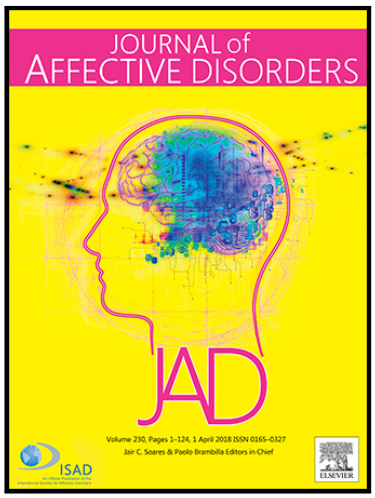

Dropout from randomised controlled trials of psychological treatments for depression in children and youth: a systematic review and meta-analyses

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Highlights

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

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 children and youth (aged up to and including 18 years) 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 for 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% (95% CI 12.0-17.4%). Dropout was equally likely from intervention and control conditions, aside from family/dyadic interventions (where dropout was more likely from control arms). There was some suggestion that interventions offering more sessions and longer duration had less dropout and of less dropout from IPT than other interventions. There were no significant associations between dropout and study quality, CBT, family or individual versus other approaches.

Limitations: Lack of consistent reporting decreased the factors which could be analysed.

Conclusions: Dropout from depression treatment in children and 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

Introduction

Depression is a disabling condition for all ages, including children and youth. The prevalence of depression in children has been found to be under 1% (Thapar, Collishaw, Pine, & Thapar, 2012), although in 13-18 year olds this rises to an estimated 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 (intended number of weeks of intervention) has been associated at trend level with higher rates of dropout in adults (Cooper & Conklin, 2015). The same study found no association between dropout and intended number of intervention sessions, however (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). Zhou and colleagues investigated both efficacy and acceptability of psychotherapies for depression in children and adolescents (Zhou et al., 2015). IPT and problem solving had significantly less all-cause discontinuation

than CBT but only IPT and CBT were significantly more effective than control conditions, they were also more effective than problem-solving therapy. To the authors‟ knowledge there have been no dropout meta-analyses incorporating investigation of moderators of dropout from depression treatment in youth.

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, in both absolute (i.e. absolute prevalence rate) and comparative terms (i.e. odds of dropout when compared to a control condition). 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. The present review focussed on randomised controlled trials as these studies are clear about which types of therapy are being offered and this is carefully controlled and standardised, allowing clear comparisons of different interventions.

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 (psychological treatment including individual and group talking therapies; for example cognitive behavioural therapy, family approaches and interpersonal psychotherapy) with participants aged up to (and including) 18 years;
- Participants met criteria for diagnosis of depression or scored above cut-off on a validated measure.

. There was no restriction placed on the type of comparison intervention or control within studies. 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. No restrictions were imposed on type of depression diagnosis or the method used to derive a diagnosis. Validated measures included self-report questionnaires with published psychometric properties and cut-off scores

(to indicate likely diagnosis or clinical level of severity, e.g. Mood and Feelings Questionnaire, Beck Depression Inventory and Hamilton Depression Scale).

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 a collaborator 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 0.75, indicating substantial agreement (Landis & Koch, 1977). Discrepancies were addressed by discussion between raters.

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 active and non-active interventions.

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 [TAU]) 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. Additionally, analyses were re-run excluding studies that scored below 3/6 on the study quality scale to assess whether this affected the pattern of results.

Deviations from the PROSPERO protocol

The inclusion of a second definition of dropout was identified during full text screening and data extraction, as several studies did not directly report treatment completion/dropout. It was considered that the review would be more complete if these studies were included, with the closest proxy for dropout possible to calculate from the available data (the second definition as stated above). Other meta-analyses of dropout have utilised this second definition (e.g. Lewis, Roberts, Gibson, &

	All studies (defined dropout and missing post-treatment data)				Defined dropout only			
	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
	48	*-0.004*	*-0.047, 0.039*	*.854*	*26*	*-0.024*	*-0.090, 0.041*	*.464*
Max sessions	48	-0.007	-0.014, -0.000	**.048**	28	-0.005	-0.016, 0.006	.406
	45	*-0.007*	*-0.014, 0.000*	*.056*	*25*	*-0.004*	*-0.015, 0.007*	*.492*
Treatment duration	50	-0.005	-0.009, 0.000	.057	28	-0.005	-0.013, 0.004	.275
	47	*-0.005*	*-0.010, -0.000*	.034	*25*	*-0.006*	*-0.014, 0.002*	*.149*
CBT vs other[a]	51	0.036	-0.040, 0.111	.355	29	0.058	-0.050, 0.166	.293
	48	*0.017*	*-0.059, 0.093*	*.665*	*26*	*0.022*	*-0.089, 0.133*	*.700*
Family approach vs other[a]	51	0.027	-0.082, 0.135	.631	29	0.186	-0.088, 0.460	.183
	48	*0.026*	*-0.081, 0.133*	*.634*	*26*	*0.184*	*-0.080, 0.448*	*.171*
IPT vs other[a]	51	-0.119	-0.227, -0.010	**.032**	29	-0.157	-0.285, -0.028	**.017**
	48	*-0.086*	*-0.204, 0.031*	*.150*	*26*	*-0.114*	*-0.258, 0.030*	*.121*
Individual vs other[a]	51	-0.020	-0.094, 0.055	.599	29	-0.064	-0.170, 0.041	.234
	48	*-0.019*	*-0.094, 0.056*	*.620*	*26*	*-0.064*	*-0.169, 0.042*	*.236*

Note. [a]Treatment of interest = 1, control = 0. CBT=Cognitive Behavioural Therapy; IPT=Interpersonal psychotherapy.

Italicised = results excluding studies that scored below 3/6 on study quality scale. Statistically significant results are in bold.

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)