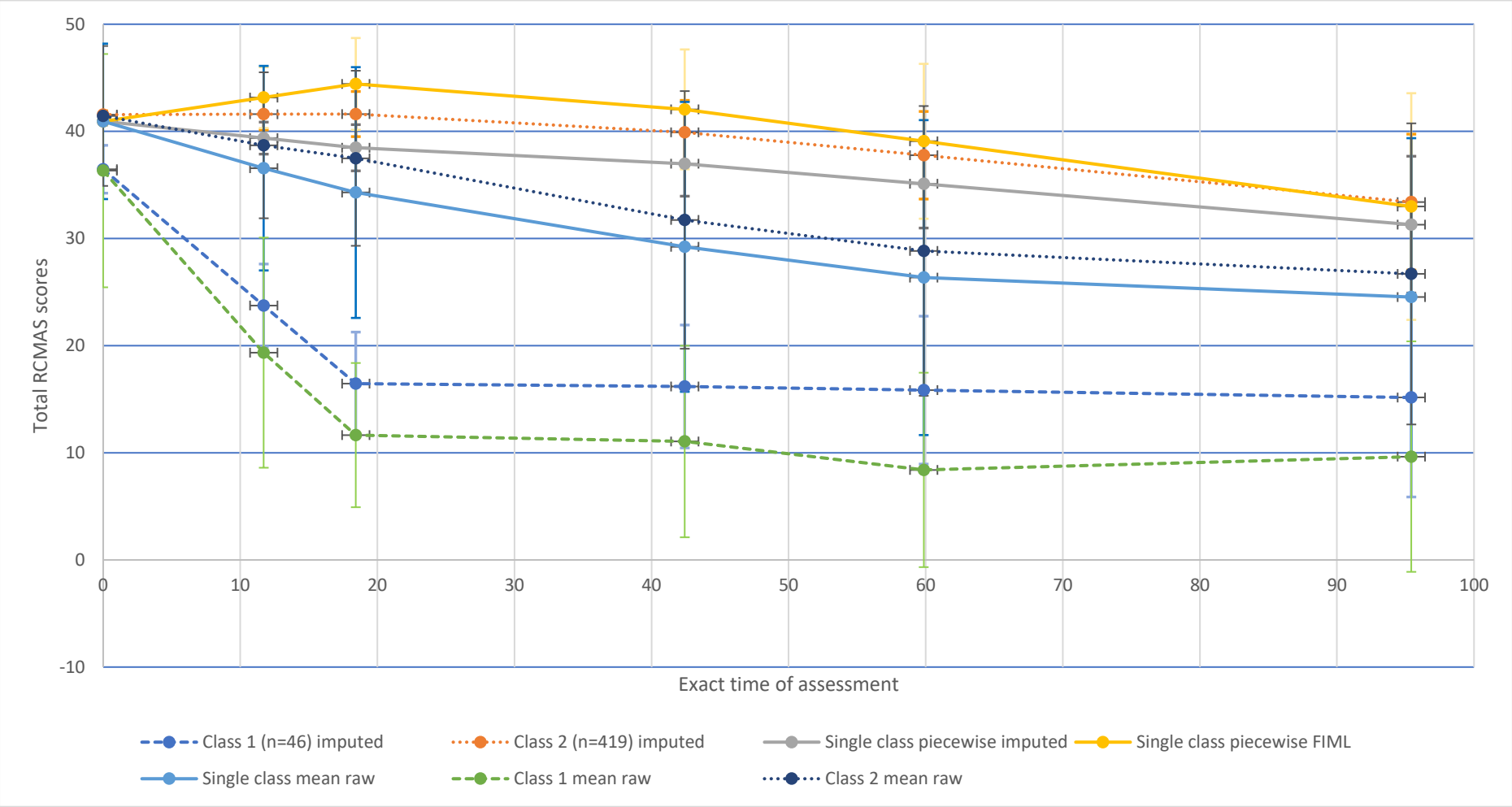


Figure 4 shows the 2-class trajectories identified through GMM using imputed data, with standard error bars. For comparison, the raw RCMAS mean scores for these identified classes and the whole sample are shown, with standard deviation error bars. Single class (whole sample) piecewise trajectories are also presented, for the imputed data and using FIML (with standard error bars).

The overlapping error bars for single-class models using FIML and imputed data indicate that both methods of accounting for missing data give comparable results. Mean RCMAS raw scores have wider error bars which overlap with both these trajectories, indicating that estimations are appropriately dealing with error due to drop out. The class 1 and class 2 (as identified using imputed data) raw means follow very similar patterns to the imputed class data but with lower scores (as in the case of the single-class model). This indicates that imputations are correcting for some of the bias in raw data (more symptomatic individuals typically drop out), making improvement seem greater than it would be if there were no dropouts.

Baseline predictors of class membership are presented in Table 11. (It was not possible to obtain exact n's or standardised coefficients due to constraints on the functions available for imputed data.) Region was a significant predictor of class. Pairwise comparisons indicated that those from the North West were more likely to be in class 1 (the smaller, improving class) compared with those from East Anglia (OR=2.05 (95% CI 1.86, 2.26), $p<.001$) or North London (OR=1.96 (95% CI 1.77, 2.19), $p<.001$). The difference between East Anglia and North London was not significant ($p=.459$). Baseline anxiety, depression, obsessions, rumination, non-suicidal self-injury and suicidal ideation all significantly predicted latent class membership, with greater severity predicting membership to the larger, non-improving class. Self-esteem significantly predicted membership to the smaller

improving class, as did being from the North West. Being female, having a longer time from randomization to starting treatment and being from East Anglia or North London also predicted membership to the larger, non-improving class.

As initial anxiety severity (RCMAS) and gender were significant, these crucial components of anxiety trajectory were added as controls when repeating the previous models. In their presence, only depression, self-esteem and suicidal ideation remained significant (Table 11). A further regression model was conducted using these variables to see which was most strongly predictive of class membership. Only depression remained significantly predictive of class membership (greater severity predicting membership to larger, non-improving class). Correlations were all less than 0.9. The maximum Variance Inflation Factor was 2.23, indicating that multicollinearity was not a problem (Chatterjee & Hadi, 2012). As the RSES correlated highly with MFQ, the correlation was re-run without this variable; without RSES all correlations were less than 0.7, only MFQ remained significantly predictive of class membership, VIF was 1.43, indicating that multicollinearity was not a problem.

Table 11: Descriptive characteristics of participants by class.

Baseline predictor	Class 1 Mean (SD) /% (small class)	Class 2 Mean (SD)/% (larger class)	Unstandardised Coefficient (95% CI)	*p*	Coefficient (95% CI) with Gender and RCMAS controlled	*p*
Age	15.52 (1.71)	15.62 (1.39)	-0.05 (-0.13, -0.04)	.301		
Gender (0=female)	52% female	77% female	1.14 (0.52, 1.76)	<.001		
Ethnicity			0.09 (-0.76, 0.94)	.839		
Index of multiple deprivation	31.08 (17.17)	26.21 (17.24)	0.02 (-0.00, 0.03)	.072	0.01 (-0.01, 0.03)	.164
Treatment arm	37% BPI, 30% CBT, 33% STPP	33% BPI, 33% CBT, 34% STPP	-0.08 (-0.23, 0.08)	.329		
Region	30% East Anglia, 22% North London, 48% North West	41% East Anglia, 28% North London, 31% North West	0.37 (0.01, 0.74)	.044	0.30 (-0.08, 0.68)	.118
Time to start treatment	4.52 (3.65)	5.04 (4.16)	-0.04 (-0.07, -0.00)	.048	-0.03 (-0.12, 0.06)	.566
Adherence to treatment	0.65 (0.45)	0.68 (0.46)	-0.11 (-0.38, 0.15)	.399		
SSRI use	21% using SSRI	22% using SSRI	-0.08 (-0.85, 0.69)	.840	-0.17 (-0.97, 0.63)	.675
RCMAS (anxiety)	36.33 (10.90)	41.42 (6.54)	-0.08 (-0.12, -0.04)	<.001	-0.01 (-0.03, 0.02)	.616
MFQ (depression)	38.35 (12.05)	46.78 (10.03)	-0.07 (-0.10, -0.04)	<.001	-0.05 (-0.09, -0.02)	.005
GAD Diagnosis	12	26	-0.94 (-1.90, 0.01)	.052	-0.70 (-1.68, 0.28)	.159
Social phobia diagnosis	13	13	-0.02 (-0.92, 0.88)	.965	0.15 (-0.79, 1.09)	.750
PTSD diagnosis	6	10	-0.57 (-2.02, 0.89)	.445	-0.23 (-1.71, 1.24)	.755
Agoraphobia, specific phobia or panic diagnosis	4	13	-1.34 (-3.16, 0.48)	.149	-1.05 (-2.90, 0.79)	.263

Baseline predictor	Class 1 Mean (SD) /% (small class)	Class 2 Mean (SD)/% (larger class)	Unstandardised Coefficient (95% CI)	*p*	Coefficient (95% CI) with Gender and RCMAS controlled	*p*
RSES (Self-esteem)	10.43 (4.14)	7.42 (4.29)	0.17 (0.09, 0.24)	<.001	0.10 (0.02, 0.19)	.018
LOI (Obsessionality)	8.27 (5.35)	10.19 (5.21)	-0.07 (-0.14, -0.01)	.020	-0.01 (-0.08, 0.06)	.791
RRS (Rumination)	82.64 (18.37)	87.65 (14.16)	-0.02 (-0.04, -0.00)	.036	-0.01 (-0.03, 0.02)	.616
BC (Behaviour checklist)	3.36 (3.01)	3.30 (3.19)	0.01 (-0.09, 0.10)	.903		
NSSI (non-suicidal self-injury)	0.43 (0.50)	0.60 (0.49)	-0.69 (-1.33, -0.06)	.033	-0.47 (-1.13, 0.20)	.169
CSSRS (Columbia Suicide Rating Scale)	2.43 (1.87)	3.43 (1.55)	-0.35 (-0.52, -0.17)	<.001	-0.29 (-0.48, -0.09)	.004

Table 12: Relationship between number of anxiety diagnoses and class over time.

	Coefficient (95% CI)	*p*
Baseline	-.57 (-1.25, 0.12)	0.105
Assessment 3 (end of treatment)	-.82 (-1.90, 0.25)	0.131
Assessment 5	-1.03 (-2.24, 0.19)	0.097

Logistic regressions indicated that there were no significant differences in the number of contemporaneous anxiety diagnoses between classes at baseline, end of treatment or end of follow up (see Table 12).

