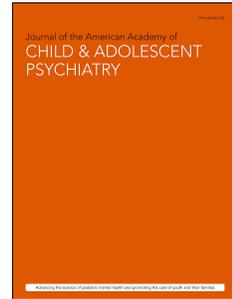# Accepted Manuscript

Prognostic Implications for Adolescents With Depression Who Drop Out of Psychological Treatment During a Randomized Controlled Trial

Sally O'Keeffe, PhD, Peter Martin, PhD, Ian M. Goodyer, MD, Raphael Kelvin, MRCPsych, Bernadka Dubicka, MD, IMPACT Consortium, Nick Midgley, PhD

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Prognostic Implications for Adolescents With Depression Who Drop Out of Psychological Treatment During a Randomized Controlled Trial
RH = Outcomes Associated With Therapy Dropout

Sally O'Keeffe, PhD, Peter Martin, PhD, Ian M Goodyer, MD, Raphael Kelvin, MRCPsych, Bernadka Dubicka, MD, IMPACT Consortium, Nick Midgley, PhD

Editorial
Supplemental Material

Drs. O'Keeffe, Midgley, and Martin are with the Child Attachment and Psychological Therapies Research Unit (ChAPTRe), Anna Freud National Centre for Children and Families, London, UK. Drs. O'Keeffe and Midgley are also with University College London, UK. Prof. Goodyer is with the University of Cambridge, UK. Dr. Kelvin is with MindEd, The Royal College of Psychiatrists, London, UK. Dr. Dubicka is with the Pennine Care NHS Foundation Trust, Lancashire, UK, and the University of Manchester, UK.

College London, Barry Widmer, BSc, University of Cambridge, Paul Wilkinson, MD, University of Cambridge, and Peter Fonagy, PhD, University College London.

Correspondence to Sally O'Keeffe, PhD, Anna Freud National Centre for Children and Families, 12 Maresfield Gardens, London, NW3 5SU, United Kingdom; e-mail: sally.okeeffe@annafreud.org

Abstract

Objective: High therapy dropout rates among adolescents have been reported, but little is known about whether dropout is associated with poor outcomes. This study aimed to examine clinical outcomes in adolescents with depression who dropped out of psychological therapy and to determine if this varied by treatment type.

Method: Data was drawn from the IMPACT study; a randomised controlled trial, comparing a Brief Psychosocial Intervention, Cognitive-Behavioral Therapy and Short-Term Psychoanalytic Psychotherapy in the treatment of adolescent major depression. The sample comprised 406 adolescents with a diagnosis of major depression, 169 of whom dropped out of treatment prior to the planned end of therapy. Primary outcome was self-report Mood and Feelings Questionnaire (MFQ); secondary outcomes were Health of the Nation Outcome Scale for Children and Adolescents, Revised Children's Manifest Anxiety Scale, Modified Leyton Obsessional Inventory and Clinical Diagnosis.

Results: During follow-up there was a non-significant trend for dropouts to report higher depressive symptoms than completers. However, modeling showed insufficient evidence for an association between dropout and outcomes.

Conclusion: In contrast to studies of adult therapy, there was no strong evidence that adolescent patients who dropped out had poorer clinical outcomes compared with those who completed therapy, when dropout was defined as ending treatment without agreement of the therapist. This challenges us to understand why adolescents stop going to therapy, how dropout should be defined, and whether what is prescribed is what is always needed.

Clinical trial registration information: Improving Mood and Preventing Relapse With Psychoanalytic Psychotherapy and Cognitive Behaviour Therapy; http://www.isrctn.com/; 83033550.

Key words: outcome, dropout, psychotherapy, depression, adolescence

Introduction

Depression has an estimated 12-month prevalence rate of 7.5% in adolescence,[1] making it one of the most common psychiatric disorders in adolescence[2] and a significant public health concern. There is now firm evidence that around 70% adolescents with depression who engage in therapy will improve up to a year after treatment.[3] There remains considerable concern however about treatment resistance including adolescents who drop out of therapy, with dropout rates estimated between 28% and 75%.[4]

Dropout has been conceptualised as a client ending therapy prematurely, where they have made the decision unilaterally without agreement of their therapist.[5] The most well accepted definition of dropout is based on therapist judgement that the client ended treatment without their agreement, although other definitions include a client ending treatment prior to completing a pre-specified number of sessions or if they fail to attend their last scheduled appointment.[6] Kazdin's risk-factor model outlines conditions that may increase the likelihood of dropout, such as socio-economic disadvantage and greater symptom severity.[7] This model has been empirically supported, at least in the treatment of conduct disorders, suggesting that it is the most troubled and disadvantaged youth who are at greatest risk of dropout.[4] Researchers have also found that greater barriers experienced when attending treatment, such as practical issues or not perceiving the treatment as relevant, increase the likelihood of dropout.[8] It is unclear whether these findings hold true for other diagnostic groups. Our previous study, drawing on the same dataset as the present study, tested the risk-factor model in adolescents receiving treatment for depression and found that increased age and antisocial behaviour were significant predictors of dropout. However, prediction of dropout from pre-treatment characteristics was overall poor, and various factors were not predictive of dropout, including sex, ethnic minority status, parental wellbeing and symptom severity (including depression, anxiety, obsessionality, self-harm, risk taking and comorbidity). Thus, there was

little evidence that it was the most impaired adolescents receiving treatment for depression who dropped out.[9]

As talking therapies have been found to be effective, it seems reasonable to expect that dropping out of treatment would be associated with poorer outcomes.[10] Adults who complete therapy for depression have consistently been found to improve more than clients who drop out.[11–13] However, we cannot assume that findings from studies with adult clients can be generalised to adolescents. Help seeking in youth often does not come from the child or adolescent themselves, but instead, is frequently initiated by an adult, such as their parent or caregiver.[7] Adolescents may be less motivated to engage in therapy than adults if they haven't sought therapy for themselves, so it cannot be assumed that the implications of dropout will be comparable for adolescents and adults.

