

Cost-effectiveness of classroom-based Cognitive Behaviour Therapy in reducing symptoms of depression in adolescents: a trial-based analysis

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Running head: Cost-effectiveness of school-based CBT for preventing depression

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Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that this study was funded by the National Institute of Health Research Health Technology Assessment programme; no relationships with any organisations that might have an interest in the submitted work in the previous 3 years; and no other financial or non-financial interests that may be relevant to the submitted work.

Ethics approval: This study was approved by the University of Bath School for Health Ethics Committee and all participants gave informed consent to have their data collected and analysed.

Sources of funding: This study was funded by the National Institute for Health Research Health Technology Assessment programme (06/37/04). After the initial grant application peer review and selection processes, the funding organisation had no role in: the study's design; the collection, analysis and interpretation of data; the writing of the report; or the decision to submit this or any other articles for publication.

Independence of the researchers from the sponsors/funders: All the researchers and co-authors are independent from the National Institute for Health Research Health Technology Assessment programme.

Access to the data: All the authors had full access to the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and accuracy of the data analysis.

Data sharing: Fuller data tables relating to the data and analyses presented in this paper are published in the NIHR HTA Programme's monograph (Stallard et al 2013). Within the constraints of the study's ethical approvals and anonymisation of participants, in principle we will consider making the individual-level data available to other researchers.

Contributorship statement: PS, AAM, KS, RAra, RA, and GL conceived and designed the study, with RA designing the resource use and health related quality of life data collection. RA processed the cost and health-related quality of life data cleaning and calculations, and worked with OU to develop and implement the statistical analysis of costs and cost-effectiveness. RP managed the trial and with JAT and AM supervised data collection. PS and KS organised the conduct of the study and led the trial teams in the south west and East Midlands. All authors had access to all study data and participated in interpretation of the findings, contributed core ideas and were involved in critically revising the paper for

important intellectual content. All authors read and approved the final manuscript. PS was principal investigator. Rob Anderson will act as guarantor for the paper.

ABSTRACT

Background – A substantial minority of adolescents suffer from depression and it is associated with increased risk of suicide, social and educational impairment, and mental health problems in adulthood. A recently conducted randomised controlled trial in England evaluated the effectiveness of a manualised universally delivered age-appropriate CBT programme in school classrooms. The cost-effectiveness of the programme for preventing low mood and depression for all participants from a health and social care sector perspective needs to be determined .

Methods - A trial-based cost-effectiveness analysis based on a cluster randomised controlled trial comparing classroom-based CBT to usual school provision of Personal Social and Health Education. Per student cost of intervention was estimated from programme records. The study was undertaken in eight mixed sex UK secondary schools, and included 3,357 school children aged 12 to 16 years (in the two trial arms evaluated in the cost-effectiveness analysis). The main outcome measures were individual self-reported data on care costs, Quality Adjusted Life-Years (QALYs, based on the EQ-5D health-related quality of life instrument) and symptoms of depression (Short Mood and Feelings Questionnaire) at baseline, 6 and 12 months.

Results – Although there was lower quality-adjusted life-years over 12 months (-0.05 QALYs per person, 95% confidence interval -0.09 to -0.005, p = 0.03) with CBT, this is a ‘clinically’ negligible difference which was not found in the complete case analyses. There was little evidence of any between-arm differences in SMFQ scores (0.19, 95% CI -0.57 to 0.95, p = 0.62), or costs (£142, 95% CI -£132 to £415, p = 0.31) per person for CBT versus usual school provision.

Conclusions: Our analysis suggests that the universal provision of classroom-based CBT is unlikely to be either more effective or less costly than usual school provision.

trial registration - ISRCTN 19083628

Key words: depression prevention, schools, CBT, cognitive behavioural therapy, cost-effectiveness, adolescents.

Abstract Word Count: 301

Funding: National Institute of Health Research Health Technology Assessment (06/37/04)

INTRODUCTION

Prevalence rates for depression in adolescents suggest that up to 5% may be affected and that it is associated with increased risk of suicide, social and educational impairment and mental health problems in adulthood (Thapar, Collishaw, Pine, & Thapar, 2012). Whilst effective psychological and pharmacological interventions are available, a sizeable proportion of adolescents do not respond to these approaches with relapse rates being high (Dunn & Goodyer, 2006; Goodyer et al., 2007; March et al., 2004). The need to reduce depression at a population level in adolescents has encouraged interest in prevention programmes. A Cochrane review concluded that there was evidence that both universal (provided for all) and targeted (upon those at risk of depression) programmes may prevent depression compared with no intervention (Merry et al., 2011). However, effect sizes are typically small, so before the widespread implementation of depression prevention programmes can be supported, effectiveness and cost-effectiveness need to be assessed under 'real life' conditions using appropriate comparisons/control groups.