Discussion

Previous research has shown that depression and anxiety are closely associated in youth, comorbidity is common and the presence of either is predictive of a later episode of either disorder (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Pine, Cohen, Gurley, Brook, & Ma, 1998). Comorbid presentations generally have a worse prognosis and the literature on intervening in the presence of comorbidity is complex. Current NICE guidance recommends psychological therapy for depression (individual CBT, interpersonal therapy, family therapy or psychodynamic psychotherapy; NICE, 2005) and CBT for anxiety (NICE, 2014); there are no recommendations for comorbid presentations. Previous research has reported conflicting findings about the impact of comorbidity on treatment effectiveness, and whether non-target symptoms are impacted by intervention.

This is the first study to assess anxiety trajectories in youth through the course of depression treatment and follow-up. After correcting for any bias due to missing data using multiple imputation, GMM revealed that a two-class model fit the data best. Ninety percent of participants were in the class which exhibited no significant change in anxiety symptoms. The smaller class (N=46) had significantly improved anxiety symptoms from beginning to end of treatment, but no change from end of treatment to follow up. Modelling techniques have been used previously in observational studies, but not to assess the impact of intervention on non-target symptoms.

After controlling for gender and baseline RCMAS, the only significant predictors of class membership were mood (MFQ), self-esteem (RSES) and suicidality (CSSRS); greater impairment predicting membership to the larger, non-improving class. There were no differences between the number of anxiety diagnoses in each class at baseline, end of treatment or end of follow-up, nor were there any effects of treatment type.

These trajectory findings are in contrast to raw data findings (Goodyer et al., 2017). In the raw data anxiety symptoms appeared significantly reduced for the psychological treatments combined versus the BPI at post-treatment, but not at 86 week follow-up. It may have been hypothesised from this that these depression treatments were promising at treating anxiety. However, the present study's use of GMM and multiple imputation to reduce potential bias due to dropout has demonstrated that this was not the case. For most youth in the IMPACT sample, depression-focused treatment had no effect on concurrent anxiety symptoms. This is contrary to previous findings (Weisz et al., 2006). It is possible that in the IMPACT sample the lack of improvement was due to greater overall severity. Alternatively, it

may be that youth with anxiety symptoms require targeted treatment to improve such symptoms. The adult literature suggests that such targeted treatment may also reduce depression symptoms (Kendall et al., 1997, 2008, 2004).

Item level examination of the content of RCMAS indicates that it captures several different aspects of worry: sensitivity, somatic symptoms, and worry about the self in a social context. These issues seem pertinent to the age range of the sample (despite the RCMAS being developed for primary aged children; Reynolds & Richmond, 1978). The mean scores of the sample in each class were substantially raised (36.3, 41.4) compared to findings from a non-clinical population of adolescents (7.0, Muris et al., 2002). It has been suggested that the vulnerabilities of social evaluative threat and reward processing may predispose anxious adolescents to depression (Silk, Davis, McMakin, Dahl, & Forbes, 2012). This corroborates previous findings that high levels of anxiety predict later high levels of depression (Cole et al., 1998). There has been some suggestion that sleep disturbance due to worry may contribute to this link (Danielsson, Harvey, MacDonald, Jansson-Frojmark, & Linton, 2013). It may be that anxiety was a common precursor to depression in the IMPACT sample and although the depression treatments successfully treated mood (Goodyer et al., 2017) the longer standing cognitive biases associated with anxiety did not shift without specific intervention. Anxiety symptoms have been shown to be persistent even following specific treatment in youth, requiring extended treatment (Ginsburg et al., 2011).

Predictors of class membership are largely consistent with prior work, and individuals scoring on multiple factors predicting the non-improving class could be targeted first for an anxiety intervention. Females were more prevalent in the larger, non-improving class, which is corroborated by previous findings that development of

anxiety symptoms is more common in girls (Mezulis et al., 2011, 2014). After controlling for baseline RCMAS and gender, MFQ, self-esteem, and suicidality were significantly predictive of class membership. Lower self-esteem was predictive of membership to the non-improving class; this is consistent with the negative social evaluation common to comorbid anxiety and depression described above (Silk et al., 2012). For many clinicians suicidality is more readily associated with depression than anxiety, in this sample baseline suicidality predicted membership to the non-improving anxiety trajectory. Previously it has been found that only mood, conduct and substance disorders are related to suicidality in teenagers (Shaffer et al., 1996). A review of suicide-related behaviours and anxiety found that there is consistent evidence for a significant association between the two (Hill, Castellanos, & Pettit, 2011). Regardless, suicidality demonstrates a high level of distress prior to a non-improving anxiety trajectory; it is possible that addressing the anxiety symptoms would in turn prevent suicidal behaviour.

A key clinical finding from this study is that improvement in depression symptoms do not necessarily generalise to anxiety. In cases where symptoms of both are present it may be necessary to use a transdiagnostic approach. Sequential focus may be beneficial, as a meta-analysis found that treating multiple problems concurrently produced smaller effects than treating any single targeted problem (Weisz et al., 2017). The present findings argue for screening for anxiety symptoms following depression treatment, not only to mitigate these symptoms in and of themselves, but also to potentially prevent a future episode of depression (Costello et al., 2003; Pine et al., 1998). The present findings also suggest that suicidality should be assessed routinely when working with anxiety. Moreover, suicidality should be considered separately from non-suicidal self-injury, which was not predictive of

class membership here, supporting the notion that the mechanisms driving these behaviours differ (Cassels & Wilkinson, 2016).

Limitations of this study include the lack of a no treatment control group, which would have allowed further elucidation of whether some change was endogenous or due to general effects of intervention. The RCMAS was originally designed as a measure of trait anxiety in schools, rather than clinical anxiety and does not map on to diagnostic categories (Reynolds & Richmond, 1978). However, it captures several different aspects of worry: sensitivity, somatic symptoms and worry about the self in a social context. These issues seem pertinent to the age range of the sample and anxiety diagnoses were also investigated using K-SADS.

In summary, the trajectories of anxiety symptoms in youth during depression treatment indicated that for most, anxiety symptoms as measured by the RCMAS were not responsive to CBT, STPP, or BPI. Youth commonly present with symptoms of anxiety and depression and each is predictive of later episodes of the other (Costello et al., 2003; Pine et al., 1998). Interventions should specifically target both and post-treatment assessments should identify residual symptoms for further intervention.

Chapter 3 References

Abbass, A. A., Rabung, S., Leichsenring, F., Refseth, J. S., & Midgley, N. (2013). Psychodynamic Psychotherapy for Children and Adolescents: A Meta-Analysis of Short-Term Psychodynamic Models. *Journal of the American Academy of Child & Adolescent Psychiatry*, *52*(8), 863–875. https://doi.org/10.1016/j.jaac.2013.05.014

Asparouhov, T., & Muthén, B. (2012). Using Mplus TECH11 and TECH14 to test the number of latent classes. Retrieved February 24, 2019, from http://www.statmodel.com/examples/webnotes/webnote14.pdf

Axelson, D. A., & Birmaher, B. (2001). Relation between anxiety and depressive disorders in childhood and adolescence. *Depression And Anxiety*, *14*, 67–78.

Bamber, D., Tamplin, A., Park, R. J., Kyte, Z. A., & Goodyer, I. M. (2002). Development of a Short Leyton Obsessional Inventory for Children and Adolescents Development of a Short Leyton Obsessional Inventory for Children and Adolescents. *Journal of American Academy of Child and Adolescent Psychiatry*, *41*(10), 1246–1252. https://doi.org/10.1097/00004583-200210000-00015

Berman, S. L., Weems, C. F., Silverman, W. K., & Kurtines, W. M. (2000). Predictors of outcome in exposure-based cognitive and behavioral treatments for phobic and anxiety disorders in children. *Behavior Therapy*, *31*(4), 713–731. https://doi.org/https://doi.org/10.1016/S0005-7894(00)80040-4

Birmaher, B., Ryan, N. D., Williamson, D. E., Brent, D. A., Kaufman, J., Dahl, R. E., … Nelson, B. (1996). Childhood and adolescent depression: a review of the past 10 years. Part I. *Journal Of The American Academy Of Child And*

Adolescent Psychiatry, *35*(11), 1427–1439.

Cassels, M., & Wilkinson, P. (2016). Non-suicidal self-injury in adolescence. *Paediatrics and Child Health*, *26*(12), 554–558.

Chatterjee, S., & Hadi, A. S. (2012). *Regression Analysis by Example.* (Fifth). New York: John Wiley & Sons.

Cole, D. A., Peeke, L. G., Martin, J. M., Truglio, R., & Seroczynski, A. D. (1998). A Longitudinal Look at the Relation Between Depression and Anxiety in Children and Adolescents. *Journal Of Consulting And Clinical Psychology*, *66*(3), 451–460. https://doi.org/10.1037/0022-006X.66.3.451

Compton, S. N., March, J. S., Brent, D., Albano, A. M., Weersing, V. R., & Curry, J. (2004). Cognitive-Behavioral Psychotherapy for Anxiety and Depressive Disorders in Children and Adolescents : An Evidence-Based Medicine Review. *Journal Of The American Academy of Child & Adolescent Psychiatry*, *43*, 930–959. https://doi.org/10.1097/01.chi.0000127589.57468.bf

Connolly Gibbons, M. B., Gallop, R., Thompson, D., Luther, D., Crits-Christoph, K., Jacobs, J., … Crits-Christoph, P. (2016). Comparative Effectiveness of Cognitive Therapy and Dynamic Psychotherapy for Major Depressive Disorder in a Community Mental Health Setting A Randomized Clinical Noninferiority Trial. *JAMA Psychiatry*, *73*(9), 904–911. https://doi.org/10.1001/jamapsychiatry.2016.1720

Costello, E. J., & Angold, A. (1988). Scales to Assess Child and Adolescent Depression: Checklists, Screens, and Nets. *Journal of the American Academy of Child & Adolescent Psychiatry*, *27*(6), 726–737. https://doi.org/10.1097/00004583-198811000-00011

Costello, J., Mustillo, S., Erkanli, A., Keeler, G., & Angold, A. (2003). Prevalence and Development of Psychiatric Disorders in Childhood and Adolescence. *Archives Of General Psychiatry*, *60*, 837–844.