Several studies found children with conduct problems (and/or their parents) who drop out have poorer clinical outcomes by the end of treatment, compared with those who complete treatment.[14–18] One study investigated longer-term outcomes associated with dropout, and found that poorer outcomes were maintained approximately 20-months after treatment began.[16] However, two of these studies reported that dropouts were more impaired at baseline, suggesting that difference in outcomes may in part be due to pre-treatment factors.[14,15] Two studies included samples of both children and adolescents (aged below 17-years) and found that those who completed treatment made greater gains than those who did not.[19,20] It cannot be assumed that findings from youth with conduct disorders generalize to those seeking treatment for depression. The phenomenology of these clinical populations differs substantially and thus the reasons for dropout may differ between them. Depression in youth is characterised by hopelessness and social withdrawal,[21] which may contribute to their decisions to drop out through feeling hopeless that it won't help. In contrast, conduct problems are characterised by antisocial and defiant behaviours[22] and so dropping out may be

a sign of acting out against the therapist or service. There may well be different influences, causes or reasons for dropout between these diagnostic groups. The models of treatment also differ, with treatment for child conduct problems placing more emphasis on parent training and parental involvement in treatment compared with interventions for adolescent depression.[22,23] The inherent differences in the phenomenology and treatment of these disorders means previous findings of outcomes in young people with conduct problems may not transfer to those with depression. Many of these studies have been conducted with younger children, yet adolescents have distinct developmental tasks,[24,25] and thus there is a strong argument for studying the implications of dropout for adolescents with depression in their own right.

Currently there is a dearth of knowledge about adolescents with depression who drop out of therapy. We addressed this gap in the literature within the context of a randomised controlled trial (RCT) evaluating the effectiveness of psychological therapies for adolescent depression.[3] This study aimed to examine the association between dropout and clinical outcomes among adolescents who received therapy for depression. In keeping with the aim of the RCT, we focused on long-term outcomes.

Method

Design

We conducted secondary analysis of the IMPACT multisite RCT comparing three psychological interventions in the treatment of moderate/severe depression in adolescents (ISRCTN register reference: ISRCTN83033550).[3,26]. Adolescents were referred from Child and Adolescent Mental Health Services across three regions in England. Inclusion criteria were a DSM-IV diagnosis of unipolar major depressive disorder,[27] measured by the Kiddie-Schedule for Affective Disorders and Schizophrenia (Kiddie-SADS),[28] and aged 11-17 years

at referral. Exclusion criteria were generalised learning difficulties, pervasive developmental disorder, eating disorder, bipolar disorder, schizophrenia, and pregnancy. Eligible patients were randomly allocated to one of three manualised treatments:

a) Brief Psychosocial Intervention (BPI). Up to 12 sessions, focused on engagement, psychoeducation about depression, problem solving, and supporting activation through engaging in interpersonal activities and physical wellbeing.

b) Cognitive-Behavioral Therapy (CBT). Up to 20 sessions, based on formulation of the adolescents' current problems, precipitating and maintaining factors, focusing on explicit, tangible and shared goals.

c) Short-Term Psychoanalytic Psychotherapy (STPP). 28 weekly sessions with the adolescent, based on close and detailed observation of the relationship the adolescent makes with their therapist, with a focus on better self-understanding of feelings and difficulties in their life.

The treatment manuals are available at: http://dev.psychiatry.cam.uk/projects

Outcome assessments took place after randomisation, at 6 and 12-weeks (during treatment), 36-weeks (completed treatment for >95%), and 52 and 86-weeks (long-term follow-ups).

All three therapies were equivalent in clinical and cost-effectiveness, with 78% of adolescents showing clinically meaningful reductions in their symptoms of depression and improved functioning approximately one-year after the end of treatment.[3] 37% of adolescents dropped out of their allocated therapy, and 10% did not take up the therapy on offer.[9] The hypothesis tested in this study was that one-year after the end of treatment for depression adolescents who dropped out of their offered therapy would have poorer outcomes than adolescents who completed therapy.

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Ethical considerations

The IMPACT study protocol was approved by the Cambridgeshire 2 Research Ethics Committee (reference:09/H0308/137). Fully informed written consent was obtained from participants, or parents for those under the age of 16.

Measures

The primary outcome was self-report depression symptoms, measured by the Mood and Feelings Questionnaire (MFQ).[29] Secondary outcomes were Health of the Nation Outcome Scale for Children and Adolescents (HoNOSCA); a measure of psychosocial impairment,[30] self-report scores on the Revised Children's Manifest Anxiety Scale (RCMAS)[31] and revised Leyton Obsessional Inventory (LOI).[32] Presence of current major depressive disorder was assessed by the Kiddie-SADS[28] at post treatment follow-ups (36, 52 and 86-weeks).

Operationalising therapy completion and dropout

Participants were retrospectively classified as dropouts if they took up the therapy on offer but ended it without the mutual agreement of their therapist, as determined by the therapist's 'end of treatment' form, regardless of how many sessions they attended. This definition was selected as is the most well accepted in the contemporary dropout literature,[9] and allows for the reality that dropout can happen after any number of sessions. To address the limitation that this definition includes adolescents that attended a significant proportion of planned sessions and those who dropped out at an early stage, sensitivity analyses were conducted to consider different approaches to defining dropout, based on when dropout occurred. In the sensitivity analyses, dropout was defined as when the ending of treatment was not agreed with the therapist, and a) it was prior to the adolescent completing 25% of their planned

sessions, b) prior to the adolescent completing 50% of their planned sessions and c) prior to the adolescent completing 75% of their planned sessions.