This paper presents the cost-effectiveness analysis from an NHS and social care perspective, of a randomised controlled trial (RCT) of a classroom-based Cognitive Behaviour Therapy (CBT) programme, the Resourceful Adolescent Programme (RAP) (Shochet & Ham, 2004). The intervention was universally delivered to young adolescents (aged 12-16 years) in eight UK secondary schools between 2009 and 2010. Further details of the intervention, the design and conduct of the trial, and the effectiveness results for the high-risk adolescents are published elsewhere (Stallard et al., 2010; Stallard & Buck, 2013; Stallard et al., 2012). The trial's effectiveness results showed similar outcomes for high-risk adolescents in all three trial arms (see Box 1, below)(Stallard et al., 2012). However this was a universally provided programme and it is therefore important to investigate the effectiveness of the intervention for all trial participants and to explore data on treatment utilization and quality of life. The aim of this paper is therefore to report the joint analysis of

costs and health-related outcomes for all trial participants, taking into account between-arm differences in selected co-variates, and possible correlation between costs and outcomes. We show results based on changes in our primary mental health outcome e (cost-effectiveness analysis) and changes in quality-adjusted life-years (often called a 'cost-utility analysis'). We also present the first estimation of the per student cost of such programmes, and a detailed breakdown of the health-related service use costs in a large school-based sample of 12-16 year olds..

METHODS

Cost-effectiveness analysis simultaneously compares the costs and effectiveness of at least two alternatives, for example to estimate the additional costs associated with any additional benefits gained by a new intervention. This cost-effectiveness analysis was based on a three-arm parallel cluster randomised controlled trial, but in the analysis presented here we omit the attention control comparator (because inclusion of this 'enhanced PSHE' (Personal Social and Health Education) trial arm was primarily to provide evidence relating to mechanisms of effectiveness). Randomisation was at the level of year group balanced on school, number of students, number of classes and frequency and timetabling of PSHE lessons, with individual participants as the unit of analysis (Stallard et al., 2010). Eligible schools were non-denominational mixed-sex secondary schools in five Local Education Authorities, incorporating urban and rural/semi-rural sites in the East Midlands and South West of England. All adolescents in Years 8-11 (aged 12-16 years) in participating schools were eligible, unless they were not attending school (e.g., long term sickness, or excluded from school) or did not participate in PSHE lessons for religious or other reasons. Interventions were delivered in the academic year September 2009 to July 2010 during PSHE lessons and are described in Box 1.

Box 1. Description of the intervention and comparators in the trial

Classroom-based CBT (The Resourceful Adolescent Programme)

The Resourceful Adolescent Programme (RAP) is a universal depression prevention programme that has been shown to be effective in Australia and New Zealand (Merry, McDowell, Wild, Bir, & Cunliffe, 2004; Shochet & Ham, 2004). The programme was developed to be delivered in schools and provided to whole classes of students. The feasibility and viability of delivering RAP in UK schools has been established (Stallard & Buck 2013).

RAP is based upon the principles of cognitive behaviour therapy (CBT) and develops skills reported to protect against the development of depression such as emotion-regulation capacities, coping mechanisms and thinking styles. RAP consists of nine modules and two booster sessions, each lasting approximately 50-60 minutes. The modules can be flexibly delivered in order to fit within the school timetable. The sessions were led by two trained facilitators working alongside the class teacher. All facilitators had at least an undergraduate university degree in a relevant discipline, appropriate professional backgrounds or experience of working with children or young people. Separate initial training and on-going supervision were provided for the facilitators in the classroom-based CBT and attention control conditions in order to avoid contamination. (NB. Treatment fidelity was assessed by independent observation of a pragmatically stratified 5% sample of classroom-based CBT sessions.)

Usual School Provision

Young people participated in the usual PSHE sessions provided by the school. The sessions were provided solely by the teacher and did not involve any external input from the research team.

Enhanced PSHE (Attention Control)

Not assessed within the cost-effectiveness analysis – see effectiveness results paper for the high risk adolescents and for a fuller description of this condition (Stallard et al., 2012).

The analysis of costs and cost-effectiveness was conducted from the perspective of their impact on health service (National Health Service (NHS) in England) and social care budgets, using prices from the year 2010. It was carried out according to current best practice methods for conducting economic evaluation alongside trials (Glick, 2007; Ramsay et al., 2005), and alongside cluster randomised controlled trials (Diaz-Ordaz, Kenward, & Grieve, 2012; Gomes, 2011).

Outcome measures

Outcomes were collected during class time by self-completed questionnaire administered to students by researchers at baseline, 6 months and 12 months follow up (Stallard et al.,

2010). The outcomes used in the cost-effectiveness analysis were: Quality Adjusted Life-Years (QALYs) from baseline to 12 months, using data from the EQ-5D questionnaire at three time-points, and; symptoms of low mood as determined by the Short Mood and Feelings Questionnaire (SMFQ) (Angold et al., 1995).

The EQ-5D is a simple and well-established 5-question health-related quality of life instrument which covers health impacts on physical mobility, self-care ability, usual activities, pain/discomfort and anxiety/depression (www.euroqol.org). Every pattern of possible EQ-5D responses can be attributed a preference weight between one (= 'full health') and zero (= as bad as being dead), and it is these weights which are used to convert life-years into quality-adjusted life-years (or 'QALYs'). The preference weights for the EQ-5D index scores were from a representative sample survey of the UK general population in 1993 (Kind, Hardman, & Macran, 1999).

The SMFQ assess symptoms of low mood and is a 13-item scale derived from the 33-item Mood and Feelings questionnaire (Angold et al., 1995, Costello & Angold 1988). Each item consists of a simple statement (e.g. 'I didn't enjoy anything at all'), which is rated as being 'true' (scores 2), 'sometimes true' (scores 1) or 'not true' (scores 0) in relation to the past two weeks). The SMFQ correlates well with other measures of depression and has good test-retest reliability, and higher scores are associated with fulfilling diagnostic criteria for clinical depression (Angold et al., 1995,).