Curry, J., Rohde, P., Simons, A., Silva, S., Vitiello, B., Kratochvil, C., … Team, T. T. (2006). Predictors and Moderators of Acute Outcome in the Treatment for Adolescents With Depression Study (TADS). *Journal of the American Academy of Child & Adolescent Psychiatry*, *45*(12), 1427–1439. https://doi.org/10.1097/01.chi.0000240838.78984.e2

Danielsson, N. S., Harvey, A. G., MacDonald, S., Jansson-Frojmark, M., & Linton, S. J. (2013). Sleep Disturbance and Depressive Symptoms in Adolescence: The Role of Catastrophic Worry. *Journal of Youth & Adolescence*, *42*(8), 1223–1233. https://doi.org/10.1007/s10964-012-9811-6

Ellis, R. E. R., Seal, M. L., Simmons, J. G., Whittle, S., Schwartz, O. S., Byrne, M. L., & Allen, N. B. (2017). Longitudinal Trajectories of Depression Symptoms in Adolescence : Psychosocial Risk Factors and Outcomes. *Child Psychiatry And Human Development*, *48*, 554–571. https://doi.org/10.1007/s10578-016-0682-z

Erskine, H. E., Moffitt, T. E., Copeland, W. E., Costello, E. J., Ferrari, A. J., Patton, G., … Scott, J. G. (2015). A heavy burden on young minds : the global burden of mental and substance use disorders in children and youth. *Psychological Medicine*, (45), 1551–1563. https://doi.org/10.1017/S0033291714002888

Ezpeleta, L., Domenech, J. M., & Angold, A. (2006). A comparison of pure and comorbid CD/ODD and depression. *Journal of Child Psychology and Psychiatry*, *7*, 704–712. https://doi.org/10.1111/j.1469-7610.2005.01558.x

Flannery-Schroeder, E., Suveg, C., Safford, S., Kendall, P. C., & Webb, A. (2004). Comorbid Externalising Disorders and Child Anxiety Treatment Outcomes. *Behaviour Change*, *21*(1), 14–25.

Ginsburg, G. S., Kendall, P. C., Sakolsky, D., Compton, S. N., Piacentini, J., Albano, A. M., … March, J. (2011). Remission after acute treatment in children and adolescents with anxiety disorders: findings from the CAMS. *Journal Of Consulting And Clinical Psychology*, *79*(6), 806–813. https://doi.org/10.1037/a0025933

Goodyer, I. M., Herbert, J., Tamplin, A., & Altham, P. M. E. (2000). First-episode major depression in adolescents Affective, cognitive and endocrine characteristics of risk status and predictors of onset. *British Journal of Psychiatry*, *176*, 142–149.

Goodyer, I. M., Reynolds, S., Barrett, B., Byford, S., Dubicka, B., Hill, J., … Kelvin, R. (2017). Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre , pragmatic , observer-blind , randomised controlled superi. *The Lancet Psychiatry*, *4*(2), 109–119. https://doi.org/10.1016/S2215-0366(16)30378-9

Goodyer, I. M., Tsancheva, S., Byford, S., Dubicka, B., Hill, J., Kelvin, R., … Fonagy, P. (2011). Improving mood with psychoanalytic and cognitive therapies (IMPACT): a pragmatic effectiveness superiority trial to investigate whether specialised psychological treatment reduces the risk for relapse in adolescents with moderate to severe unipolar depres. *Trials*, *12*. https://doi.org/10.1186/1745-6215-12-175

Gould, M. S., King, R., Greenwald, S., Fisher, P., Schwab-Stone, M., Kramer, R., … Shaffer, D. (1998). Psychopathology Associated With Suicidal Ideation and Attempts Among Children and Adolescents. *Journal of the American Academy of Child & Adolescent Psychiatry*, *37*(9), 915–923. https://doi.org/https://doi.org/10.1097/00004583-199809000-00011

Hill, R. M., Castellanos, D., & Pettit, J. W. (2011). Suicide-related behaviors and anxiety in children and adolescents : A review. *Clinical Psychology Review*, *31*(7), 1133–1144. https://doi.org/10.1016/j.cpr.2011.07.008

Kaufman, J., Birmaher, B., Brent, D., Rao, U. M. A., Flynn, C., Moreci, P., … Ryan, N. (1997). Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): Initial Reliability and Validity Data. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*(7), 980–988. https://doi.org/10.1097/00004583-199707000-00021

Kendall, P. C., Brady, E. U., & Verduin, T. L. (2001). Comorbidity in Childhood Anxiety Disorders and Treatment Outcome. *Journal of the American Academy of Child & Adolescent Psychiatry*, *40*(7), 787–794. https://doi.org/https://doi.org/10.1097/00004583-200107000-00013

Kendall, P. C., Flannery-Schroeder, E., Panichelli-Mindel, S. M., Southam-Gerow, M., Henin, A., & Warman, M. (1997). Therapy for Youths With Anxiety Disorders : A Second Randomized Clinical Trial. *Journal Of Consulting And Clinical Psychology*, *65*(3), 366–380.

Kendall, P. C., Hudson, J. L., Gosch, E., Flannery-Schroeder, E., & Suveg, C. (2008). Cognitive – Behavioral Therapy for Anxiety Disordered Youth : A

Randomized Clinical Trial Evaluating Child and Family Modalities. *Journal Of Consulting And Clinical Psychology*, *76*(2), 282–297. https://doi.org/10.1037/0022-006X.76.2.282

Kendall, P. C., Safford, S., Flannery-Schroeder, E., & Webb, A. (2004). Child Anxiety Treatment : Outcomes in Adolescence and Impact on Substance Use and Depression at 7 . 4-Year Follow-Up. *Journal Of Consulting And Clinical Psychology*, *72*(2), 276–287. https://doi.org/10.1037/0022-006X.72.2.276

Kertz, S. J., Sylvester, C., Tillman, R., & Luby, J. L. (2017). Latent Class Profiles of Anxiety Symptom Trajectories From Preschool Through School Age. *Journal of Clinical Child & Adolescent Psychology*, 1–16. https://doi.org/10.1080/15374416.2017.1295380

Kessler, R. C., Avenevoli, S., Mclaughlin, K. A., Green, J. G., Lakoma, M. D., & Petukhova, M. (2012). Lifetime co-morbidity of DSM-IV disorders in the US National Comorbidity Survey Replication Adolescent Supplement (NCS-A). *Psychological Medicine*, *42*, 1997–2010. https://doi.org/10.1017/S0033291712000025

Kim, S. (2014). Determining the number of latent classes in single- and multi-phase growth mixture models. *Structural Equation Modelling*, *21*(2), 263–279. https://doi.org/10.1080/10705511.2014.882690.Determining

Leichsenring, F., Rabung, S., & Leibing, E. (2004). The Efficacy of Short-term Psychodynamic Psychotherapy in Specific Psychiatric Disorders. *Archives Of General Psychiatry*, (61), 1208–1216.

Leichsenring, F., Salzer, S., Jaeger, U., Kächele, H., Kreische, R., Leweke, F., … Leibing, E. (2009). Short-term Psychodynamic Psychotherapy and Cognitive-

Behavioral Therapy in Generalized Anxiety Disorder : A Randomized , Controlled Trial. *American Journal of Psychiatry*, (166), 875–881.

Little, R. J. A. (1988). A Test of Missing Completely at Random for Multivariate Data with Missing Values. *Journal Of The American Statistical Association*, *83*(404), 1198–1202.

Merikangas, K. R., Zhang, H., Avenevoli, S., Acharyya, S., Neuenschwander, M., & Angst, J. (2003). Longitudinal Trajectories of Depression and Anxiety in a Prospective Community Study. *Archives Of General Psychiatry*, *60*, 993–1000.

Mezulis, A., Funasaki, K., & Hyde, J. S. (2011). Negative Cognitive Style Trajectories in the Transition to Adolescence. *Journal of Clinical Child & Adolescent Psychology*, *40*(2), 318–331. https://doi.org/10.1080/15374416.2011.546048

Mezulis, A., Salk, R. H., Hyde, J. S., Priess-Groben, H. A., & Simonson, J. L. (2014). Affective , Biological , and Cognitive Predictors of Depressive Symptom Trajectories in Adolescence. *Journal Of Abnormal Child Psychology*, *42*, 539–550. https://doi.org/10.1007/s10802-013-9812-2

Muris, P., Merckelbach, H., Ollendick, T., King, N., & Bogie, N. (2002). Three traditional and three new childhood anxiety questionnaires: their reliability and validity in a normal adolescent sample. *Behaviour Research And Therapy*, *40*, 753–772.

Muthén, L. K., & Muthén, B. O. (2017). *Mplus User's Guide.* (Eighth). Los Angeles, CA: Muthén & Muthén.

NICE. (2005). Depression in children and young people: identification and

management. Retrieved January 28, 2019, from https://www.nice.org.uk/guidance/cg28

NICE. (2014). Anxiety disorders. Retrieved January 28, 2019, from https://www.nice.org.uk/guidance/qs53

Noble, M., McLennan, D., Wilkinson, K., Whitworth, A., Barnes, H., & Dibben, C. (2008). *The English Indices of Deprivation 2007*. London.

Nolen-Hoeksema, S., & Morrow, J. (1991). A Prospective Study of Depression and Posttraumatic Stress Symptoms After a Natural Disaster : The 1989 Loma Prieta Earthquake. *Journal of Personality and Social Psychology*, *61*(1), 115–121.

Ohannessian, C. M., Milan, S., & Vannucci, A. (2017). Gender Differences in Anxiety Trajectories from Middle to Late Adolescence. *Journal of Youth & Adolescence*, *46*, 826–839. https://doi.org/10.1007/s10964-016-0619-7

Park, R. J., Goodyer, I. M., & Teasdale, J. D. (2005). Self-devaluative dysphoric experience and the prediction of persistent first-episode major depressive disorder in adolescents. *Psychological Medicine*, *35*(4), 539–548. https://doi.org/DOI: 10.1017/S003329170400371X

Penninx, B. W. J. H., Nolen, W. A., Lamers, F., Zitman, F. G., Smit, J. H., Spinhoven, P., … Beekman, A. T. F. (2011). Two-year course of depressive and anxiety disorders : Results from the Netherlands Study of Depression and Anxiety (NESDA). *Journal of Affective Disorders*, *133*, 76–85. https://doi.org/10.1016/j.jad.2011.03.027

Pine, D. S., Cohen, P., Gurley, D., Brook, J., & Ma, Y. (1998). The Risk for Early-

Adulthood Anxiety and Depressive Disorders in Adolescents With Anxiety and Depressive Disorders. *Archives Of General Psychiatry*, *55*, 56–64.

Posner, K., Brown, G. K., Stanley, B., Brent, D. A., Yershova, K. V, Oquendo, M. A., … Mann, J. J. (2011). The Columbia-Suicide Severity Rating Scale: Initial Validity and Internal Consistency Findings From Three Multisite Studies With Adolescents and Adults. *American Journal of Psychiatry*, (168), 1266–1277. https://doi.org/10.1176/appi.ajp.2011.10111704

Reynolds, C. R., & Richmond, B. O. (1978). What I Think and Feel : A Revised Measure of Children's Manifest Anxiety. *Journal Of Abnormal Child Psychology*, *6*(2), 271–280.