Participants were classified as treatment completers if their therapist recorded that treatment had ended as planned or by mutual agreement.

Participants were classified as non-starters if they did not attend any therapy sessions. Non-starters do not take up the treatment on offer, which is considered as representing a distinct phenomenon from that of dropout.[33]

Statistical analysis

Data analyses were conducted in R V3.3.2.[34] Multilevel modelling was used to examine whether dropouts and completers differed in their rate of change between treatment arms. Treatment arms, therapy ending and time were tested as predictors of outcomes for the continuous outcome variables (MFQ; HoNOSCA; RCMAS; LOI). Therapy ending was a dichotomous variable (0=completed; 1=dropped out). The models had a three-level structure, with repeated measures nested within participants, who in turn were nested within therapists. For 22 participants the therapist was unknown; these were treated as their therapists' only case. Participant random slopes for the Time variable were included in all models, to allow for variation in the rate of change between participants. In addition, age and antisocial behaviour (measured using the Antisocial Behaviour Questionnaire)[3] were controlled for as they were known to differ between completers and dropouts.[9]

The relationship between time and outcome was not expected to be linear. To account for greater rate of change early in treatment, time was log-transformed, using the equation log(Time+1). This enabled the non-linear relationship between time and outcomes (MFQ, HoNOSCA, RCMAS and LOI) to be modeled using linear regression. Square-root transformation of time yielded a better fit for modeling outcomes on the RCMAS according

to Akaike's Information Criterion (AIC; Akaike, 1973) and Bayesian Information Criterion (BIC; Schwarz, 1978). Square-root transformation of time was therefore used for modeling outcomes on the RCMAS. The best fitting model was selected using likelihood ratio tests, the AIC and BIC, with a smaller AIC and BIC representing a better fitting model.

To investigate whether risk of meeting diagnostic criteria for depression at 36, 52 and 86-weeks differed between completers and dropouts, in each treatment arm, mixed effect logistic regression analyses were used. All participants met diagnostic criteria for depression at baseline, so logistic regression analyses were used to test dropout as a predictor of depression at the long-term follow-up assessments. Mixed effect models were used to account for therapist effects. The dependent variable was depression diagnosis (measured by the Kiddie-SADS), and predictor variables were interaction terms for Treatment Arm X Therapy Ending. Models were run with completers in each treatment arm coded as the reference group, to estimate the association between dropout and outcomes in each treatment arm. Age and antisocial behavior were included as covariates.

Sensitivity analyses were conducted to test whether the conclusions were sensitive to how dropout was defined.

Results

Participants

The IMPACT sample consisted of 465 participants, as previously reported.[3] Cases were excluded if it was unknown how therapy ended, due to incomplete therapist records ($n = 12$), or if they did not start treatment ($n = 47$), providing a sample of 406 participants for the present study.

Participants ranged from 11 to 17-years (M=15.56, SD=1.44) at baseline. 303 (75%) were female participants and 103 (25%) were male participants. Ethnicity was 81% white, 7% mixed ethnic background, 2% Asian, 3% black, 3% other and 4% ethnicity unknown.

Dropout rates, treatment duration and session attendance

Of the 406 participants, 237 completed therapy and 169 dropped out. Dropout by treatment arm, number of sessions attended and treatment durations are shown in Table S1 (available online). On average, participants in all three arms attended far fewer sessions than the manuals prescribed. The majority of dropouts in all treatment arms attended less than 50% of the prescribed sessions, whereas completers tended to attend more than 50% of intended sessions. Treatment duration from the first to last session was substantially lower for dropouts compared with completers, indicating that dropout tended to occur early in therapy.

Clinical outcomes associated with dropout

Descriptive statistics on each outcome measure for dropouts and completers in the three treatment arms, at each timepoint, show little difference in baseline scores between completers and dropouts (Table 1). In CBT and STPP, dropouts tended to have slightly poorer outcomes than completers; in BPI, outcome differences between dropouts and completers were smaller and sometimes in the opposite direction, with dropouts sometimes having better outcomes.

[Table 1]

To model outcomes on the MFQ, Model 1 predicted the trajectory of change in MFQ scores with Time (Log(Time+1)), Treatment Arms and Therapy Ending as the independent variables, with random intercepts for therapists and participants, and participant random slopes for the effect of time, controlling for age and antisocial behaviour. This assumed the

rate of change was the same for all groups. In Model 2, two-way interaction terms (Time X Treatment Arms; Time X Therapy Ending) were added to the model, which tested whether change was dependent on therapy ending and treatment arm, without an interaction between therapy ending and treatment arm. This did not improve the model fit, according to the AIC, BIC and a likelihood ratio test (LRT(3)=2.82, p=0.42). In Model 3, three-way interaction terms (Time X Treatment Arms X Therapy Ending) were added to the model, to test whether the association between dropout and outcomes differed between the treatment arms. This did not improve the model fit, based on the AIC, BIC and a likelihood ratio test (LRT(4)=6.01, p=0.20). Therefore we found no strong evidence for an association of dropout with MFQ across all three treatments, nor for an association of dropout with MFQ for any treatment arm (for model estimates, see Table S2; available online). Model 3 is plotted in Figure 1.

[Figure 1]

Outcomes on the HoNOSCA, RCMAS and LOI were modeled using the same strategy described above. Adding two-way interaction terms and three-way interaction terms did not improve the fit of the models, for any of the outcome measures (for model estimates, see Tables S3-S5; available online). Thus, no strong evidence was found for an association between dropout and outcomes on any of the outcome measures.