This paper examines the cost-effectiveness of a universally delivered school based intervention and so data from all students in participating classes were included.

Service use data

Data on the use of a wide range of health and social care services were collected from the pupils using an adapted and age-appropriate self-completed version of the Client Services Receipt Inventory (CSRI) (Beecham & Knapp, 2001). This self-completed version had been

used and amended in the pilot study (Stallard & Buck, 2013). This cost of service use data from all three time-points (baseline, 6 and 12 months) were included in the cost-effectiveness analysis. Details of the services and resources assessed are summarised in Table 1.

***** TABLE 1 ABOUT HERE *****

The unit costs applied to the different types of health service use, or for visits to see different types of care professionals about anxiety or depression are provided in Table B (in the online Appendix). The two main sources for the unit costs were the Department of Health's National Schedule of Reference Costs (for Primary Care Trusts and NHS Trusts combined) and the Personal Social Services Research Unit's *Unit Costs of Health and Social Care* (hourly costs of patient or client contact for various types of health or social care professional)(Curtis, 2011; Department of Health, 2011).

The reason given for each reported inpatient stay was assessed as being either elective or non-elective and relevant unit costs applied. For the very small minority (<1%) of participants who reported taking medication for anxiety or depression, the information provided on medication names and how long they had been taken was too unreliable to use as a basis for estimating these costs. For example, the type of medicine taken was simply recorded by some as 'don't know' or 'can't remember', or stated 'paracetamol' or other over-the-counter medications or herbal remedies, which would have no cost implications for the NHS. The self-reported medication data were therefore excluded from further analysis.

Costing the interventions

The resource use involved in providing the classroom-based CBT programme was costed using detailed project records of staff time and other expenditure. This included the paid time of facilitators delivering the programme, cost of their training and ongoing supervision and management, travel costs, printing costs of course booklets, and an apportionment of the

cost of recruiting schools. The calculated intervention costs excluded the costs of developing or adapting the new materials (these were treated as ‘sunk costs’ – it is assumed they would not be incurred again) or the estimated proportions of people’s time which are due to the research/trial context of programme delivery. The costs did, however, include a share of the initial training costs of the facilitators (time of trainers and facilitators, room hire and subsistence). Usual provision of PSHE lessons involved no intervention costs.

All costs were calculated as either the amount of resource used multiplied by a unit cost, or as the total amount incurred over the trial period divided by the number of pupils in participating classes, number of sessions delivered, or number of schools, depending on the level at which the cost was incurred. Table A (online supporting materials) shows the key data and costs that were used to calculate the mean intervention cost per student.

Statistical analysis of the cost-effectiveness data

The cleaning and correction of resource use and EQ-5D data, and the calculation of service use costs were conducted in PASW Statistics v18 (www.SPSS.com). The models for analysing incremental cost-effectiveness were fitted using Stata 12 software (www.stata.com). Given the relatively short timeframe of the trial and follow-up, neither costs nor outcomes were discounted to present values (i.e. preferences over the timing of future costs and outcomes would have a negligible impact on the results).

Two cost-effectiveness analyses were conducted, one using the SMFQ score (the primary outcome measure for the effectiveness trial) and another using quality-adjusted life-years (QALYs) based on responses to the EQ-5D questionnaire. The derivation of the per person QALYs from baseline to 12 months involved: calculating the social preference weight (or utility) for all those who completed the EQ-5D at each of the three time points; estimating the ‘area under the curve’ between baseline and 6 months and between 6 months and 12 months, and summing them. QALYs were therefore calculated only for students who had complete EQ-5D data at all three time points.

Incremental costs, incremental effects, and where relevant, incremental cost-effectiveness ratios (ICERs) were estimated, comparing the classroom-based CBT arm to the Usual School Provision arm. The incremental cost per unit decrease in the SMFQ score (since lower scores on the SMFQ indicate better outcome) and the incremental cost per unit QALY increase were estimated. Both unadjusted and adjusted analyses were carried out, adjusting for Year level for all outcomes and additionally for SMFQ score at baseline when analysing the SMFQ outcome. The remaining factors used to balance the randomisation were not adjusted for due to the relatively small number of clusters.

In the complete case analyses, random effects bivariate linear regression models were fitted to model cost and effectiveness (SMFQ or QALY) simultaneously, allowing for correlation within randomised clusters and correlation between cost and effectiveness score within participants (Goldstein, 2003). These models produced estimates of: the mean difference in cost and its standard error; the mean difference in effect and its standard error; and (indirectly via the variance-covariance matrix of the regression coefficients) the correlation between the mean cost difference and the mean effect difference.

Note that because the cost of the intervention must be apportioned across all participants in a given trial arm, both the SMFQ- and QALY-based cost-effectiveness results are based on the whole sample who had valid cost and outcome data i.e. not just those assessed as high risk (SMFQ) at baseline, as in the primary effectiveness analysis(Stallard et al. 2012).

The findings reported here are based on analyses of multiple imputed data, making the assumption that the any missing cost or effect data are missing at random. Imputation and analysis models that explicitly allow for the clustered design were used (Diaz-Ordaz et al., 2012). The following variables were included in the imputation model: cost, SMFQ scores and QALY scores at each of baseline, 6 months and 12 months; trial arm status; and the variables used to balance the randomisation. The data were imputed and analysed using the software REALCOM Impute package (www.bristol.ac.uk/cmm/software/realcom/) in

conjunction with Stata software, version 12 (www.stata.com). The imputed datasets were analysed in Stata using the *mi* commands. Findings from the complete case analyses of non-imputed data indicated essentially the same interpretation as the reported analyses based on imputed data (see Appendix 1).