Rohde, P., Clarke, G. N., Lewinsohn, P. M., Seeley, J. R., & Kaufman, N. K. (2001). Impact of Comorbidity on a Cognitive-Behavioral Group Treatment for Adolescent Depression. *Journal of the American Academy of Child & Adolescent Psychiatry*, *40*(7), 795–802. https://doi.org/10.1097/00004583-200107000-00014

Rosenberg, M. (1965). *Society and the adolescent self-image.* Princeton, NJ: Princeton University Press.

Shaffer, D., Gould, M. S., Fisher, P., Trautman, P., Moreau, D., Kleinman, M., & Flory, M. (1996). Psychiatric Diagnosis in Child and Adolescent Suicide. *Archives of General Psychiatry*, *53*(4), 339–348. https://doi.org/10.1001/archpsyc.1996.01830040075012

Sharratt, K., Boduszek, D., Jones, A. D., & Gallagher, B. (2014). Construct validity, dimensionality and factorial invariance of the Rosenberg Self-Esteem Scale: a bifactor modelling approach among children of prisoners. *Current Issues in*

Personality Psychology, *2*(4), 1–9. https://doi.org/10.5114/cipp.2014.47447

Silk, J. S., Davis, S., McMakin, D. L., Dahl, R. E., & Forbes, E. E. (2012). Why do anxious children become depressed teenagers?: The role of social evaluative threat and reward processing. *Psychological Medicine*, *42*(10), 2095–2107. https://doi.org/10.1017/S0033291712000207.Why

StataCorp. (2017). Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.

Stice, E., Burton, E., Bearman, S. K., & Rohde, P. (2007). Randomized Trial of a Brief Depression Prevention Program: An Elusive Search for a Psychosocial Placebo Control Condition. *Behaviour Research And Therapy*, *45*(5), 863–876.

Trowell, J., Joffe, I., Campbell, J., Clemente, C., Almqvist, F., Soininen, M., … Tsiantis, J. (2007). Childhood depression : a place for psychotherapy An outcome study comparing individual psychodynamic psychotherapy and family therapy. *European Child & Adolescent Psychiatry*, (16), 157–167. https://doi.org/10.1007/s00787-006-0584-x

Vostanis, P., Feehan, C., & Grattan, E. (1998). Two-year outcome of children treated for depression. *European Child & Adolescent Psychiatry*, *7*(1), 12–18.

Weisz, J. R., Kuppens, S., Ng, M. Y., Eckshtain, D., Ugueto, A. M., Vaughn-Coaxum, R., … Fordwood, S. R. (2017). What five decades of research tells us about the effects of youth psychological therapy: A multilevel meta-analysis and implications for science and practice. *The American Psychologist*, *72*(2), 79–117. https://doi.org/10.1037/a0040360

Weisz, J. R., Mccarty, C. A., & Valeri, S. M. (2006). Effects of Psychotherapy for

Depression in Children and Adolescents : A Meta-Analysis. *Psychological Bulletin*, *132*(1), 132–149. https://doi.org/10.1037/0033-2909.132.1.132

White, I. R., Royston, P., & Wood, A. M. (2011). Multiple imputation using chained equations: Issues and guidance for practice. *Statistics In Medicine*, *30*, 377–399. https://doi.org/10.1002/sim.4067

Wickrama, T., & Wickrama, K. A. S. (2010). Heterogeneity in Adolescent Depressive Symptom Trajectories : Implications for Young Adults ' Risky Lifestyle. *Journal of Adolescent Health*, *47*, 407–413. https://doi.org/10.1016/j.jadohealth.2010.02.013

Wilkinson, P. O., & Goodyer, I. M. (2008). The effects of cognitive-behavioural therapy on mood-related ruminative response style in depressed adolescents. *Child and Adolescent Psychiatry and Mental Health*, *2*(1), 3. https://doi.org/10.1186/1753-2000-2-3

Wood, A., Kroll, L., Moore, A., & Harrington, R. (1995). Properties of the Mood and Feelings Questionnaire in Adolescent Psychiatric Outpatients: A Research Note. *Journal of Child Psychology and Psychiatry*, *36*(2), 327–334.

Chapter 4: Extended Methodology

This chapter will provide a description of how and why statistical procedures were undertaken in greater detail than in the empirical paper. This includes a description of analytical methods and underlying concepts. All information necessary to interpret analyses and results is within the empirical paper, this chapter is supplementary.

Missing data

Missing data can have a profound impact on the results of analyses and introduce bias, affecting the conclusions drawn. It is essential for careful consideration to be given to decide on the most appropriate way of dealing with missing data in any dataset, as different methods can yield different results (e.g. (Houck et al., 2004). This is a particular issue with longitudinal studies, where the richness of the dataset and patterns across time cannot be fully explored without accounting for missingness (Gibbons et al., 1993). Choice of method for dealing with missing data should be informed by the nature or mechanism of missingness in the data (Rubin, 1976). If data is missing completely at random (MCAR) this means that missingness does not depend on (cannot be predicted by) observed or unobserved data. Data can also be missing at random (MAR); this means that missingness can depend on observed, but not unobserved data (once the observed variables are controlled for, the missingness appears to be random). The third mechanism of missingness is missing not at random (MNAR), where missingness depends on unobserved data (Graham, 2009).

Little's Test is a single global test statistic to assess MCAR that uses all of the available data (Little, 1988). A significant result indicates that data are MAR.

There are several methods available for accounting for missing data. Last observation carried forward (LOCF), where missing values are replaced with the participant's previous score, has been widely used in clinical trials (Lachin, 2016). This approach has been criticised for assuming that data are MCAR and that a participant's responses would have been constant from their last assessment to the end of the trial, assumptions which are not reliable and can bias estimates of effects and standard errors (Mallinckrodt et al., 2003). Also LOCF does not allow for estimation of how a participant's scores may have changed over time, which is essential to fully understand the impact of an intervention (Gibbons et al., 1993). Mean substitution is another method, where missing values are replaced with the mean of non-missing values of the given variable. It assumes that data are MCAR, yielding biased means when this is false. Mean substitution also reduces the variance of the variables and is not recommended (Graham, 2009; Schlomer, Bauman, & Card, 2010). Complete cases analysis involves exclusion of participants who have any missing data from analyses (also called listwise deletion) which results in a loss of statistical power (Schlomer et al., 2010). If data are not MCAR, the remaining cases will produce a biased result (Croy & Novins, 2005). It has been suggested that this approach may be reasonable if the difference between participants who do and do not have missing data can be fully explained by baseline variables, and these variables included as covariates (Graham, 2009).

More recent methods for estimating the values of missing data have developed from likelihood-based mixed effects models, including fixed (e.g. treatment group, baseline severity) and random (e.g. participant) effects (Mallinckrodt et al., 2003). These methods are valid if data are MCAR or MAR. Maximum likelihood approaches involve use of observed data to estimate

parameters, which are then used to estimate the missing data (Schlomer et al., 2010). Full Information Maximum Likelihood (FIML) does not impute missing values, but incorporates computation of a case wise likelihood function from observed variables and analysis within the same step (Schlomer et al., 2010). An alternative strategy to this is Multiple Imputation (MI). MI is a regression-based approach which includes random error variance (single imputation results always lie on the regression line, real data do not, Graham, 2009). An advantage of MI over FIML is the ability to easily include auxiliary variables into the missing data model (Collins, Schafer, & Kam, 2001). Auxiliary variables are not part of the model being tested but are highly correlated to variables in the model. Currently it is not possible to incorporate auxiliary variables into latent class models using FIML; it is possible to do this with MI (Graham, 2009).

Little's MCAR test was significant for the raw RCMAS scores in the IMPACT data, indicating that data is MAR. As outlined above, MI is an appropriate way of dealing with this type of missingness. The imputations utilised in the empirical paper were run by a collaborator (Sharon Neufeld) as part of a wider set of imputations on the IMPACT dataset for several studies.

Mixed models

Mixed models were run to examine the patterns of diagnoses over the course of treatment and follow-up assessments. Mixed models contain both fixed and random effects. Fixed effects are factors which have systemic and predictable influence on the data, whereas modelling random effects takes account of individual random differences between participants. Mixed models can help to understand variation at different levels or hierarchies, between participants and groups within

the data. This is a particularly useful method for longitudinal data, as repeated measurement of participants (the non-independence of their data) is taken into account (Verbeke, 1997).

Growth Mixture Modelling

Growth mixture modelling (GMM) is a type of growth curve modelling that allows identification of unobserved sub-groups of individuals based on their characteristics and how a parameter, such as symptoms, changes over time (Ram & Grimm, 2009).

In the empirical paper, different types of model trajectory were compared (linear, quadratic and piecewise), based on examination of the mixed model findings and previous literature. Initially, baseline single-group growth curve models were obtained, which served as a starting point for identification of unobserved groups. A series of different growth models were fitted to all data to see which best described the overall pattern of change in the whole group. The aim was to find the most complete way of representing the data, including allowing for the possibility of multiple unobserved groups (it may be that several lines represent the data better than a single line, each line representing a sub-group of participants). Models were fitted with increasing numbers of groups, until statistical evidence was found that the addition of another group did not provide better fit.

The GMM was estimated using maximum likelihood (this method maximises the agreement between data and the model, ensuring that the model is a good representation of the data). Mplus uses an expectation-maximisation procedure, which finds maximum likelihood estimates in models that depend on unobserved latent variables (sub-groups within the participants, Muthén & Muthén, 2017).

Iterative procedures are used to obtain estimates of probability of individuals' membership in each of the possible groups.

The final step was model selection and interpretation, determination of which model provided the best representation of the observed data, considering the optimal number of unobserved groups and the type and extent of differences between and within groups. Model selection was based on theory, past findings, model results and fit statistics. Possible models were checked carefully to ensure that they made sense mathematically (e.g. no negative variance). Fit statistics such as the Bayesian Information Criteria were compared across models, a lower value indicating a better fit. (Fit statistics summarise the discrepancy between observed values in the data and values predicted by the applied model). The confidence with which individuals were classified as belonging to groups was explored. This was measured using entropy, an indicator of the probabilities of individuals' group membership. Models with higher entropy, and therefore less variability in class membership, were favoured where possible. Likelihood ratio tests were used to compare the model of interest with a model containing one less class/group. One example is the Vuong-Lo-Mendell-Rubin likelihood ratio test (VLMR-LRT). If the likelihood ratio test was significant, the model of interest was selected (rather than the alternative with one less group). Finally, group trajectories were plotted and examined, checking that the groups were distinct and that the separation and patterns made sense theoretically.