Finally, mixed effect logistic regression analyses were used, testing the main effects of each treatment arm and interaction terms for Treatment Arm X Dropout as predictors of depression diagnosis at 36, 52 and 86-weeks (Table 2). At 36-weeks, those who dropped out of BPI were estimated to be 71% less likely to meet diagnostic criteria for depression compared with those who completed BPI (OR=0.29, CI 0.10:0.82), showing evidence contrary to our hypothesis. This association was not maintained in the longer term, as the BPI X Dropout terms were not significant at 52 and 86-weeks. In CBT and STPP, some evidence was found for an association between dropout and outcomes in the expected direction. At 36-

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weeks, those who dropped out of STPP were estimated to be 2.7 times more likely to meet diagnostic criteria for depression compared with those who completed STPP (OR=2.67, CI 1.11:6.41). A longer-term association of dropout and depression diagnosis was not found in STPP, as the STPP X Dropout terms were not significant at 52 and 86-weeks. In CBT, there was not a significant effect of dropout at 36-weeks on the odds of meeting diagnostic criteria for depression. However, at 52-weeks, dropping out of CBT was estimated to increase the odds of meeting diagnostic criteria for depression six-fold (OR=6.09, CI 2.05:18.10). This difference was statistically significant, yet the confidence intervals were rather wide, indicating that this association could not be estimated with a great deal of precision, and should be viewed with caution. This association between dropout and depression diagnosis was not maintained in the longer-term, at 86-week follow-up (Table 2).

[Table 2]

Exploratory Analysis

The trial was not designed to have sufficient power for these secondary analyses. We considered that the findings presented may be due to inadequate power to detect an association between dropout and outcomes, overall or separately for the three treatments. We decided to present coefficient estimates from Model 2 and Model 3, as an exploratory analysis.

Table 3 shows estimated difference in MFQ scores between dropouts and completers in each treatment arm. The estimates of the association between dropout and outcome (not accounting for treatment arm) were derived from Model 2, and estimates for each treatment arm were derived from Model 3. In BPI and STPP, dropout estimates showed little indication of an association of dropout with MFQ scores at 36, 52 and 86-weeks, as the 95% confidence intervals contained zero. In CBT however, the confidence intervals did not contain zero and

contained the value of five (considered to be an important difference on the MFQ[3]). This shows some weak evidence for an association of dropout with MFQ scores in CBT, but should be viewed cautiously due to the exploratory nature of these analyses. On the RCMAS, the same pattern was observed: the 95% confidence intervals for dropout estimates contained zero for the BPI and STPP arms at all time-points, but not for CBT. This provides some indication of a possible association of dropout on outcomes on the RCMAS in the CBT arm, at 36, 52 and 86-weeks. On the HoNOSCA and LOI, the 95% confidence intervals for dropout estimates at all timepoints and all three treatment arms contained zero, providing no evidence for an association of dropout and outcomes on these measures.

Table 3 also shows estimated differences in outcome scores between dropouts and completers in each treatment arm at the 6 and 12-week assessments, to explore whether progress (or lack of) during treatment was associated with dropout. The confidence intervals all contain zero, thus there is no strong evidence for a difference between dropouts and completers in the rate of change in the early part of treatment.

[Table 3]

Sensitivity analyses were conducted to test whether the conclusions were sensitive to how dropout was defined. The results were found to be robust, as they did not change when dropouts were re-classified as completers if they attended more than 25%, 50% and 75% of the planned sessions. No evidence was found for therapist effects in any of the models.

Discussion

The IMPACT trial investigated psychological therapies in the treatment of adolescent depression, and found no statistically significant difference in clinical outcomes between three treatment arms.[3] The present study investigated whether dropout was associated with outcomes by conducting secondary analysis of the IMPACT dataset. It was hypothesised that

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adolescents who dropped out of therapy would have poorer long-term outcomes compared with those who completed therapy, in the three treatments.

Modeling showed insufficient evidence to conclude an association between dropout and outcomes, for four of the five outcome measures investigated, based on the planned analyses. The only outcome measure where there was statistically significant evidence that dropout may be associated with poorer outcomes was depression diagnosis, in CBT and STPP. CBT dropouts were estimated to be six times more likely to meet diagnostic criteria for depression at 52-weeks compared with completers, yet this could not be estimated with a great deal of precision, and any association was not maintained at 86-weeks. STPP dropouts were estimated to be 2.7 times more likely to meet diagnostic criteria for depression at 36-weeks than completers, but this difference was not maintained at the longer-term follow-ups. Counter to our hypothesis, BPI dropouts were estimated to be 71% less likely to meet diagnostic criteria at 36-weeks than completers. No such difference in depression diagnosis between BPI dropouts and completers was observed at the later follow-ups. Thus, there was some evidence for an association between dropout and outcomes in CBT and STPP after the end of treatment, yet at 86-weeks, there were no significant differences between dropouts and completers in any treatment arm.

As these were secondary analyses of the IMPACT dataset, we were mindful this study was likely to be underpowered. To provide an indication of power, we explored the estimated difference in outcomes between dropouts and completers with confidence intervals in each treatment arm. Based on dropout estimates, some evidence for an association of dropout with outcome was found in the CBT arm, weaker evidence in the STPP arm, and little evidence in the BPI arm. This evidence must be considered weak because the association between dropout and outcomes were estimated from models that were rejected due to insignificant results. The wide confidence intervals of dropout estimates show we were unable to estimate

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differences in outcomes associated with dropout with good precision, due to the sample size. However, these estimates may be useful for future researchers conducting systematic reviews or meta-analyses, to obtain better estimates of the association of therapy dropout with outcomes in adolescents.