RESULTS

Of the 5,503 eligible students, 5,030 (91%) consented to participate in the trial, of whom 3,357 (1,753 CBT arm and 1,604 control arm) were allocated to the two trial arms analysed here. Of these, 2,237 had valid cost data, 2,767 had valid SMFQ data at 12 months and 2,087 had valid EQ-5D (QALY) outcome data (i.e., at all three time points). All participants (including those with missing data) were included in the analyses of imputed data.

The classroom-based CBT intervention costs an estimated £41.96 per student, most of which was due to the cost of facilitator time to deliver the sessions (see Table 2). Note that the training costs within these per student costs reflect the relatively high ratio of the number of facilitators to total number of classes delivered (39 facilitators to deliver 787 sessions to 79 classes for classroom-based CBT), which might not be as high if the classroom-based CBT programme were rolled out on a larger scale and for a longer period of time. Table 3 shows the very similar health and social care service usage and care costs for the two trial arms in the six months before, during and after the intervention.

*** TABLE 2 ABOUT HERE ***

*** TABLE 3 ABOUT HERE ***

Table 4 summarises the comparison between the classroom-based CBT and usual school provision arms with respect to cost for the 12-month period of the trial, SMFQ score at 12 months and QALYs (from 0 to 12 months). Incremental analyses which are either unadjusted or adjusted for covariates are shown. Incremental analysis compares the gain or loss in effectiveness with the additional costs, or cost savings, with one intervention compared with another. The point estimates indicate that CBT is more costly

and less effective than usual school provision, with respect to both SMFQ and QALYs, but these differences are both very small and uncertain (with the 95% confidence intervals spanning zero for both costs and SMFQ differences). Although the analysis in Table 4 shows a small negative mean difference in QALYs (-0.05), which is statistically significant in the adjusted analysis ($p= 0.03$), this is the only finding amongst all the adjusted or unadjusted, and imputed dataset or complete case analyses which shows a statistically significant result; the magnitude of this difference is also smaller than most estimates of the 'minimally important difference' for the EQ-5D (Walters & Brazier 2005, Le et al 2013). Thus we conclude that classroom-based CBT is highly unlikely to be cost-effective.

*** TABLE 4 ABOUT HERE ***

DISCUSSION

Despite high levels of fidelity and adherence, the main trial indicated that a universally provided classroom-based CBT depression prevention programmes delivered in schools was not effective for adolescents at high-risk of depression (data reported elsewhere) (Stallard et al., 2012). Taking into account the data on both costs and effects for all trial participants from a health and social care perspective, the cost-effectiveness analysis reported here has provided little evidence that universal classroom-based CBT is likely to be either more effective or associated with lower costs than usual school provision.

While this cost-effectiveness result might seem an obvious implication of the main effectiveness results from the trial, this is not always the case, for the following reasons. First, unlike RCTs of effectiveness, economic evaluations are primarily about estimation rather than hypothesis testing in their analytical approach. Secondly, the sample sizes of RCTs are typically powered on the basis of expected effects on the primary clinical outcome, and not on expected differences in costs. Thirdly, because individual level costs and effectiveness are often correlated, so too are incremental costs and effects, and the direction

and strength of correlation can substantially alter the likelihood that that an intervention may be judged as cost-effective – even in the context of a statistically non-significant effectiveness result for the primary outcome. For these reasons health economists recommend the conduct of a full cost-effectiveness analysis, as we have presented here, even in the context of no statistically significant impact on the primary clinical outcomes (Drummond et al 2005).

This cost-effectiveness analysis is based on the first large-scale pragmatic randomised trial to compare a universal depression focused classroom-based CBT programme with usual school provision on symptoms of low mood/depression in adolescents. The collection of cost data and the cost-effectiveness analyses were carried out according to current best practice methods for conducting economic evaluation alongside randomised trials (Diaz-Ordaz et al., 2012; Glick, 2007; Gomes, 2011; Ramsay et al., 2005). The statistical methods of the cost-effectiveness analysis have accounted for the clustered nature of the data and any correlation between costs and effects. Analysis was based on effectiveness measures of established validity and reliability, and the self-report data were relatively complete. It incorporated a detailed ‘bottom-up’ costing of classroom-based CBT based on accurate records of staffing, resources and other activities involved. We have also adjusted for or omitted those intervention costs (‘protocol-driven’ costs) which would, in all likelihood, not be incurred outside of a research trial context; and those which would not be incurred with the widespread roll-out of such interventions (e.g. adaptation of course materials).

The main study limitations relate to the trial design and conduct include: the CBT programme evaluated was developed for use with children aged 12-15 years of age and the inclusion of 16 year olds could have reduced the effects; the approach of delivering the intervention to all children in order to prevent depression in the minority who are at high risk of depression may have affected the overall potency of the intervention; and participants were not blinded to treatment allocation. There are also some limitations specific to the cost-effectiveness

analysis. The requirement that participants self-report relevant cost and effectiveness data (i.e., EQ-5D responses) inevitably results in some missing data. In accordance with current best practice methods, we have imputed missing cost and effect data for the analysis presented here; but we also (in Appendix 1) show that results based on analysis of complete cases are very similar, and support identical conclusions. Lastly, without linked data collection from health or other support services, it is not possible to assure the validity and reliability of the self-report of service use data from children of these ages. Other research, in adults, suggests that patient self-report agrees closely with service/provider records for hospital use, with recall periods of up to six months, but that for medication and other care products patient recall can be quite incomplete (van den Brink, van den hout, Stigglebout, van de Velde, & Kievit, 2004).