Regressions

Regressions were used to examine the relationship between outcome measures and class membership, to see which variables predicted membership to each trajectory.

Multicollinearity

Multicollinearity is present when there are high correlations between independent variables in a regression model. This is problematic because it is harder to estimate the independent effects of variables within the model, coefficient estimates become less precise and the statistical power of the model is reduced (Thompson, Seon Kim, Aloe, & Becker, 2017). Multicollinearity was found not to be problematic within the regression models tested in the empirical study, as the Variance Inflation Factors (VIF) were within acceptable ranges (Chatterjee & Hadi, 2012).

Chapter 4 References

Chatterjee, S., & Hadi, A. S. (2012). *Regression Analysis by Example.* (Fifth). New York: John Wiley & Sons.

Collins, L. M., Schafer, J. L., & Kam, C.-M. (2001). A Comparison of Inclusive and Restrictive Strategies in Modern Missing Data Procedures. *Psychological Methods*, *6*(4), 330–351. https://doi.org/10.1037/1082-989X.6.4.330

Croy, C. D., & Novins, D. K. (2005). Methods for Addressing Missing Data in Psychiatric and Developmental Research. *Journal of the American Academy of Child & Adolescent Psychiatry*, *44*(12), 1230–1240. https://doi.org/10.1097/01.chi.0000181044.06337.6f

Gibbons, R. D., Hedeker, D., Elkin, I., Waternaux, C., Kraemer, H. C., Greenhouse, J. B., … Watkins, J. T. (1993). Some Conceptual and Statistical Issues in Analysis of Longitudinal Psychiatric Data: Application to the NIMH Treatment of Depression Collaborative Research Program Dataset. *Archives of General Psychiatry*, *50*(9), 739–750. https://doi.org/10.1001/archpsyc.1993.01820210073009

Graham, J. W. (2009). Missing Data Analysis : Making It Work in the Real World. *Annual Review Of Psychology*, (60), 549–576. https://doi.org/10.1146/annurev.psych.58.110405.085530

Houck, P. R., Mazumdar, S., Koru-Sengul, T., Tang, G., Mulsant, B. H., Pollock, B. G., & Reynolds, C. F. (2004). Estimating treatment effects from longitudinal clinical trial data with missing values : comparative analyses using different methods. *Psychiatry Research*, *129*, 209–215. https://doi.org/10.1016/j.psychres.2004.08.001

Lachin, J. M. (2016). Fallacies of Last Observation Carried Forward. *Clinical Trials*, *13*(2), 161–168. https://doi.org/10.1177/1740774515602688.Fallacies

Little, R. J. A. (1988). A Test of Missing Completely at Random for Multivariate Data with Missing Values. *Journal of the American Statistical Association*, *83*(404), 1198–1202.

Mallinckrodt, C. H., Sanger, T. M., Dube, S., Debrota, D. J., Molenberghs, G., Carroll, R. J., … Tollefson, G. D. (2003). Assessing and Interpreting Treatment Effects in Longitudinal Clinical Trials with Missing Data. *Biological Psychiatry*, (53), 754–760. https://doi.org/10.1016/S0006-3223(03)01867-X

Muthén, L. K., & Muthén, B. O. (2017). *Mplus User's Guide.* (Eighth). Los Angeles, CA: Muthén & Muthén.

Ram, N., & Grimm, K. J. (2009). Growth Mixture Modeling: A Method for Identifying Differences in Longitudinal Change Among Unobserved Groups. *International Journal of Behavioural Development*, *33*(6), 565–576. https://doi.org/10.1177/0165025409343765.Growth

Rubin, D. B. (1976). Inference and Missing Data. *Biometrika*, *63*(3), 581–592. https://doi.org/10.2307/2335739

Schlomer, G. L., Bauman, S., & Card, N. A. (2010). Best Practices for Missing Data Management in Counseling Psychology. *Journal of Counseling Psychology*, *57*(1), 1–10. https://doi.org/10.1037/a0018082

Thompson, C. G., Seon Kim, R., Aloe, A. M., & Becker, B. J. (2017). Extracting the Variance Inflation Factor and Other Multicollinearity Diagnostics from Typical Regression Results. *Basic and Applied Social Psychology*, *39*(2), 81–90.

Verbeke, G. (1997). Linear Mixed Models for Longitudinal Data. In *Linear Mixed Models in Practice. Lecture Notes in Statistics, vol 126.* New York: Springer.

Chapter 5: Discussion and Critical Evaluation

While efficacy is clearly a key element when assessing the utility of a psychological therapy, it is also important to investigate the acceptability of such interventions and the impact they have on comorbid symptoms. If a treatment is not acceptable clients will stop attending and therefore not benefit. If a treatment successfully impacts on only a subset of the client's symptoms their level of functioning may not be increased post-intervention and they are likely to relapse. Findings have been presented investigating these two important areas in the context of depression treatment in youth.

Meta-analytic techniques provide greater power than individual studies to find effects and compare different interventions. They were used here to explore dropout rates from depression treatment in youth. The overall dropout rate from interventions was 14.6%, where dropout was found to be equally likely across intervention and active control conditions. Dropout was more likely from wait list/treatment as usual than family/dyadic interventions. Interventions which offered a greater number of sessions were associated with less dropout. No significant links were found between dropout and study quality, treatment duration, CBT, family or individual versus other approaches.

The impact of effective depression treatments on non-target anxiety symptoms was investigated, using growth mixture modelling. For most young people (90% of participants) these treatments did not impact on concurrent anxiety symptoms. Factors associated with ongoing anxiety included greater initial severity of mood and anxiety symptoms, low self-esteem, suicidality and being female.

Both studies contribute novel findings about the psychological treatment of depression in youth. Dropout from depression treatment had not been investigated before with a youth sample; findings indicated that the rate was similar to that found in adult studies (Cooper & Conklin, 2015; Swift & Greenberg, 2014) and slightly less than the adolescent dropout rate from antidepressant drug treatment (Rohden et al., 2017). Longitudinal trajectory modelling of non-target symptoms during depression treatment in youth had not been conducted previously. The existing evidence gave conflicting messages about the efficacy of interventions on comorbid symptoms. The finding that most participants' anxiety symptoms did not improve was contrary to previously reported findings from the raw data of the same sample (Goodyer et al., 2017).

A strength of both studies was the use of analyses to optimise statistical power. The aggregation of data across several trials allowed questions to be addressed which are not possible within a single trial, namely proportion meta-analyses, odds ratios and meta-regressions. The empirical paper utilised multiple imputation to estimate the values of missing data (with consideration of other variables) to account for potential bias in the raw data. As alluded to above, the use of multiple imputations and growth mixture modelling demonstrated that examination of the raw RCMAS scores did not give an accurate representation of overall change in anxiety scores over time, due to missing data. Previously some researchers expressed concern about the use of multiple imputation, including that it uses simulation and adds noise to the data. Other issues included computing storage and practical difficulties creating the imputations. These concerns have been robustly addressed; imputation seeks to represent rather than create information and simulates only the missing data, meaning that it is more efficient than other simulation

methods such as bootstrapping (Rubin, 1996). Computing capabilities are increasing constantly and imputation is now supported across several statistical packages and researchers are encouraged to use multiple imputation routinely to deal with missing data (Graham, 2009). See extended methodology section for thorough discussion of the rationale for use of multiple imputation in the empirical paper.

Both studies reported here have limitations. The IMPACT trial did not include a no intervention control group, so it was not possible to compare anxiety trajectories across young people who were and were not receiving treatment. Therefore some of the observed patterns may be due to endogenous factors. It seems unlikely that those without treatment would show an improving trajectory for anxiety symptoms, as comorbid anxiety and depression diagnoses have been associated with longer duration and greater impairment compared to either disorder alone (Birmaher et al., 1996; Ezpeleta, Domenech, & Angold, 2006) and it seems reasonable that this would extend to sub-diagnostic anxiety symptoms. It is worth noting that the RCMAS was originally designed as a measure of trait anxiety in schools, rather than clinical anxiety and does not map on to diagnostic categories. However, it captures several different aspects of anxiety: worry, sensitivity, somatic symptoms and worry about the self in a social context. These issues seem pertinent to the age range of the sample and anxiety diagnoses were also investigated using K-SADS.

Limitations of the systematic review include the inability to investigate the reasons for dropout, as few studies reported these. It would be beneficial for treatment trials to report characteristics of participants who dropout, reasons for dropout and the exact stage at which this occurs to allow exploration of whether aspects of treatment may be unacceptable to participants. It was beyond the scope of the review presented here, but future work may combine investigation of efficacy

and dropout. It may be that participants are more likely to dropout from treatments that they are not gaining benefit from. Or conversely depression treatment may have initially increased awareness of the situation; some participants may find this a difficult but helpful motivator for change but others may find this too aversive and discontinue treatment.

The main clinical implication of the systematic review was that psychological therapies for depression in youth are broadly acceptable, with minimal dropout. Participants were more likely to engage in interventions with more sessions. Wait-lists were also acceptable (few people discontinued waiting). Therefore offering interventions with greater numbers of sessions may decrease dropout from depression interventions, even if participants have to wait to access these. No factors were identified indicating which treatment options may be best suited to different individuals; to maximise the likelihood of engagement it may be best to offer a variety of evidence based interventions to give choice. Findings from the empirical paper highlighted the need for thorough assessment pre and post intervention, particularly of symptoms associated to the main presenting problem but not targeted by treatment as effects may not generalise to non-target symptoms.

Overall it may be necessary to broaden out depression treatments for young people. The majority of CAMHS patients present with comorbidity, difficulties in several areas and require input from multiple agencies (e.g. family workers, social care, school inclusion services). The provision of effective intervention would have the potential to reduce long-term treatment cost and re-referral and decrease impact of mental health issues on development and other areas of life including friendships, school attainment and parental productivity. A study which compared outcomes for youth treated for depression in community services to youth treated using CBT in

depression trials found that those treated in services had significantly worse outcomes (Weersing & Weisz, 2002). It is important to increase the use of effective therapies in community clinic settings, with awareness of the complexity of presentations.

There is some suggestion that young people referred to NHS CAMHS with a depression presentation may differ to those in clinical trials; investigation at one CAMHS site found that less than half met diagnostic criteria, 42% of the adolescents met criteria for depression as a primary disorder. Of the adolescents that did meet criteria for depression, 54% had comorbid anxiety disorder (Orchard, Pass, Marshall, & Reynolds, 2017). Therefore a more flexible, formulation or problem based approach to intervention, drawing on a range of evidence-based treatments may be more effective than focussing primarily on a single disorder.