Given that the interventions were designed to improve depressive pathology and wellbeing, it was surprising to find limited evidence of an association between dropout and adolescents' long-term outcomes. This raises important questions about how dropout is defined and why adolescents drop out of therapy. Previous research cited not perceiving need for further treatment as a common reason clients give for stopping therapy.[24,37] It is possible that some young people dropped out because they did not feel in need of further treatment or because they perceived it was not helping. However, our exploratory analyses found no strong evidence for a difference between dropouts and completers in the rate of symptom change in the 6 and 12-week assessments. Future research should include adolescents' perspectives as to the reasons they dropped out of therapy.

Interestingly, and in contrast to the results presented here, research with child and adult patients has found dropout to be associated with poorer clinical outcomes.[11,13–20] This age effect may reflect a developmental difference in the meaning of depressive symptoms and/or syndrome. Adolescents have distinctive developmental tasks, including formation of identity, becoming more autonomous and questioning adult authority.[24,25] Perhaps therapists need to be sensitive to and assess the nature of adolescent maturation and how this may impact on the planned treatment. For example, if becoming independent from adults becomes apparent during treatment, this may enable the decision to stop therapy and be more autonomous in subsequent recovery.[24] This would support the notion that dropping out of therapy may not always be a bad thing for adolescents. Further research is required to test this

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developmentally sensitive speculation including for treatments of adolescents presenting with other disorders.

It is important to acknowledge the episodic nature of depression, as the likelihood of recurrence and relapse within one year, even in successfully treated depression, is estimated between 50-75%.[38] Improvements observed may in part reflect the natural course of the disorder, and some adolescents may recover regardless of whether they complete treatment or not. We also note there were relatively few pre-treatment differences between completers and dropouts, as dropouts were not found to have greater symptom severity than completers at baseline.[9] However, at baseline, age and antisocial behavior were higher for dropouts than completers. These variables were included as control variables,[9] and may moderate the relation between dropout and outcome.

This was the first known study to investigate clinical outcomes associated with dropout in adolescents receiving therapy for depression. While absence of strong evidence is not evidence of absence of an effect, these findings challenge common assumptions that dropout equates to poor clinical outcomes. Research is needed to further investigate the implications of dropout.

This study had several limitations. It was not designed (or powered) to formally test or confirm these secondary hypotheses. These findings must be viewed with caution and further research is required to test the association between dropout and clinical outcomes. The 86-week follow-up may be too short for some dropout manifestations to be measured. This study was also limited by our models not taking into account the point at which dropout occurred, as we did not have a measure of outcome at the point of dropout.

Dropout was defined as the adolescent ending therapy without the therapist's agreement. The limitation of this definition is that it is highly dependent on the therapists' views about the appropriateness of ending treatment. Moreover, it does not account for when

dropout occurred. To overcome this issue, sensitivity analyses were conducted to consider whether the findings differed as a function of the definition, which they did not. It was surprising that little evidence for an association of dropout and outcomes was found, given that dropout was based on therapists' judgement as to whether they agreed with the ending. This calls into question issues regarding operational definitions of dropout, and more broadly, about the nature of dropout itself. It must be acknowledged that it is unknown how representative this sample was of the population, as it was based on recruitment from specialist adolescent mental health services and was not designed to be representative of these forms of major depression in the community. This means we can only comment on drop out from therapy of those young people with depression in the community who are able to access treatment. In addition, as these findings were in the context of an RCT, it is unknown how generalizable they are to routine clinical practice, but provide an important starting point in the study of dropout and outcome.

We note that the dropout rate in this sample (37%) was substantially higher than the rate of consent withdrawal (10.9%) reported in the TADS trial for adolescent depression.[39] This may be due to the short treatment duration in TADS compared with the IMPACT trial. However, these groups are not directly comparable, as TADS only reported the consent withdrawal rate, whereas dropout was operationally defined in this study based on the ending of treatment not being agreed with the therapist. This means some adolescents were classified as having dropped out as they stopped attending their sessions or were discharged due to non-attendance, without necessarily having formally withdrawn consent for treatment. This is likely to have contributed to the marked difference in dropout rates in our study compared with TADS. This reflects issues with inconsistency in how dropout is operationally defined in the literature. There is a need for standardized reporting of treatment dropout in clinical trials,[40] to facilitate dropout comparisons across studies.

In conclusion, dropout is a common phenomenon in adolescents receiving therapy for depression.[9] Given that psychotherapy is generally associated with positive clinical outcomes, it is usually assumed that dropping out of psychotherapy is an undesirable way for it to conclude. Most studies of dropout and outcome with children and adults have supported this assumption.[11,13–20] However, little evidence for an association of dropout and clinical outcomes was found in this study, particularly by the final follow-up at 86-weeks, suggesting that dropping out of treatment for many adolescents with depression may not be a signature of poor long-term outcome, when defined as ending treatment without agreement from the therapist. These findings should be viewed as exploratory and a sufficiently powered study to test the prognostic implications of treatment dropout is required.

References

1. Avenevoli S, Swendsen J, He JP, Burstein M, Merikangas K. Major depression in the National Comorbidity Survey- Adolescent supplement: Prevalence, correlates, and treatment. *J Am Acad Child Adolesc Psychiatry*. 2015;54(1):37-44.

2. Costello E, Erkanli A, Angold A. Is there an epidemic of child or adolescent depression? *J Child Psychol Psychiatry*. 2006;47(12):1263-1271.

3. Goodyer IM, Reynolds S, Barrett B, et al. 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*. 2017;4(2):109–119.

4. de Haan AM, Boon AE, de Jong JTVM, Hoeve M, Vermeiren RRJM. A meta-analytic review on treatment dropout in child and adolescent outpatient mental health care. *Clin Psychol Rev*. 2013;33(5):698-711.

5. Pekarik G. The effects of employing different termination classification criteria in dropout research. *Psychother Theory, Res Pract Train*. 1985;22(1):86-91.