There are currently very few economic evaluations of similar group-CBT programmes for low mood or depression, and only one that is for depression prevention which targets children or adolescents (Lynch et al., 2005). This cost-effectiveness study was of a 15-session group CBT intervention for the 13 to 18 year-old children of depressed parents, in a large health maintenance organisation in the USA; the incremental cost, incremental cost per depression-free day or the incremental cost per QALY were not statistically significantly different from usual care (based on 95% confidence intervals). Overall, it is not possible to judge whether our findings are consistent with those of similar studies because of the lack of trial-based economic evaluations of group-CBT to prevent depression, or of other interventions to prevent low mood and anxiety in children.

We estimated that the per student costs of the CBT programme were approximately £40 per student. With these modest per student programme costs even small mean QALY gains – *if gained with greater certainty* – would be judged as cost-effective by NHS policy makers in England. For example, an 0.005 QALY gain per student for an additional cost of £40 implies an incremental cost-effectiveness ratio of only £8,000 per QALY gained; this is well under

the usual threshold (£20,000 per QALY) regarded by the National Institute of Health and Care Excellence as separating cost-effective from non-cost-effective use of NHS resources. The CBT programme costs would be further reduced if the cost of training each facilitator was spread across more sessions delivered per facilitator. Nevertheless, such speculation is only useful in the context of more certain differences in effectiveness and impact on quality of life than our randomised trial actually found.

In conclusion, we found no evidence to suggest that a universally delivered classroom-based CBT programme designed to prevent symptoms of depression in adolescents was cost-effective over a one year time period. The clear implication for policy makers at this time is therefore that such programmes should not be implemented. Future studies of such programmes should always incorporate and report well designed and properly conducted cost-effectiveness analysis, in order to compare any detected health gains with the opportunity costs and savings of delivering the programme.

Contributors

Paul Stallard, Alan Montgomery, Kapil Sayal, Ricardo Araya, Rob Anderson, Glyn Lewis conceived and designed the study. Rob Anderson and Obi Ukoumunne calculated the individual-level costs and QALYs and conducted the incremental cost-effectiveness analysis. Rhiannon Phillips managed the trial and with John Taylor and Abigail Millings supervised data collection. Paul Stallard and Kapil Sayal organised the conduct of the study and led the trial teams in the South West and East Midlands. Alan Montgomery and Melissa Spears undertook the statistical analysis of effectiveness. All authors have read and approved the final manuscript. Rob Anderson was the health economist investigator on the trial and will act as guarantor for this paper.

Conflicts of Interest

R Anderson, OU, PS, AAM, KS, RP, R Araya, GL, JT, AM & MS declare no conflicts of interest.

Acknowledgements

This study was funded by the National Institute for Health Research Health Technology Assessment (06/37/04). The authors would like to thank the schools and students who participated in this project, the facilitators who helped with intervention delivery and to the East Midlands Hub of the NIHR Mental Health Research Network for their administrative and research support. We are grateful for the advice of Professor Ian Shochet who developed the Resourceful Adolescent Programme. We acknowledge the support and guidance of the Trial Steering Committee and Data Monitoring Ethic Committee and in particular their respective chairs, Professor Laurence Moore and Professor David Gunnell. OU is supported by the Peninsula Collaboration for Leadership in Applied Health Research and Care (CLAHRC), a collaboration between the University of Exeter, University of Plymouth, and National Health Service South West, funded by the National Institute for Health Research. KS is partly funded by CLAHRC Nottinghamshire, Derbyshire, Lincolnshire.

Key Points

A substantial minority of adolescents suffer from depression, yet there are few proven approaches to preventing low mood and depression in this age group.

This study evaluated the cost-effectiveness of a universally provided classroom-based group CBT intervention, based on a high quality cluster-randomised trial in 8 secondary schools in England.

This study yielded no evidence that the intervention was cost-effective over a one-year time period in this school-based sample of 12-16 year olds

Our findings suggest that classroom-based universal CBT interventions should not be routinely implemented, and the effectiveness and cost-effectiveness of similar programmes should be rigorously evaluated

