PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cost-effectiveness of a community-delivered multi-component intervention compared with enhanced standard care of obese adolescents: cost-utility analysis alongside a randomised controlled trial (the HELP Trial)
AUTHORS	Panca, Monica; Christie, Deborah; Cole, Tim; Costa, Silvia; Gregson, John; Holt, Rebecca; Hudson, Lee; Kessel, Anthony; Kinra, Sanjay; Mathiot, Anne; Nazareth, Irwin; Wataranan, Jay; Wong, Ian; Viner, Russell; Morris, Stephen

VERSION 1 – REVIEW

REVIEWER	Thomas J. Hoerger RTI International, USA
REVIEW RETURNED	23-Aug-2017

GENERAL COMMENTS	This paper examines the cost-effectiveness of the Healthy Eating Lifestyle Programme (HELP) compared to enhanced standard care for obese adolescents. The paper found that the intervention had significantly higher costs but no evidence of higher quality of life; therefore, it concluded that the intervention was unlikely to be cost-effective. The conclusion about cost-effectiveness was hardly surprising, once the results of the clinical trial of the intervention was completed. In the clinical trial, the intervention had no effect on its primary outcome, BMI at 6 months, nor did it have significant effects on any of the clinical and psychological secondary outcomes. Thus, significant improvements in quality of life were unlikely. Because the intervention was clearly expensive, and average medical costs for adolescent individuals (even those who are obese) are generally low, incremental net costs were very likely to be high and significant. Therefore, in this case, the formal cost-effectiveness analysis does not add much new information beyond what one get from a back-of-the-envelope pronouncement (the intervention doesn't have an effect on outcomes and it costs money, so it is very unlikely to be cost-effective). Nevertheless, the authors should probably get some credit for going ahead with their planned economic evaluation. The paper quantifies the large costs of the 12-visit intervention, shows that there were not significant medical costs in the year after the intervention began, and confirmed that there were not significant effects on quality of life. The paper applied state-of-the art cost estimation, using a generalized linear model with gamma family and log link (almost overkill, given that there was randomization and a small sample size).

	It used multiple imputation to adjust for a relatively large percentage of missing cost and QALY variables; they also provided results based on individuals with complete information, which was helpful for showing that the imputations were unlikely to change the study's conclusions. The paper presents results point estimates and confidence intervals for incremental costs and incremental QALYs. The paper's cost-effectiveness conclusion is based on the intervention's significant increase in cost and its insignificant effect on QALYs. One small criticism of this approach is that the paper does not formally calculate an incremental cost-effectiveness ratio or estimate the probability that the intervention is cost-effective giving varying willingness-to-pay values for QALYs. In general, you can have interventions that have a higher than 50% probability of being cost-effective, even if they have an insignificant effect on incremental QALYs. However, this is unlikely to be the case for this intervention, given the high incremental costs and the wide confidence interval for incremental QALYs. Nonetheless, because the authors have done all the work already, it would be easy to calculate the incremental cost-effectiveness ratio and show the cost-effectiveness acceptability curve. Minor Points 1. It might be useful to explicitly clarify that the intervention was provided during 1-on-1 meetings between a provider and the adolescent and parent(s). This made the intervention relatively resource-intensive. Possibly, the costs could be reduced if the intervention was provided in a group setting, though it is not clear that the motivational interviewing could be provided in such a setting. 2. Intervention costs might also be higher because 21 providers were trained to meet with 87 participants. In a real-world setting, it would be unreasonable for a provider to have an average caseload of 4 patients. This would not affect the in-person and travel cost of each visit, but it would lower the average training cost. 3. The section on resource use for the intervention (or Table 2) might show labor costs per hour for providers. Table 1's presentation on medical care use does a nice job of showing both unit costs and resource use. 4. For unit costs (top of p. 8) it might be more complete to show which costs came from published sources, and which came from local sources, and what those local sources were.