6. Warnick EM, Gonzalez A, Weersing VR, Scahill L, Woolston J. Defining dropout from youth psychotherapy: how definitions shape the prevalence and predictors of attrition. *Child Adolesc Ment Health*. 2012;17(2):76-85.

7. Kazdin AE. Dropping out of child psychotherapy: Issues for research and implications for practice. *Clin Child Psychol Psychiatry*. 1996;1(1):133-156.

8. Kazdin AE, Holland L, Crowley M. Family experience of barriers to treatment and premature termination from child therapy. *J Consult Clin Psychol*. 1997;65(3):453-463.

9. O'Keeffe S, Martin P, Goodyer I, Wilkinson P, IMPACT Consortium, Midgley N.

Predicting dropout in adolescents receiving therapy for depression. *Psychother Res*. 2017;28(5):708-721.

10. Weisz JR, Kuppens S, Ng MY, et al. What five decades of research tells us about the effects of youth psychological therapy: A multilevel meta-analysis and implications for science and practice. *Am Psychol*. 2017;72(2):79-117.

11. Cahill J, Barkham M, Hardy G, et al. Outcomes of patients completing and not completing cognitive therapy for depression. *Br J Clin Psychol*. 2003;42(2):133-143.

12. Persons JB, Burns DD, Perloff JM. Predictors of dropout and outcome in cognitive therapy for depression in a private practice setting. *Cognit Ther Res*. 1988;12(6):557-575.

13. Saatsi S, Hardy GE, Cahill J. Predictors of outcome and completion status in cognitive therapy for depression. *Psychother Res*. 2007;17(2):185-195.

14. Kazdin AE, Mazurick JL, Siegel TC. Treatment outcome among children with externalizing disorder who terminate prematurely versus those who complete psychotherapy. *J Am Acad Child Adolesc Psychiatry*. 1994;33(4):549-557.

15. Kazdin AE, Wassell G. Treatment completion and therapeutic change among children referred for outpatient therapy. *Prof Psychol Res Pract*. 1998;29(4):332-340.

16. Boggs SR, Eyberg M, Edwards L, et al. Outcomes of Parent-Child Interaction Therapy: A comparison of treatment completers and study dropouts one to three years later. *Child Fam Behav Ther*. 2005;26(4):1-22.

17. Danko CM, Garbacz LL, Budd KS. Outcomes of Parent-Child Interaction Therapy in an urban community clinic: A comparison of treatment completers and dropouts. *Child Youth Serv Rev*. 2016;60:42-51.

18. Luk ESL, Staiger PK, Mathai J, Wong L, Birleson P, Adler R. Children with persistent conduct problems who dropout of treatment. *Eur Child Adolesc Psychiatry*.

2001;10(1):28-36.

19. Lai KY, Chan TS, Pang AHT, Wong CK. Dropping out from child psychiatric treatment: reasons and outcome. *Int J Soc Psychiatry*. 1997;43(3):223-229.

20. Jensen-Doss A, Weisz JR. Diagnostic agreement predicts treatment process and outcomes in youth mental health clinics. *J Consult Clin Psychol*. 2008;76(5):711-722.

21. Midgley N, Parkinson S, Holmes J, Stapley E, Eatough V, Target M. Beyond a diagnosis: The experience of depression among clinically-referred adolescents. *J Adolesc*. 2015;44:269-279.

22. NICE. *Antisocial Behaviour and Conduct Disoders in Children and Young People: Recognition and Management*. London: National Institute for Health and Care Excellence; 2017.

23. NICE. *Depression in Children and Young People: Identification and Management in Primary, Community and Secondary Care*. London: National Institute for Health and Care Excellence.; 2005.

24. Block AM, Greeno CG. Examining outpatient treatment dropout in adolescents: A literature review. *Child Adolesc Soc Work J*. 2011;28(5):393-420.

25. Erikson EH. *Childhood and Society*. Vol 1st ed. New York, NY: Norton; 1950.

26. Goodyer IM, Tsancheva S, Byford S, et al. 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*. 2011;12(1):175.

27. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*. Washington, DC: American Psychiatric Association; 2000.

28. Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and

Schizophrenia for School-Age Children Present and Lifetime version (K-SADS-PL): Initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry*. 1997;36(7):980-988.

29. Angold A, Costello EJ, Pickles A, Winder F. *The Development of a Questionnaire for Use in Epidemiological Studies in Children and Adolescents.* London: MRC Child Psychiatry Research Unit; 1987.

30. Garralda ME. Child and adolescent mental health service use: HoNOSCA as an outcome measure. *Br J Psychiatry*. 2000;177(1):52-58.

31. Reynolds CR, Richmond BO. What I think and feel: A Revised Measure of Children's Manifest Anxiety. *J Abnorm Psychol*. 1978;6(2):271-280.

32. Bamber D, Tamplin A, Park R, Kyte ZA, Goodyer IM. Development of a short Leyton Obsessional Inventory for children and adolescents. *J Am Acad Child Adolesc Psychiatry*. 2002;41(10):1246-1252.

33. Garfield SL. Research on client variables in psychotherapy. In: Garfield & Bergin, ed. *Handbook of Psychotherapy and Behavior Change*. Vol 3rd ed. New York: Wiley; 1986:213-256.

34. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2016.

35. Akaike H. Information theory and an extension of the maximum likelihood principle. In: Petrov BN, Csaki F, eds. *Second International Symposium on Information Theory*. Vol Budapest: Akadémiai Kiado; 1973:267-281.

36. Schwarz G. Estimating the dimension of a model. *Ann Stat*. 1978:461–464.

37. Garcia JA, Weisz JR. When youth mental health care stops: Therapeutic relationship problems and other reasons for ending youth outpatient treatment. *J Consult Clin Psychol*. 2002;70(2):439-443.