REFERENCES

- Angold, A., Costello, E., Messer, S., Pickles, A., Winder, F., & Silver, D. (1995). Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. . *International Journal of Methods in Psychiatric Research*, 5, 237-249.
- Beecham, J., & Knapp, M. (2001). Costing psychiatric interventions. In G. Thornicroft (Ed.), *Measuring Mental Health Needs*. London: Gaskell.
- Costello E, Angold A. (1988) Scales to assess child and adolescent depression: checklist, screens and nets. *Journal of the American Academy of Child & Adolescent Psychiatry* 27, 726–37.
- Curtis, L. (2011). Unit Costs of Health and Social Care 2010. Canterbury, Kent: Personal Social Services Research Unit.
- Department of Health. (2011). NHS reference costs 2009-2010 [for NHS Trust and PCT combined]. Retrieved 12 January 2012, from Department of Health, England
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_123459
- Diaz-Ordaz, K., Kenward, M., & Grieve, R. (2012). Handling missing values in cost-effectiveness analyses that use data from cluster randomised trials. *RSS Journal Series A, EarlyView Online*.
- Dunn, V., & Goodyer, I. (2006). Longitudinal investigation into childhood- and adolescence-onset depression: psychiatric outcome in early adulthood. *British Journal of Psychiatry*, 188, 216-222.
- Glick, H. A., Doshi, J.A., Sonnad, S.S., Polsky, D. (2007). *Economic Evaluation in Clinical Trials*: Oxford University Press.
- Goldstein, H. (2003). *Multilevel Statistical Models (3rd Edition)*. London: Arnold.
- Gomes, M., Grieve, R., Nixon, R., Edmunds, W.J. (2011). Statistical Methods for Cost-Effectiveness Analyses That Use Data from Cluster Randomized Trials: A Systematic Review and Checklist for Critical Appraisal. *Medical Decision Making*, 12.
- Goodyer, I., Dubicka, B., Wilkinson, P., Kelvin, R., Roberts, C., Byford, S., . . . Harrington, R. (2007). Selective serotonin reuptake inhibitors (SSRIs) and routine specialist care with and without cognitive behaviour therapy in adolescents with major depression: randomised controlled trial. *British Medical Journal*, 335(7611), 142-146A. doi: 10.1136/bmj.39224.494340.55

- Kent L, Vostanis P, Feehan C. (1997) Detection of major and minor depression in children and adolescents: evaluation of the mood and feelings questionnaire. *Journal of Child Psychology & Psychiatry* 38, 565–73.
- Kind, P., Hardman, G., & Macran, S. (1999). UK Population Norms for EQ-5D. *Discussion Paper 172* Retrieved January, 2012, from
<http://www.york.ac.uk/media/che/documents/papers/discussionpapers/CHE%20Discussion%20Paper%20172.pdf>
- Lynch, F. L., Hornbrook, M., Clarke, G., Perrin, N., Polen, M. R., O'Connor, E., & Dickerson, J. (2005). Cost-effectiveness of an intervention to prevent depression in at-risk teens. *Archives of General Psychiatry*, 62, 1241-1248.
- March, J., Silva, S., Petrycki, S., Curry, J., Wells, K., Fairbank, J., . . . Treatment Adolescent Depression, S. (2004). Treatment for adolescents with depression study (TADS) team . Fluoxetine, cognitive-behavioural therapy, and their combination for adolescents with depression; Treatment for adolescents with depression study (TADS) randomized controlled trial. *JAMA*, 292, 807-820.
- Merry, S., McDowell, H., Wild, C. J., Bir, J., & Cunliffe, R. (2004). A randomized placebo-controlled trial of a school-based depression prevention program. *Journal of the American Academy of Child and Adolescent Psychiatry*, 43(5), 538-547.
- Merry, S. N., Hetrick, S. E., Cox, G. R., Brudevold-Iversen, T., Bir, J. J., & McDowell, H. (2011). Psychological and educational interventions for preventing depression in children and adolescents (Review). *Cochrane Database of Systematic Reviews*, (12). Retrieved from <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003380.pub3/pdf> website: doi:10.1002/14651858.CD003380.pub3.
- Le, Q.A., Doctor, J.N., Zoellner, L.A., Feeny,N.C. (2013). Minimally important clinical differences for the EQ-5D and QWB-SA in Post-Traumatic Stress Disorder (PTSD): results from a Doubly Randomized Preference Trial (DRPT) *Health and Quality of Life Outcomes*, 11: 59
- Ramsay, S., Willke, R., Briggs, A., Brown, R., Buxton, M., Chawla, A., . . . Reed, S. (2005). Good research practices for cost-effectiveness analysis alongside clinical trials: The ISPOR RCT-CEA Task Force Report. *Value in Health*, 8(5), 521-520.
- Shochet, I., & Ham, D. (2004). Universal school-based approaches to preventing adolescent depression: past findings and future directions of the Resourceful Adolescent Program. *International Journal of Mental Health Promotion*, 6(3), 17-25.

- Stallard, P. and Buck, R., 2013. Preventing depression and promoting resilience : Feasibility study of a school-based cognitive-behavioural intervention. *The British Journal of Psychiatry*, 202 (Supplement 54), s18-s23.
- Stallard, P., Montgomery, A., Araya, R., Anderson, R., Lewis, G., Sayal, K., . . . Taylor, J. (2010). Protocol for a randomised controlled trial of a school based cognitive behaviour therapy (CBT) intervention to prevent depression in high risk adolescents (PROMISE). *Trials*, 11(114).
- Stallard, P., Phillips, R., Montgomery, A., Anderson, R., Taylor, J., Araya, R., . . . Sayal, K. (2013). A cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of classroom-based Cognitive Behavioural Therapy (CBT) in reducing symptoms of depression in high-risk adolescents. *Health Technology Assessment*. 17 (47).
- Stallard, P., Sayal, K., Phillips, R., Taylor, J., Spears, M., Anderson, R., . . . Montgomery, A. (2012). Classroom based cognitive behaviour therapy in reducing symptoms of depression in high risk adolescents: pragmatic randomised controlled trial *BMJ* (Vol. 345, pp. e6058).
- Thapar A, McGuffin P. (1998) Validity of the shortened Mood and Feelings Questionnaire in a community sample of children and adolescents: a preliminary research note. *Psychiatry Research* 81, 259–68.
- Thapar, A., Collishaw, S., Pine, D., & Thapar, A. (2012). Depression in adolescence. *Lancet*, 379, 1056-1067.
- van den Brink, M., van den hout, W. B., Stigglebout, A. M., van de Velde, C. J. H., & Kievit, J. (2004). Cost measurement in economic evaluations of health care: whom to ask? *Medical Care*, 42(8), 740-746.
- Walters, S.J., Brazier, J.E. (2005). Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D *Quality of Life Research*, 14(6), 1523-1532.