REVIEWER	Julie Ratcliffe University of South Australia, Australia
REVIEW RETURNED	29-Sep-2017

GENERAL COMMENTS	Thank you for the opportunity to review this interesting paper on this important topic. This is a clear and well written paper and reflects a soundly conduced economic evaluation conducted alongside an RCT of a community delivered intervention for obese adolescents. I have a few minor comments

	1. We are informed in the methods section of the paper that resource use data was collected retrospectively via trial questionnaires sent to participants at baseline, 6 and 12 months. I took from this statement that participant recollection of resource use items was undertaken as the main mechanism for establishing health care utilisation costs. However this perspective conflicts with the statement made in the discussion section that 'the use of participant level data allowed a comprehensive and accurate assessment of all healthcare costs that was more reliable and less biased than that of self-reported data'. Can the authors please clarify? 2. In relation to this issue if participant recall was utilised without any triangulation of this data to check accuracy e.g. in relation to frequency and length of hospitalisations then the possibility of recall bias should be acknowledged as a limitation. 3. It may also be a stretch to indicate that participant level data was utilised at every stage as it appears that the intervention was costed using a uniform assessment of the time spent by providers in delivering the intervention also of travel time spent etc? Whilst I understand that this is a pragmatic and acceptable approach to costing the intervention it is not individualised as we would expect to see some variability at an individual level here -although I know it is unlikely to affect the overall findings this point still needs acknowledging for clarity. 4. If word limits allow in my view it would add to the paper if the authors can offer any additional insights from their own experience of being involved in this trial and from participants feedback as to why the intervention as delivered was not cost-effective? Could e.g. greater involvement and integration of obese adolescent and families in the co-design and delivery of targeted weight loss interventions prove more cost effective? If not, what different approaches to this problem could potentially be adopted with greater levels of success?

VERSION 1 – AUTHOR RESPONSE

Response to Reviewer 1

1. It might be useful to explicitly clarify that the intervention was provided during 1-on-1 meetings between a provider and the adolescent and parent(s). This made the intervention relatively resource-intensive. Possibly, the costs could be reduced if the intervention was provided in a group setting, though it is not clear that the motivational interviewing could be provided in such a setting.
• The text was amended and reviewer's recommendation included.

2. Intervention costs might also be higher because 21 providers were trained to meet with 87 participants. In a real-world setting, it would be unreasonable for a provider to have an average caseload of 4 patients. This would not affect the in-person and travel cost of each visit, but it would lower the average training cost.
• This is due to high staff turnover during the study period.
• The text was amended and the issue was addressed in the Limitation section.

3. The section on resource use for the intervention (or Table 2) might show labor costs per hour for providers. Table 1's presentation on medical care use does a nice job of showing both unit costs and resource use.
• A table with the labor cost was created and the text was amended.

4. For unit costs (top of p. 8) it might be more complete to show which costs came from published sources, and which came from local sources, and what those local sources were.
• Resource use were costed using the published sources and are included in Table 1 for healthcare professionals contacts outside the study team.
• Local costs refer to payments made for staff, room rentals and materials and they were covered by the study funds.

* One small criticism of this approach is that the paper does not formally calculate an incremental cost-effectiveness ratio or estimate the probability that the intervention is cost-effective giving varying willingness-to-pay values for QALYs
• Text amended with calculated ICER and CEAC presented.

Response to Reviewer 2

1. We are informed in the methods section of the paper that resource use data was collected retrospectively via trial questionnaires sent to participants at baseline, 6 and 12 months. I took from this statement that participant recollection of resource use items was undertaken as the main mechanism for establishing health care utilisation costs. However this perspective conflicts with the statement made in the discussion section that 'the use of participant level data allowed a comprehensive and accurate assessment of all healthcare costs that was more reliable and less biased than that of self-reported data'. Can the authors please clarify?
• Wrong statement; has been deleted.

2. In relation to this issue if participant recall was utilised without any triangulation of this data to check accuracy e.g. in relation to frequency and length of hospitalisations then the possibility of recall bias should be acknowledged as a limitation.
• The text was amended and the issue addressed in the Discussion section.

3. It may also be a stretch to indicate that participant level data was utilised at every stage as it appears that the intervention was costed using a uniform assessment of the time spent by providers in delivering the intervention also of travel time spent etc? Whilst I understand that this is a pragmatic and acceptable approach to costing the intervention it is not individualised as we would expect to see some variability at an individual level here -although I know it is unlikely to affect the overall findings this point still needs acknowledging for clarity.
• The text was amended and reviewer's recommendation addressed.