38. Goodyer IM, Wilkinson PO. Practitioner Review: Therapeutics of unipolar major depressions in adolescents. *J Child Psychol Psychiatry*. 2018.

39. Treatment for Adolescents with Depression Study Team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents With depression. *J Am Med Assoc*. 2004;292(7):807-820. doi:10.1001/jama.292.7.807.

40. Cooper AA, Kline AC, Baier AL, Feeny NC. Rethinking research on prediction and prevention of psychotherapy dropout: A mechanism-oriented approach. *Behav Modif*. 2018.

Table 1: Outcomes at Each Timepoint, for Dropouts and Completers in Each Treatment Arm

Outcome	Timepoint	BPI		CBT		STPP	
		Dropouts	**Completers**	**Dropouts**	**Completers**	**Dropouts**	**Completers**
MFQ	Baseline (N=406)	46.53	46.28	45.49	46.18	44.77	44.66
	6-weeks (n=285)	39.02	36.26	38.43	33.40	34.05	37.35
	12-weeks (n=301)	35.76	34.66	38.06	29.27	32.82	34.60
	36-weeks (n=289)	26.66	32.20	27.50	23.40	30.89	23.80
	52-weeks (n=297)	25.96	24.94	30.57	22.61	25.80	21.33
	86-weeks (n=319)	22.53	24.32	26.31	19.60	24.68	18.27
HoNOSCA	Baseline (n=380)	19.89	18.48	19.00	17.62	18.09	18.38
	6-weeks (n=252)	15.50	14.51	15.28	13.47	14.13	15.01
	12-weeks (n=271)	17.46	13.16	14.28	11.10	12.11	13.36
	36-weeks (n=241)	11.94	11.69	9.81	9.70	12.26	8.99
	52-weeks (n=235)	8.78	9.95	12.09	7.62	10.41	7.15
	86-weeks (n=250)	7.72	8.48	9.01	6.36	8.35	7.54
Modified LOI	Baseline (n=402)	11.07	9.45	10.15	11.08	9.40	8.68

	6-weeks (n=282)	9.32	7.32	8.50	6.79	7.43	7.97
	12-weeks (n=298)	7.97	6.37	7.83	6.21	7.13	7.52
	36-weeks (n=283)	6.54	6.02	5.50	4.28	5.90	4.65
	52-weeks (n=281)	7.19	5.00	5.28	4.83	5.07	4.61
	86-weeks (n=298)	5.79	4.75	5.39	4.54	4.20	3.46
RCMAS	Baseline (n=405)	42.37	40.42	40.72	41.71	40.44	40.10
	6-weeks (n=283)	36.39	36.20	39.34	35.90	35.58	38.70
	12-weeks (n=299)	35.24	35.09	38.95	32.91	34.02	34.79
	36-weeks (n=285)	29.46	33.23	29.54	25.96	29.67	27.89
	52-weeks (n=285)	26.27	27.75	31.21	24.39	27.19	24.19
	86-weeks (n=301)	24.00	25.57	28.41	22.59	24.52	22.60
% meeting criteria for depression	6-weeks (n=268)	78%	67%	74%	52%	64%	61%
	12-weeks (n=282)	52%	56%	65%	41%	57%	56%
	36-weeks (n=263)	22%	52%	36%	28%	49%	26%
	52-weeks (n=247)	32%	29%	54%	17%	31%	22%
	86-weeks (n=262)	15%	31%	37%	18%	19%	9%

Note: BPI =Brief Psychosocial Intervention; CBT = Cognitive-Behavioral Therapy; HoNOSCA = Health of the Nation Outcomes Scales Child and Adolescent; LOI = Leyton Obsessional Inventory; MFQ = Mood and Feelings Questionnaire; RCMAS = Revised Children's Manifest Anxiety Scale; STPP = Short Term Psychoanalytic Psychotherapy.

Table 2. Mixed Effects Logistic Regression Analyses Predicting Depression Diagnosis at 36, 52 and 86-weeks

	Variable	36-weeks (n=260)	52-weeks (n=245)	86-weeks (n=237)
		OR (95% CI)	OR (95% CI)	OR (95% CI)
Fixed effects	Constant	2.31 (0.11:49.36)	0.11 (0.00:3.43)	0.05 (0.00:2.31)
	Age	0.96 (0.79:1.17)	1.10 (0.89:1.36)	1.16 (0.91:1.47)
	Anti-social behaviour	0.96 (0.88:1.05)	0.94 (0.84:1.04)	0.98 (0.87:1.11)
	Dropout	0.29* (0.10:0.82)	1.29 (0.44:3.81)	0.44 (0.13:1.49)
	CBT	0.39* (0.18:0.83)	0.51 (0.21:1.22)	0.54 (0.22:1.30)
	CBT X Dropout	5.01* (1.15:21.84)	4.72* (1.02:21.84)	6.01* (1.19:30.43)
	STPP	0.34*** (0.16:0.76)	0.74 (0.30:1.81)	0.24* (0.07:0.76)
	STPP X Dropout	9.26*** (2.38:36.04)	1.10 (0.25:4.82)	5.39 (0.89:32.72)
Random effects	Therapist variance (SD)	0.00	0.00	0.00

ORs for Treatment Arm X Dropout interaction terms

Reference group:				
BPI Completers	BPI X Dropout	0.29* (0.10:0.82)	1.29 (0.44:3.81)	0.44 (0.13:1.49)
CBT Completers	CBT X Dropout	1.44 (0.51:4.09)	6.09*** (2.05:18.10)	2.63 (0.93:7.50)

STPP Completers	STPP X Dropout	2.67* (1.11:6.41)	1.42 (0.52:3.90)	2.36 (0.62:8.96)

Note: Mixed effects logistic regression models predicted depression diagnosis (measured by the Kiddie-SADS [Kiddie Schedule for Affective

Disorders and Schizophrenia]), with therapist effects and controlling for age and antisocial behaviour. Sample based on the number of

participants who completed the Kiddie-SADS at that timepoint. BPI = Brief Psychosocial Intervention; CBT = Cognitive-Behavioral Therapy;

OR = odds ratio. STPP = Short Term Psychoanalytic Psychotherapy.