Depression and anxiety have been associated with similar cognitive biases in adolescents, though depression has been shown to be associated more with a self-referential memory bias while anxiety has been shown to be associated more so with an interpretive bias in a community sample (Smith, Reynolds, Orchard, Whalley, & Wy, 2018). More generally, a negative interpretation bias has been associated with both anxiety and depression symptoms in adolescents (Orchard, Pass, & Reynolds, 2016). High levels of anxiety have been found to be predictive of later depression in adolescents (Cole, Peeke, Martin, Truglio, & Seroczynski, 1998); it may be that adolescents have typically been anxious for some years before developing depression.

Despite some cognitive overlap in presentation, treatment protocols for depression and anxiety treatment are typically quite different. Depression treatments

generally involve some form of behavioural activation, and brief behavioural activation has been found to be an effective standalone treatment for adolescent depression, 65% of a sample from NHS clinic required no further psychological intervention (Warwick et al., 2017). A review found that behavioural activation may be effective, but further research is needed in this area (Tindall et al., 2017). Anxiety interventions generally involve some form of graded exposure using a hierarchy, modifying cognitions at each step. CBT for anxiety in young people has been found to have 48 to 66% full recovery rates (from all anxiety diagnoses, not just the primary diagnosis) in a meta-analysis (Warwick et al., 2017). The same study found full recovery rates of up to 21% in wait list and active treatment comparisons. A Cochrane review of anxiety disorders in children and adolescents published before this was not so definitive and found that CBT was effective but that there was not much evidence to say that CBT was more effective than active controls or TAU (James, James, Cowdrey, Soler, & Choke, 2015). A large meta-analysis exploring five decades of youth psychological therapy found strongest effect sizes for anxiety treatment, weakest for depression and non-significant for multiple problem treatment (Weisz et al., 2017). This indicates that both depression and anxiety can be sensitive to treatment, but it may be better to focus on each sequentially.

A modular transdiagnostic approach tailored to individual presentation with re-assessment, formulation and treatment planning at regular stages may enhance overall effectiveness and decrease relapse or re-referral. In the adult literature a unified protocol for the transdiagnostic treatment of emotional disorders has been found to be effective in a randomized controlled trial (Farchione et al., 2012). The unified protocol targets a common feature of many disorders; emotional reactivity, aversion to these experiences and attempts to alter, avoid or control emotional

responding (Barlow, Allen, & Choate, 2004). An alternative approach allowing sequential selection from several standardised modules based on client presentation and formulation is currently being evaluated for adults (Black et al., 2018). The authors state that this method of transdiagnostic intervention allows for incorporation of existing evidence-based manualised treatments into a single treatment package. This format may provide an efficient and effective way to intervene in the presence of complexity. In the youth literature an adapted version of the unified protocol (targeting emotional reactivity and responses to this) has been developed (Ehrenreich, Goldstein, Wright, & Barlow, 2009) and authors state that a trial would be the next step. One modular psychotherapy protocol for youths has been developed; the *Modular Approach to Therapy for Children with Anxiety, Depression, Trauma or Conduct Problems* (MATCH) (Chorpita & Weisz, 2009). MATCH was designed for 6-15 year olds and consists of 33 practice elements (e.g. behavioural activation, exposure, reward system). Flowcharts are provided to help clinicians customise treatment plans. MATCH has outperformed disorder specific manuals and usual care on clinical and functional outcomes (Weisz et al., 2012); including at 2 year follow up (Chorpita et al., 2013). In another trial MATCH outperformed usual care on clinical and functional outcomes, reduced treatment duration and reduced use of other mental health services (Chorpita et al., 2017). Practitioner advice for intervening in a transdiagnostic manner advocates careful selection of treatment targets at appropriate stages throughout treatment, use of standardised measures and regular supervision to balance adherence and flexibility (Marchette & Weisz, 2017). A potential next step for youth treatment could be the adaptation or consolidation of MATCH (Chorpita & Weisz, 2009) and adult modular

(Black et al., 2018) protocols to develop and trial a modular transdiagnostic intervention for adolescents.

In conclusion, findings have been presented from two studies indicating that present psychological treatments for depression in youth are acceptable but may not impact on concurrent anxiety symptoms. A substantial proportion of youth referred to mental health services for depression treatment do not meet diagnostic criteria for depression, and concurrent anxiety symptoms and diagnoses are common (Orchard et al., 2017). Therefore interventions aimed solely at depression are unlikely to provide maximum benefit. A more flexible, formulation or problem based approach to intervention, drawing on a range of evidence-based treatments may be more effective, with problems tackled sequentially. A transdiagnostic approach targeting emotional reactivity has demonstrated effectiveness in adults (Farchione et al., 2012), and investigation of a modular transdiagnostic treatment package for adults is currently underway (Black et al., 2018). A modular transdiagnostic treatment has been shown to be effective in 6-15 year olds (Chorpita & Weisz, 2009). The development of a modular transdiagnostic intervention for adolescents, potentially drawing upon those already developed primarily for children (Chorpita & Weisz, 2009) and adults (Black et al., 2018) could be a next step for youth treatment. This could enable incorporation of a range of evidence based treatments into a single package, allowing clinicians to adapt interventions to individual clients whilst still delivering treatments with demonstrated effectiveness.

Chapter 5 References

Barlow, D. H., Allen, L. B., & Choate, M. L. (2004). Toward a Unified Treatment for Emotional Disorders. *Behavior Therapy*, *35*, 205–230.

Birmaher, B., Ryan, N. D., Williamson, D. E., Brent, D. A., Kaufman, J., Dahl, R. E., … Nelson, B. (1996). Childhood and adolescent depression: a review of the past 10 years. Part I. *Journal Of The American Academy Of Child And Adolescent Psychiatry*, *35*(11), 1427–1439.

Black, M., Hitchcock, C., Bevan, A., Leary, C. O., Clarke, J., Elliott, R., … Dalgleish, T. (2018). The HARMONIC trial : study protocol for a randomised controlled feasibility trial of Shaping Healthy Minds — a modular transdiagnostic intervention for mood, stressor-related and anxiety disorders in adults. *BMJ Open*, *8*(e024546.), doi:10.1136/ bmjopen-2018-024546. https://doi.org/10.1136/bmjopen-2018-024546

Chorpita, B. F., Daleiden, E. L., Park, A. L., Ward, A. M., Levy, M. C., Cromley, T., … Krull, J. L. (2017). Child STEPs in California: A cluster randomized effectiveness trial comparing modular treatment with community implemented treatment for youth with anxiety, depression, conduct problems, or traumatic stress. *Journal Of Consulting And Clinical Psychology*, *85*(1), 13–25. https://doi.org/10.1037/ccp0000133

Chorpita, B. F., & Weisz, J. R. (2009). *Modular approach to therapy for children with anxiety, depression, trauma or conduct problems (MATCH-ADTC).* Satellite Beach, FL: PracticeWise.

Chorpita, B. F., Weisz, J. R., Daleiden, E. L., Schoenwald, S. K., Palinkas, L. A., Miranda, J., … Gibbons, R. D. (2013). Long-term outcomes for the Child

STEPs randomized effectiveness trial: a comparison of modular and standard treatment designs with usual care. *Journal Of Consulting And Clinical Psychology*, *81*(6), 999–1009. https://doi.org/10.1037/a0034200

Cole, D. A., Peeke, L. G., Martin, J. M., Truglio, R., & Seroczynski, A. D. (1998). A Longitudinal Look at the Relation Between Depression and Anxiety in Children and Adolescents. *Journal Of Consulting And Clinical Psychology*, *66*(3), 451–460. https://doi.org/10.1037/0022-006X.66.3.451

Cooper, A. A., & Conklin, L. R. (2015). Dropout from individual psychotherapy for major depression : A meta-analysis of randomized clinical trials. *Clinical Psychology Review*, *40*, 57–65. https://doi.org/10.1016/j.cpr.2015.05.001

Ehrenreich, J. T., Goldstein, C. R., Wright, L. R., & Barlow, D. H. (2009). Development of a Unified Protocol for the Treatment of Emotional Disorders in Youth. *Child & Family Behavior Therapy*, *31*(1), 20–37. https://doi.org/10.1080/07317100802701228

Ezpeleta, L., Domenech, J. M., & Angold, A. (2006). A comparison of pure and comorbid CD/ODD and depression. *Journal of Child Psychology and Psychiatry*, *7*, 704–712. https://doi.org/10.1111/j.1469-7610.2005.01558.x

Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Thompson-hollands, J., Carl, J. R., … Barlow, D. H. (2012). Unified Protocol for Transdiagnostic Treatment of Emotional Disorders: A Randomized Controlled Trial. *Behavior Therapy*, *43*(3), 666–678. https://doi.org/10.1016/j.beth.2012.01.001.Unified

Goodyer, I. M., Reynolds, S., Barrett, B., Byford, S., Dubicka, B., Hill, J., … Kelvin, R. (2017). Cognitive behavioural therapy and short-term psychoanalytical

psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre , pragmatic , observer-blind , randomised controlled superi. *The Lancet Psychiatry*, *4*(2), 109–119. https://doi.org/10.1016/S2215-0366(16)30378-9

Graham, J. W. (2009). Missing Data Analysis : Making It Work in the Real World. *Annual Review Of Psychology*, (60), 549–576. https://doi.org/10.1146/annurev.psych.58.110405.085530

James, A., James, G., Cowdrey, F. A., Soler, A., & Choke, A. (2015). Cognitive behavioural therapy for anxiety disorders in children and adolescents.(Review). *Cochrane Database of Systematic Reviews*, (2).

Marchette, L. K., & Weisz, J. R. (2017). Practitioner Review: Empirical evolution of youth psychotherapy toward transdiagnostic approaches. *The Journal of Child Psychology and Psychiatry.*, *58*(9), 970–984. https://doi.org/10.1111/jcpp.12747

Orchard, F., Pass, L., Marshall, T., & Reynolds, S. (2017). Clinical characteristics of adolescents referred for treatment of depressive disorders. *Child And Adolescent Mental Health*, *22*(2), 61–68. https://doi.org/10.1111/camh.12178

Orchard, F., Pass, L., & Reynolds, S. (2016). Associations Between Interpretation Bias and Depression in Adolescents. *Cognitive Therapy And Research*, *40*, 577–583. https://doi.org/10.1007/s10608-016-9760-6

Rohden, A. I., Benchaya, M. C., Camargo, R. S., Moreira, T. de C., Barros, H. M. T., & Ferigolo, M. (2017). Dropout Prevalence and Associated Factors in Randomized Clinical Trials of Adolescents Treated for Depression: Systematic Review and Meta-analysis. *Clinical Therapeutics*, *39*(5), 971–992.e4.

https://doi.org/10.1016/j.clinthera.2017.03.017

Rubin, D. B. (1996). Multiple Imputation after 18+ years. *Journal Of The American Statistical Association*, *91*(434), 473–489.