Table 1: Details of service and resource use recorded

Type of service use	Details recorded	Notes or limits
Overnight hospital stays	Reason, and no. of days in hospital	For up to 3 stays
Accident and Emergency visits	No. of visits, reasons for visits	Up to 3 reasons
Hospital outpatient appointments	No. of visits, reasons for visits	Up to 3 reasons
Visits to the GP	No. of visits, no. of visits for worry anxiety or unhappiness	
"Seen anyone else for psychological problems (such as worry, anxiety or unhappiness)"	No. of times seen (for each of: Nurse at a GP practice, School nurse, Counsellor, Child Mental Health Service, Child psychologist, Social worker, or "Someone else, please say who")	
Taking medication (for anxiety or depression)	Name of medicine, how long taken	Up to 2 medicines

Table 2: Per student cost (£) of delivering classroom-based CBT

Type of cost	classroom-based CBT
Cost of training and managing facilitators	9.84
Cost of facilitator time delivering the intervention	29.37
Intervention booklet (printing) costs per child	1.41
Travel costs of facilitators	1.23
Allocation of school recruitment costs	0.12
Cost per child receiving intervention	41.96

Table 3. Number of students and cost of using health care over the study period.

(a) baseline (i.e. pre-intervention, from -6 to 0 months):

Type of care use	CBT		Usual PSHE	
	No. (%)	Mean cost £ (SE)	No. (%)	Mean cost £ (SE)
Inpatient stays	45 (4.5)	72.09 (16.4)	33 (3.1)	50.48 (14.8)
A&E attendances	167 (16.6)	26.93 (2.6)	169 (15.8)	25.19 (2.2)
Outpatient visits	226 (22.5)	46.25 (3.9)	234 (21.9)	37.21 (3.4)
TOTAL hospital use/costs	328 (32.6)	145.27 (18.8)	335 (31.4)	112.89 (16.6)
GP (for any reason)	448 (44.5)	28.76 (1.7)	440 (41.2)	25.49 (1.6)
GP (for psychological problems)	33 (3.3)	1.94 (0.4)	29 (2.7)	1.41 (0.3)
GP Nurse	26 (2.6)	.51 (0.1)	12 (1.1)	.17 (0.1)
School Nurse	30 (3.0)	.76 (0.2)	18 (1.7)	.97 (0.4)
Counsellor	14 (1.4)	2.80 (1.0)	7 (0.7)	1.07 (0.5)
CMHS	6 (0.6)	.81 (0.4)	5 (0.5)	.81 (0.4)
Child Psychologist	7 (0.7)	3.06 (1.7)	2 (0.2)	1.14 (1.0)
Social Worker	4 (0.4)	1.63 (0.9)	6 (0.6)	.70 (0.3)
Other professional	64 (6.4)	9.58 (2.5)	43 (4.0)	4.86 (1.5)
TOTAL all service use/costs	607 (60.3)	183.61 (19.6)	615 (57.6)	143.24 (17.0)

(b) from 0 to 6 months:

Type of care use	CBT		Usual PSHE	
	No. (%)	Mean cost £ (SE)	No. (%)	Mean cost £ (SE)
Inpatient stays	36 (3.6)	43.62 (9.1)	27 (2.5)	52.66 (16.3)
A&E attendances	158 (15.7)	22.93 (2.1)	144 (13.5)	21.43 (2.2)

Outpatient visits	212 (21.1)	47.93 (4.8)	227 (21.3)	39.80 (3.6)
TOTAL hospital use/costs	309 (30.7)	114.48 (12.5)	311 (29.1)	113.89 (18.0)
GP (for any reason)	404 (40.2)	26.24 (1.9)	445 (41.7)	25.70 (1.4)
GP (for psychological problems)	35 (3.5)	1.92 (0.4)	27 (2.5)	1.78 (0.5)
GP Nurse	21 (2.1)	.46 (0.1)	11 (1.0)	.25 (0.1)
School Nurse	15 (1.5)	.39 (0.1)	5 (0.5)	.24 (0.1)
Counsellor	17 (1.7)	4.37 (1.5)	10 (0.9)	2.60 (1.2)
CMHS	5 (0.5)	1.24 (0.8)	4 (0.4)	.45 (0.2)
Child Psychologist	4 (0.4)	2.62 (1.5)	1 (0.1)	.08 (0.1)
Social Worker	4 (0.4)	1.53 (1.1)	3 (0.3)	.35 (0.2)
Other professional	51 (5.1)	11.50 (3.6)	27 (2.5)	4.01 (1.3)
TOTAL all service use/costs	579 (57.6)	152.22 (13.6)	608 (57.0)	143.60 (18.2)

(c) from 6 to 12 months:

Type of care use	CBT		Usual PSHE	
	No. (%)	Mean cost £ (SE)	No. (%)	Mean cost £ (SE)
Inpatient stays	30 (3.0)	59.71 (19.8)	20 (1.9)	21.78 (6.9)
A&E attendances	145 (14.4)	21.30 (2.2)	126 (11.8)	16.12 (1.7)
Outpatient visits	179 (17.8)	36.41 (3.5)	198 (18.6)	33.68 (3.1)
TOTAL hospital use/costs	275 (27.3)	117.42 (21.8)	273 (25.6)	71.58 (8.5)
GP (for any reason)	368 (36.6)	22.30 (1.5)	427 (40.0)	21.89 (1.1)
GP (for psychological problems)	36 (3.6)	2.35 (0.5)	17 (1.6)	.97 (0.3)
GP Nurse	28 (2.8)	.46 (0.1)	19 (1.8)	.40 (0.1)
School Nurse	14 (1.4)	.65 (0.3)	18 (1.7)	.43 (0.1)
Counsellor	21 (2.1)	4.42 (1.2)	14 (1.3)	2.43 (0.8)
CMHS	10 (1.0)	.72 (0.3)	2 (0.2)	.22 (0.2)

Child Psychologist	2 (0.2)	.40 (0.3)	3 (0.3)	1.21 (0.8)
Social Worker	4 (0.4)	.26 (0.1)	4 (0.4)	.20 (0.1)
Other professional	56 (5.6)	8.94 (2.5)	39 (3.7)	4.91 (1.4)
TOTAL all service use/costs	529 (52.6)	148.66 (22.3)	585 (54.8)	98.38 (8.8)

Percentages are of all those who adequately completed the service and resource use questionnaire for that period.

A&E = Accident and Emergency. GP = General Practitioner. CMHS = Community Mental Health Service. SE = Standard Error of the mean.

Table 4: Incremental per student effectiveness and costs of classroom-based CBT versus usual school provision (control)

Outcome	CBT	Control	unadjusted	adjusted		
			mean (SD)*	mean (SD)*	mean difference	mean difference (95% CI)
Cost (in £)	553 (1392)	406 (1240)	167		142 (-132 to 415)	0.31
SMFQ score	3.9 (5.4)	3.2 (4.5)	0.48		0.19 (-0.57 to 0.95)	0.62
QALYs	0.90 (0.12)	0.91 (0.12)	-0.06		-0.05 (-0.09 to -0.005)	0.03

* Mean and standard deviations (SD) calculated based on non-missing participants only; between arm comparisons based on analysis of imputed data.

Table A and B below to be made available as an online Appendix

Table A Costs and other key data for calculating the per student intervention costs

Type of cost or other resource relevant data	Classroom-based- CBT
Hours of coordinator time to organise staff	150
Total no. of classes receiving the intervention	79
Total no. of students in the programme*	2,030
Mean no. of students per class (all on roll)	25.7
Total no. of sessions delivered	787
Mean no. of sessions received per class	9.96
Total no. of facilitators who delivered sessions	39
No. of sessions delivered per school visit (for travel costs)	3
Total salary cost of those providing the intervention	£59,621
Total cost of training facilitators	£18,418
Cost of staff time recruiting each school to the programme	£60
Cost of travel for recruiting each school to the programme	£20

*NB: This differs from the numbers in the trial arms because the intervention costs must be shared amongst all who received the intervention, not just those who consented to involvement in the study and also completed the assessment booklets.

Table B. Unit costs applied for each type of service use (in 2010 £)

Q No.	Resource type and unit	Unit cost (£)	Source
Q6-11	Inpatient stays – elective	781 per day	NSRC2009-10 See note c
Q6-11	Inpatient stays – non-elective short-stay (1 day/night)	520 per day	NSRC2009-10 See note c
Q6-11	Inpatient stays – non-elective long-stay (>1 day/night)	386 per day	NSRC2009-10 See note c
Q13-16	A & E attendances	103	NSRC2009-10 A&E Services not leading to Admitted (Sheet: TPCTAandEMSNA)
Q18-21	Hospital outpatient clinics	99	NSRC2009-10 face to face outpatient appointments (weighted average, consultant and non-consultant-led, first attendance and follow-ups)
Q23 & 24	Visit to GP	32	UC2010 Section 2.8 (11.7 minute consultation) ^a
Q25a	GP practice nurse consultation	10	UC2010 Section 10.6 (Nurse GP Practice, per consultation) ^a
Q25b	School nurse time (per hour)	64	UC2010 (Community Nurse, per hour with patient, £16 per 15 minute appointment) ^a
Q25c	Counsellor (per hour) ^b	44	UC2010 Section 2.14 (Counselling services in primary medical care, per hour with patient or per contact hour) ^a
Q25d	Child Mental Health Service (per hour) ^b	48	UC2010 (Mental Health Nurse, per hour with patient) ^a
Q25e	Child psychologist (per hour) ^b	81	UC2010 Section 9.5 (Clinical Psychologist, per hour with patient) ^a
Q25f	Social worker (per hour) ^b	53	UC2010 Section 11.3 (Social worker (children), per hour with client) ^a

^a Including direct care staff costs, but excluding qualification/training costs.

^b Appointments assumed to last an average of one hour with these practitioners, except for school nurses (15 minutes)

^c After deleting HRG codes and costs for inpatient stay reasons which are either (i) extremely unlikely to be applicable to children aged 13-14 years, or (ii) which are specific codes for those aged 19 years or older.

Abbreviations: NSRC = National Schedule of Reference Costs for PCTs and NHS Trusts combined (20); UC2010 = Unit Costs of Health and Social Care, 2010