*$p < .05$, ***$p < .001$

Table 3: Mean Estimated Difference in Outcomes Associated With Dropout With Confidence Intervals, in Each Treatment Arm

Measure	Timepoint	Overall dropout effect[a] (95% CI)	BPI dropout effect[b] (95% CI)	CBT dropout effect[b] (95% CI)	STPP dropout effect[b] (95% CI)
MFQ	6-weeks	0.47 (-1.56:2.49)	-1.22 (-4.73:2.29)	2.78 (-0.76:6.32)	-0.19 (-3.60:3.21)
	12-weeks	0.92 (-1.21:3.04)	-1.53(-5.23:2.17)	3.70 (-0.00:7.40)	0.52 (-3.03:4.08)
	36-weeks	1.81 (-0.86:4.49)	-2.13 (-6.82:2.56)	5.51 (0.86:10.16)	1.93 (-2.52:6.39)
	52-weeks	2.13 (-0.82:5.08)	-2.35 (-7.52:2.83)	6.16 (1.03:11.28)	2.44 (-2.47:7.35)
	86-weeks	2.60 (-0.80:6.00)	-2.67 (-8.65:3.30)	7.12 (1.21:13.03)	3.19 (-2.47:8.85)
HoNOSCA	6-weeks	0.69 (-0.37:1.74)	0.75 (-1.07:2.56)	1.39 (-0.46:3.23)	-0.11 (-1.90:1.68)
	12-weeks	0.72 (-0.31:1.76)	0.44 (-1.36:2.23)	1.43 (-0.39:3.24)	0.26 (-1.48:2.00)
	36-weeks	0.79 (-0.41:2.00)	-0.17 (-2.28:1.93)	1.51 (-0.61:3.63)	0.98 (-1.02:2.97)
	52-weeks	0.82 (-0.49:2.13)	-0.39 (-2.69:1.91)	1.54 (-0.79:3.86)	1.24 (-0.94:3.41)
	86-weeks	0.86 (-0.66:2.37)	-0.72 (-3.36:1.93)	1.58 (-1.10:4.26)	1.62 (-0.88:4.12)
LOI – adolescent version	6-weeks	0.58 (-0.34:1.49)	1.18 (-0.41:2.76)	0.12 (-1.49:1.72)	0.41 (-1.15:1.97)
	12-weeks	0.64 (-0.25:1.54)	1.09 (-0.47:2.65)	0.37 (-1.19:1.93)	0.45 (-1.07:1.97)
	36-weeks	0.78 (-0.17:1.72)	0.93 (-0.74:2.60)	0.87 (-0.77:2.52)	0.52 (-1.07:2.11)

	52-weeks	0.83 (-0.16:1.82)	0.87 (-0.88:2.63)	1.05 (-0.67:2.77)	0.55 (-1.12:2.21)
	86-weeks	0.90 (-0.18:1.98)	0.79 (-1.14:2.71)	1.32 (-0.56:3.19)	0.59 (-1.22:2.39)
RCMAS	6-weeks	0.23 (-1.26:1.73)	0.51 (-3.12:2.10)	1.61 (-1.00:4.23)	-0.44 (-2.94:2.07)
	12-weeks	0.48 (-1.19:2.15)	-0.98 (-3.91:1.96)	2.55 (-0.36:5.46)	-0.19 (-2.97:2.60)
	36-weeks	0.97 (-1.33:3.27)	-1.89 (-5.95:2.18)	4.40 (0.42:8.39)	0.30 (-3.52:4.12)
	52-weeks	1.14 (-1.43:3.72)	-2.21 (-6.77:2.34)	5.07 (0.60:9.53)	0.48 (-3.80:4.75)
	86-weeks	1.40 (-1.61:4.41)	-2.70 (-8.03:2.62)	6.05 (0.83:11.27)	0.74 (-4.26:5.73)

Note: Mixed model estimates of mean differences for dropouts compared with completers at 6, 12, 36, 52 and 86-weeks. Analysis used therapist, participant and slope random effects, and tested three-way interactions Time(log-transformed) X Treatment arm X Dropout, controlling for age and antisocial behaviour. BPI = Brief Psychosocial Intervention; CBT = Cognitive-Behavioral Therapy; HoNOSCA = Health of the Nation Outcome Scale for Children and Adolescents; LOI = Leyton Obsessional Inventory; MFQ = Mood and Feelings Questionnaire; RCMAS = Revised Children's Manifest Anxiety Scale; STPP = Short Term Psychoanalytic Psychotherapy.

[a]Derived from Model 2 (which tested two-way interactions: Time X Treatment Arms; Time X Therapy Ending);

[b]Derived from Model 3 (which tested three-way interactions: Time X Treatment Arms X Therapy Ending).

Figure 1. Estimated Change in Mood and Feelings Questionnaire (MFQ) Scores Over

Time for Completers and Dropouts in Each Treatment Arm

Note: BPI = Brief Psychosocial Intervention; CBT = Cognitive-Behavioral Therapy; STPP =

Short Term Psychoanalytic Psychotherapy.

Prognostic Implications for Depressed Adolescents Who Drop Out of Psychological Treatment During a Randomised Controlled Trial

Sally O'Keeffe, PhD, Peter Martin, PhD, Ian M Goodyer, MD, Raphael Kelvin, MRCPsych, Bernadka Dubicka, MD, IMPACT Consortium, Nick Midgley, PhD

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