Smith, E. M., Reynolds, S., Orchard, F., Whalley, H. C., & Wy, S. (2018). Journal of A ff ective Disorders Cognitive biases predict symptoms of depression , anxiety and wellbeing above and beyond neuroticism in adolescence. *Journal of Affective Disorders*, *241*(August), 446–453. https://doi.org/10.1016/j.jad.2018.08.051

Swift, J. K., & Greenberg, R. P. (2014). A Treatment by Disorder Meta-Analysis of Dropout From Psychotherapy. *Journal of Psychotherapy Integration*, *24*(3), 193–207.

Tindall, L., Mikocka-Walus, A., McMillan, D., Wright, B., Hewitt, C., & Gascoyne, S. (2017). Is behavioural activation effective in the treatment of depression in young people? A systematic review and meta-analysis. *Psychology And Psychotherapy*, *90*(4), 770–796. https://doi.org/10.1111/papt.12121

Warwick, H., Reardon, T., Cooper, P., Murayama, K., Reynolds, S., Wilson, C., & Creswell, C. (2017). Complete recovery from anxiety disorders following Cognitive Behavior Therapy in children and adolescents : A meta-analysis. *Clinical Psychology Review*, *52*, 77–91. https://doi.org/10.1016/j.cpr.2016.12.002

Weersing, V. R., & Weisz, J. R. (2002). Community clinic treatment of depressed youth: benchmarking usual care against CBT clinical trials. *Journal Of Consulting And Clinical Psychology*, *70*(2), 299–310.

Weisz, J. R., Chorpita, B. F., Palinkas, L. A., Schoenwald, S. K., Miranda, J., Bearman, S. K., … Health, the R. N. on Y. M. (2012). Testing Standard and Modular Designs for Psychotherapy Treating Depression, Anxiety, and Conduct Problems in Youth. *Archive of General Psychiatry*, *69*(3), 274–283.

Weisz, J. R., Kuppens, S., Ng, M. Y., Eckshtain, D., Ugueto, A. M., Vaughn-Coaxum, R., … Fordwood, S. R. (2017). What five decades of research tells us about the effects of youth psychological therapy: A multilevel meta-analysis and implications for science and practice. *The American Psychologist*, *72*(2), 79–117. https://doi.org/10.1037/a0040360

Appendices

Appendix A: Author instructions for Journal of Affective Disorders

A summary of the relevant manuscript preparation instructions is provided below, copied from the journal website. For full author guidelines, see: https://www.elsevier.com/journals/journal-of-affective-disorders/01650327/guide-for-authors

Types of Papers

The Journal primarily publishes:

Full-Length Research Papers (up to 5000 words, excluding references and up to 6 tables/figures)

Review Articles and Meta-analyses (up to 8000 words, excluding references and up to 10 tables/figures)

Short Communications (up to 2000 words, 20 references, 2 tables/figures)

Correspondence (up to 1000 words, 10 references, 1 table/figure).

At the discretion of the accepting Editor-in-Chief, and/or based on reviewer feedback, authors may be allowed fewer or more than these guidelines.

Preparation of Manuscripts

Articles should be in English. The title page should appear as a separate sheet bearing title (without article type), author names and affiliations, and a footnote with the corresponding author's full contact information, including address, telephone and fax numbers, and e-mail address (failure to include an e-mail address can delay processing of the manuscript).

Papers should be divided into sections headed by a caption (e.g., Introduction, Methods, Results, Discussion). A structured abstract of no more than 250 words should appear on a separate page with the following headings and order: Background, Methods, Results, Limitations, Conclusions (which should contain a statement about the clinical relevance of the research). A list of three to six key words should appear under the abstract. **Authors should note that the 'limitations' section both in the discussion of the paper AND IN A STRUCTURED ABSTRACT are essential. Failure to include it may delay in processing the paper, decision making and final publication.**

Figures and Photographs

Figures and Photographs of good quality should be submitted online as a separate file. Please use a lettering that remains clearly readable even after reduction to about 66%. For every figure or photograph, a legend should be

provided. All authors wishing to use illustrations already published must first obtain the permission of the author and publisher and/or copyright holders and give precise reference to the original work. This permission must include the right to publish in electronic media.

Tables

Tables should be numbered consecutively with Arabic numerals and must be cited in the text in sequence. Each table, with an appropriate brief legend, comprehensible without reference to the text, should be typed on a separate page and uploaded online. Tables should be kept as simple as possible and wherever possible a graphical representation used instead. Table titles should be complete but brief. Information other than that defining the data should be presented as footnotes.

Colour reproduction

The Journal of Affective Disorders is now also included in a new initiative from Elsevier: 'Colourful e-Products'. Through this initiative, figures that appear in black & white in print can appear in colour, online, in ScienceDirect at http://www.sciencedirect.com.

There is no extra charge for authors who participate.

For colour reproduction in print, you will receive information regarding the costs from Elsevier after receipt of your accepted article. Please indicate your preference for colour in print or on the Web only. Because of technical complications which can arise by converting colour figures to "grey scale" (for the printed version should you not opt for colour in print) please submit in addition usable black and white versions of all the colour illustrations. For further information on the preparation of electronic artwork, please see http://authors.elsevier.com/artwork/jad.

Abstract

A concise and factual abstract is required. The abstract should state briefly the purpose of the research, the principal results and major conclusions. An abstract is often presented separately from the article, so it must be able to stand alone. For this reason, References should be avoided, but if essential, then cite the author(s) and year(s). Also, non-standard or uncommon abbreviations should be avoided, but if essential they must be defined at their first mention in the abstract itself.

Highlights

Highlights are mandatory for this journal. They consist of a short collection of bullet points that convey the core findings of the article and should be submitted in a separate editable file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point). You can view example Highlights on our information site.

Keywords

Immediately after the abstract, provide a maximum of 6 keywords, using American spelling and avoiding general and plural terms and multiple concepts (avoid, for example, 'and', 'of'). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. These keywords will be used for indexing purposes.

Reference style

Text: All citations in the text should refer to:
1. *Single author:* the author's name (without initials, unless there is ambiguity) and the year of publication;
2. *Two authors:* both authors' names and the year of publication;
3. *Three or more authors:* first author's name followed by 'et al.' and the year of publication.

Citations may be made directly (or parenthetically). Groups of references can be listed either first alphabetically, then chronologically, or vice versa. Examples: 'as demonstrated (Allan, 2000a, 2000b, 1999; Allan and Jones, 1999)…. Or, as demonstrated (Jones, 1999; Allan, 2000)… Kramer et al. (2010) have recently shown …'

List: References should be arranged first alphabetically and then further sorted chronologically if necessary. More than one reference from the same author(s) in the same year must be identified by the letters 'a', 'b', 'c', etc., placed after the year of publication.

Examples:

Reference to a journal publication:
Van der Geer, J., Hanraads, J.A.J., Lupton, R.A., 2010. The art of writing a scientific article. J. Sci. Commun. 163, 51–59. https://doi.org/10.1016/j.Sc.2010.00372.

Reference to a journal publication with an article number:
Van der Geer, J., Hanraads, J.A.J., Lupton, R.A., 2018. The art of writing a scientific article. Heliyon. 19, e00205. https://doi.org/10.1016/j.heliyon.2018.e00205.

Reference to a book:
Strunk Jr., W., White, E.B., 2000. The Elements of Style, fourth ed. Longman, New York.

Reference to a chapter in an edited book:
Mettam, G.R., Adams, L.B., 2009. How to prepare an electronic version of your article, in: Jones, B.S., Smith , R.Z. (Eds.), Introduction to the Electronic Age. E-Publishing Inc., New York, pp. 281–304.

Reference to a website:
Cancer Research UK, 1975. Cancer statistics reports for the UK. http://www.cancerresearchuk.org/aboutcancer/statistics/cancerstatsreport/ (accessed 13 March 2003).

Reference to a dataset:
[dataset] Oguro, M., Imahiro, S., Saito, S., Nakashizuka, T., 2015. Mortality data for Japanese oak wilt disease and surrounding forest compositions. Mendeley Data, v1. https://doi.org/10.17632/xwj98nb39r.1.

Appendix B: Supplementary material to be submitted with meta-analysis (Chapter 1) to Journal of Affective Disorders

Table 13: Quality scoring table, active psychotherapy arms only.

Study	Active psychotherapy/psychotherapies	Intent to treat analysis	CONSORT diagram presented	Treatment completion defined	Treatment manual	Therapists trained in intervention	Treatment integrity checked	Study Quality
(Ackerson et al., 1998)	Cognitive bibliotherapy	0	0	0	1	1	1	3
(D. A. Brent et al., 1997)	Individual CBT; Systemic Behaviour Family Therapy	1	0	0	1	1	1	4
(D. Brent et al., 2008)	Venlafaxine + CBT; SSRI + CBT	1	1	0	1	1	1	5
(G. N. Clarke et al., 1999)	Group CBT; Group CBT + parent group	0	0	0	1	1	1	3
(G. Clarke et al., 2016)	TAU + CBT	1	1	1	1	1	1	6
(G. Clarke et al., 2005)	Brief CBT + TAU SSRIs	1	0	0	1	1	1	4

Study	Active psychotherapy/psychotherapies	Intent to treat analysis	CONSORT diagram presented	Treatment completion defined	Treatment manual	Therapists trained in intervention	Treatment integrity checked	Study Quality
(G. S. Diamond et al., 2002)	Attachment Based Family Therapy	0	0	0	1	1	1	3
(Fristad et al., 2016)	Psychoed Psychotherapy + placebo; Omega 3 + Psychoed Psychotherapy	1	1	0	1	1	1	5
(Gaete et al., 2016)	Group CBT	1	1	0	1	1	1	5
(I M Goodyer et al., 2008)	SSRI + CBT	1	1	0	1	1	1	5
(Ian M Goodyer et al., 2017)	CBT; Short-term psychoanalytic psychotherapy	1	1	0	1	1	1	5
(Iftene et al., 2015)	Rational-Emotive CBT group; REBT/CBT group + medication	1	1	0	1	1	1	5
(Israel & Diamond, 2013)	Attachment Based Family Therapy	1	1	0	1	1	1	5