4. If word limits allow in my view it would add to the paper if the authors can offer any additional insights from their own experience of being involved in this trial and from participants feedback as to why the intervention as delivered was not cost-effective? Could e.g. greater involvement and integration of obese adolescent and families in the co-design and delivery of targeted weight loss interventions prove more cost effective?
If not, what different approaches to this problem could potentially be adopted with greater levels of success?
• The text was amended.

Response to Editor

- Please revise the 'Strengths and Limitations' section on page 4. Many of the points are a summary of the study and its findings rather than specific strengths or limitations of the study. As a reminder, this section should contain up to five short bullet points, no longer than one sentence each, that relate specifically to the methods of the study reported (see: http://bmjopen.bmj.com/site/about/guidelines.xhtml#articletypes).
• 'Strengths and Limitations' section changed.

- The introduction section is very brief. Can this section be expanded to provide a more extensive overview of the background literature on this topic and the rationale for carrying out the study?
• The ‘Introduction’ section was expanded.

- Please clarify why some items in the CHEERS checklist have not been completed. Are these items not applicable to your study?
• Empty spaces suggest that the statements in CHEERS checklist are not applicable for our study.
• New CHEERS checklist created due to changes in main text

VERSION 2 – REVIEW

REVIEWER	Thomas Hoerger RTI International USA
REVIEW RETURNED	28-Nov-2017

GENERAL COMMENTS	The authors have been responsive in addressing my comments. I now have a couple of minor comments and one concern. The Concern. The revised Results section states "The incremental cost-effectiveness ratio (ICER) of HELP intervention versus enhanced standard care was £6,155 (95%CI -£5,318 to £17,323) at a maximum willingness-to-pay for a QALY of £20,000 and £7,578 (95%CI -£6,741 to £28,746) at a maximum willingness-to pay for a QALY of £30,000." It isn't clear whether this is really an ICER or a net benefits ratio. If it were an ICER, the units would be pounds/QALY, and the ratio would be calculated independently of the maximum willingness-to-pay per QALY. If it were a net benefits estimate (= incremental QALYs * willingness-to-pay - incremental costs), the units would be in pounds and we would probably expect the value to be negative. It's possible that the calculations are being messed up because some of the incremental QALYs are (a) negative and/or (b) sometimes very close to zero. Both factors can mess up ratios. Minor comments 1. the abstract can be modified to say that ICERs were calculated, and these showed that the intervention really was not cost-effective. Currently, it just says that the intervention is unlikely to be cost-effective. 2. P.19. A paragraph begins "In our study, one possible explanation..." but the sentence goes on to offer several possible explanations. Finally, on P.9, change "pblished" to "published".

VERSION 2 – AUTHOR RESPONSE

Reviewer

Thank you for your comments and valuable suggestions.

1. The Concern. The revised Results section states "The incremental cost-effectiveness ratio (ICER) of HELP intervention versus enhanced standard care was £6,155 (95%CI -£5,318 to £17,323) at a maximum willingness-to-pay for a QALY of £20,000 and £7,578 (95%CI -£6,741 to £28,746) at a maximum willingness-to pay for a QALY of £30,000." It isn't clear whether this is really an ICER or a net benefits ratio. If it were an ICER, the units would be pounds/QALY, and the ratio would be calculated independently of the maximum willingness-to-pay per QALY. If it were a net benefits estimate (= incremental QALYs * willingness-to-pay - incremental costs), the units would be in pounds and we would probably expect the value to be negative. It's possible that the calculations are being messed up because some of the incremental QALYs are (a) negative and/or (b) sometimes very close to zero. Both factors can mess up ratios.
• We present the results as reviewer suggested and also amended the Abstract

Minor comments
2. the abstract can be modified to say that ICERs were calculated, and these showed that the intervention really was not cost-effective. Currently, it just says that the intervention is unlikely to be cost-effective.
• Reviewer's suggestion addressed in the Abstract

3. P.19. A paragraph begins "In our study, one possible explanation..." but the sentence goes on to offer several possible explanations.
• Changed the sentence to eliminate confusion.

4. Finally, on P.9, change "pblished" to "published".
• Corrected the error.

Editor
• I have changed the name of one of the co-authors (Lee Hudson changed in Lee D Hudson)

VERSION 3 – REVIEW

REVIEWER	Thomas Hoerger RTI International USA
REVIEW RETURNED	02-Jan-2018

GENERAL COMMENTS	The authors have addressed my comments on the previous version.