Study	Active psychotherapy/psychotherapies	Intent to treat analysis	CONSORT diagram presented	Treatment completion defined	Treatment manual	Therapists trained in intervention	Treatment integrity checked	Study Quality
(J. L. Luby et al., 2018)	Parent-Child Interaction Therapy	0	0	0	1	1	1	3
(J. Luby et al., 2012)	Parent-Child Interaction Therapy	0	1	1	1	1	1	5
(March et al., 2004)	Fluoxetine + CBT; CBT	1	1	0	1	1	0	4
(McCauley et al., 2016)	Behavioural Activation	1	1	1	1	1	1	6
(Melvin et al., 2006)	CBT; CBT + Sertraline	1	1	0	1	1	0	4
(Merry et al., 2012)	Computerised CBT (SPARX)	1	1	1	1	1	1	6
(L Mufson et al., 1999)	Interpersonal psychotherapy for depressed adolescents	1	0	0	1	1	1	4
(Laura Mufson et al., 2004)	Interpersonal psychotherapy for depressed adolescents	1	1	0	1	1	1	5
(Nelson et al., 2003)	CBT via video; CBT face to face	0	0	1	0	0	0	1

Study	Active psychotherapy/psychotherapies	Intent to treat analysis	CONSORT diagram presented	Treatment completion defined	Treatment manual	Therapists trained in intervention	Treatment integrity checked	Study Quality
(O'Shea et al., 2015)	Group Interpersonal Psychotherapy; Individual Interpersonal Psychotherapy	1	0	0	1	1	1	4
(Poole et al., 2018)	Multi-family group intervention (BEST MOOD)	1	1	0	1	1	1	5
(Reynolds & Coats, 1986)	CBT group	0	0	0	1	1	1	3
(Rickhi et al., 2015)	Online spirituality/compassion programme (LEAP)	1	1	1	1	1	1	6
(Rosselló et al., 2012)	Individual CBT; Group CBT; Individual Interpersonal Psychotherapy; Group Interpersonal Psychotherapy	1	1	0	1	1	1	5
(Smith et al., 2015)	Computerised CBT (Stressbusters)	1	1	0	1	1	1	5
(Stallard et al., 2011)	Computerised CBT (Think, Feel, Do)	0	1	0	1	1	1	4

Study	Active psychotherapy/psychotherapies	Intent to treat analysis	CONSORT diagram presented	Treatment completion defined	Treatment manual	Therapists trained in intervention	Treatment integrity checked	Study Quality
(Stasiak et al., 2014)	Computerised CBT (The Journey)	1	1	1	1	1	1	6
(Tang et al., 2009)	Interpersonal psychotherapy for depressed adolescents with suicidal risk	0	0	0	1	1	0	2
(Tompson et al., 2017)	Family Focussed Treatment for Childhood depression	1	1	1	1	1	1	6
(Topooco et al., 2018)	Online CBT (including chat sessions)	1	1	0	1	1	1	5
(Trowell et al., 2007)	Individual Psychodynamic Psychotherapy; Family Therapy	1	1	0	1	1	0	4
(Wilkinson & Goodyer, 2008)	SSRI + psychoed as usual + CBT	0	0	0	1	1	1	3
(Wood et al., 1996)	CBT	1	0	0	1	1	1	4
(Wright et al., 2017)	Computerised CBT (Stressbusters)	0	1	1	1	1	1	5

Appendix C: Author instructions for Journal of Clinical Child & Adolescent Psychology

A summary of the relevant manuscript preparation instructions is provided below, copied from the journal website. For full author guidelines, see: https://www.tandfonline.com/action/authorSubmission?journalCode=hcap20&page=instructions

Preparing Your Paper

Regular Articles, Brief Reports, Future Directions

- Should be written with the following elements in the following order: title page; abstract; main text; references; appendices (as appropriate); table(s) with caption(s) (on individual pages); figures; figure captions (as a list)
- Should contain an unstructured abstract of 250 words.
- Read making your article more discoverable, including information on choosing a title and search engine optimization. A Regular Article may not exceed 11,000 words (i.e., 35 pages), including references, footnotes, figures, and tables. Brief Reports include empirical research that is soundly designed, but may be of specialized interest or narrow focus. Brief Reports may not be submitted in part or whole to another journal of general circulation. Brief Reports may not exceed 4,500 words for text and references. These limits do not include the title page, abstract, author note, footnotes, tables, and figures. Manuscripts that exceed these page limits and that are not prepared according to the guidelines in the Manual will be returned to authors without review. Future Directions submissions are written by leading scholars within the field. These articles provide a brief summary of important advances that are needed within a specific research or practice area pertinent to clinical child and adolescent psychology. Future Directions submissions are by invitation only and undergo peer review. All Regular Article and Brief Report submissions must include a title of 15 words or less that identifies the developmental level of the study participants (e.g., children, adolescents, etc.). JCCAP uses an unstructured abstract format. For studies that report randomized clinical trials or meta-analyses, the abstract also must be consistent with the guidelines set forth by CONSORT or MARS, respectively. The Abstract should include up to 250 words, presented in paragraph form. The Abstract should be typed on a separate page (page 2 of the manuscript), and must include each of the following label sections: 1) Objective (i.e., a brief statement of the purpose of the study); 2) Method (i.e., a detailed summary of the participants, N, age, gender, ethnicity, as well as a summary of the study design, measures, and procedures; 3) Results (i.e., a detailed summary of the primary findings that clearly articulate comparison groups (if relevant); 4) Conclusions (i.e., a description of the research and clinical implications of the findings). Avoid abbreviations, diagrams, and reference to the text in the abstract. JCCAP will scrutinize manuscripts for a clear theoretical framework that supports central study hypotheses. In addition, a clear developmental rationale is required for the selection of participants at a specific age. The Journal is making diligent efforts to insure that there is an appropriately detailed description of the sample, including a) the population from which the sample was drawn; b) the number of participants; c) age, gender, ethnicity, and SES of participants; d) location of sample, including country and community type (rural/urban), e) sample identification/selection; f) how participants were contacted; g) incentives/rewards; h) parent consent/child assent procedures and rates; i) inclusion and exclusion criteria; j) attrition rate. The Discussion section should

include a comment regarding the diversity and generality (or lack thereof) of the sample. The Measures section should include details regarding item content and scoring as well as evidence of reliability and validity in similar populations. All manuscripts must include a discussion of the clinical significance of findings, both in terms of statistical reporting and in the discussion of the meaningfulness and clinical relevance of results. Manuscripts should a) report means and standard deviations for all variables, b) report effect sizes for analyses, and c) provide confidence intervals wherever appropriate (e.g., on figures, in tables), particularly for effect sizes on primary study findings. In addition, when reporting the results of interventions, authors should include indicators of clinically significant change. Authors may use one of several approaches that have been recommended for capturing clinical significance, including (but not limited to) the reliable change index (i.e., whether the amount of change displayed by a treated individual is large enough to be meaningful, the extent to which dysfunctional individuals show movement to the functional distribution). All manuscripts should conform to the criteria listed in Table 1 of the 2008 APA Publications and Communications Board Working Group on Journal Article Reporting Standards (published in American Psychologist). These reporting standards apply to all empirical papers. In addition, JCCAP requires that reports of randomized clinical trials conform to CONSORT reporting standards (http://www.consort-statement.org/index.aspx?o=2965), including the submission of a flow diagram and checklist. Nonrandomized clinical trials must conform to TREND criteria (see http://www.cdc.gov/trendstatement/docs/AJPH_Mar2004_Trendstatement.pdf) and meta-analyses should conform to MARS standards (see Table 4 in 2008 American Psychologist article).

Taylor & Francis quick layout guide

These general article layout guidelines will help you to format your manuscript so that it is ready for you to submit it to a Taylor & Francis journal. Please also follow any specific Instructions for Authors provided by the Editor of the journal, which are available on the journal pages at www.tandfonline.com. Please also see our guidance on putting your article together, defining authorship and anonymizing your article for peer review.

We recommend that you use our templates to prepare your article, but if you prefer not to use templates this guide will help you prepare your article for review.

If your article is accepted for publication, the manuscript will be formatted and typeset in the correct style for the journal.

Article layout guide

Font: Times New Roman, 12-point, double-line spaced. Use margins of at least 2.5 cm (or 1 inch). Guidance on how to insert special characters, accents and diacritics is available here.

Title: Use bold for your article title, with an initial capital letter for any proper nouns.

Abstract: Indicate the abstract paragraph with a heading or by reducing the font size. Check whether the journal requires a structured abstract or

graphical abstract by reading the Instructions for Authors. The Instructions for Authors may also give word limits for your abstract. Advice on writing abstracts is available here.

Keywords: Please provide keywords to help readers find your article. If the Instructions for Authors do not give a number of keywords to provide, please give five or six. Advice on selecting suitable keywords is available here.

Headings: Please indicate the level of the section headings in your article:

1. First-level headings (e.g. Introduction, Conclusion) should be in bold, with an initial capital letter for any proper nouns.
2. Second-level headings should be in bold italics, with an initial capital letter for any proper nouns.
3. Third-level headings should be in italics, with an initial capital letter for any proper nouns.
4. Fourth-level headings should be in bold italics, at the beginning of a paragraph. The text follows immediately after a full stop (full point) or other punctuation mark.
5. Fifth-level headings should be in italics, at the beginning of a paragraph. The text follows immediately after a full stop (full point) or other punctuation mark.

Tables and figures: Indicate in the text where the tables and figures should appear, for example by inserting [Table 1 near here]. You should supply the actual tables either at the end of the text or in a separate file and the actual figures as separate files. You can find details of the journal Editor's preference in the Instructions for Authors or in the guidance on the submission system. Ensure you have permission to use any tables or figures you are reproducing from another source.

Appendix D Supplementary material to be submitted with empirical paper (Chapter 3) to Journal of Clinical Child & Adolescent Psychology

Table 14: Percentage of raw data missing for each anxiety diagnosis (measured using the K-SADS-PL).

	Baseline %missing	6 weeks %missing	12 weeks %missing	36 weeks %missing	52 weeks %missing	86 weeks %missing
Anxiety type						
Separation	3	38	35	39	42	39
GAD	11	43	40	43	46	42
Panic	1	37	35	40	43	38
Agoraphobia	25	52	52	49	52	45
PTSD	17	45	41	45	49	43
Social phobia	0	38	35	40	43	38
Specific phobia	13	45	42	44	47	42
Agoraphobia/ Specific phobia/ Panic	21	48	48	46	50	45

Table 15: RCMAS scores across time, raw data.

RCMAS	Baseline	6 weeks	12 weeks	36 weeks	52 weeks	86 weeks
Mean	40.93	36.56	34.29	29.22	26.35	24.53
(SD)	(7.25)	(9.54)	(11.70)	(13.52)	(14.70)	(14.83)