Reviewer's report

Title: Cost-effectiveness analysis of supported self-management compared with treatment as usual in CFS/ME patients in primary care.

Version: 1 Date: 11 September 2012

Reviewer: Andrew Stoddart

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Main comments:

I have assessed the Health Economic aspects of the paper. The paper is generally well written and the interpretation of the results seem generally reasonable. It is difficult to comment on the adequacy of the methodology as some elements could use clarification. However I expect that in most cases once these have been made clearer the techniques applied will be revealed to have been suitable. I hope my comments are found to be useful.

Discretionary Revisions

1. Labelling of Usual Care on Graphs does not match the term treatment as usual (TAU) in text. While it is obvious that usual care and treatment as usual are the same thing (and it is unlikely this would confuse a reader) the paper would benefit from consistency.

2. The reader is offered very short descriptions of the interventions being assessed which do not include specific details of the interventions' key cost elements, instead they are referred to the clinical paper. While a full description is clearly unnecessary given that it has been previously published, the brief addition of specific details regarding the number of and length of visits in each intervention would aid the readers understanding of how the intervention costs are constituted without needing to look elsewhere.

3. Table 2 is cumbersome and difficult to read due to large number of boxes, while it provides an excellent source of information, consider formatting the table more clearly. Perhaps even just putting brackets around SDs to differentiate from the means would help.

Minor Essential Revisions

1 Several items on Table 1 are not referenced to a source. While these are likely to be the NHS Reference costs 2007/8, this is not technically specified. Items include: Cost per elective bed day, Cadiac Intensive Care Unit, Outpatient, Daycase procedure, A&E and phlebotomy. Additionally Neither the PSSRU unit costs or the Reference costs 2007/8 appear in the references for the paper despite being referenced as sources in Table 1.
2 The “Cost GBP” label on Fig 1 is unclear/backwards (ie reads up rather than down and letters partially merge making it difficult to read).

Major Compulsory Revisions

1 In general the methodology around the economic impact of CFE/ME on the patient and family is not specified clearly with considerable omissions.

a) The data collection methodology, though presumably recorded by patient recall like the NHS costs have been, is not stated. The paper only states that “data was collected” though in the discussion a questionnaire is mentioned.

b) Any price weights applied these items are not specified. These could easily be added to the bottom of Table 1. How lost Income has been calculated in particular is unclear. What theoretical basis was used (presumably a human capital approach) and did this include absenteeism as well as presenteeism? How were these measured and what wage rate was used? Or were patients perhaps asked directly about the cost itself?

c) Similarly the discussion around testing non-NHS costs refers to a significant difference in medians of lost leisure time but no units of measurement or quantities lost are stated. The results in Table 2 include lost earnings which may incorporate leisure time if leisure has been priced at the same rate of lost work but if so this does not disentangle the leisure time specifically.

While I expect that standard/accepted techniques will have been applied here, and I realise that increasing detail too much could dominate the text, there is presently insufficient information given in the paper to allow the analysis approach used to be assessed. Also any limitations of any techniques used (such as a human capital approach) are not discussed.

2 Cost data for weeks 20 – 44 were not recorded. To compensate for this the authors have imputed costs for this period based on trends in the observed periods. The fact that this happened is not explained in the methods section but rather in the results. The methods sections ought really to specify the time points/periods at which data was collected, that the mid-period was imputed and ideally how this was done. Any assumptions made in this imputation are not specified. This time period unfortunately directly follows the intervention period and it is during this time (judging by the EQ-5D and main clinical results) it is believed that the benefits of the PR intervention diminish. However the trajectory of this deterioration is presumably unknown. Similarly with EQ-5D having only been measured at weeks 0, 20 and 70, QALYs estimated from the EQ-5D results has an implicit assumption of a straight line depreciation between weeks 20 and 70 (see fig 2). While this may be a reasonable approximation since the results appear to converge at week 70 it may also be impossible to tell. Consideration over how assumptions used in imputing costs for this time period or applying a straight line to EQ-5D results between weeks 20 and 70 are not discussed. Given the small absolute magnitudes of the effect sizes it is possible that differences in this period from the imputed values or peaks/troughs in EQ-5D scores could
have an effect on the results. That said the absence of evidence of long term benefit of PR over usual care (TAU) may limit the appeal of PR even if a short lived QALY gain were reported and it would be reasonable to consider such a point against this limitation if it is discussed.

3 A minor revision which is related to the above issue (and I apologise if this seems petty), it is technically unclear what has been done for the complete case sensitivity analysis for costs during the unrecorded period weeks 20 to 44 (which reports not to have used imputation). This is due to the unfortunate need to use the word “impute” for both filling in the missing time period and filling in missing follow up data. While I expect that costs at weeks 20 to 44 have been imputed for all patients but only the results from patients with no missing week 20 or 70 questionnaires have been included in the complete case analysis, Table 4’s reference to the complete case analysis as being “without imputation” may be misinterpreted by some readers. The paper would benefit from clarifying this point.

4 The authors use a base year of 2008/09 however many of their price weights in Table 1 reference PSSRU 2010 (which uses a base year of 2009/10) and do not claim to have made any inflation adjustment. As far as I can see they may have missreferenced the source or simply made a small typographical error on the table both of which could be easily amended. But there is a risk that they may have used different PSSRU reports for different variables cases and not always inflated/deflated to the 2008/9 base year.

To give two quick examples:

a) GP home visits are priced at £117 per visit and referenced to PSSRU 2010. The figure in the 2010 edition of PSSRU is £120 (page 167) where as the figure in the 2009 PSSRU is infact £117 (page 121). Several other items referenced to PSSRU 2010 appear to also be the 2009 edition (District Nurse, practice nurse, Nurse specialist and physiotherapist at least) and if so can easily be fixed by correcting the source referenced.

b) General Practitioner (presumably surgery) visits are priced at £36 per visit, which is the PSSRU 2010 price (page 167) rather than £35 in PSSRU 2009 (page 121). It is likely this may simply be a typographical error on the value on the table but if not then they have used the wrong base year on this item. Admittedly a £1 difference on a single item shouldn’t change the results a great deal but it may be indicative that other items have not been adjusted to the correct base year. Particularly in light of the absence of quoted sources for some items (see above).

Before the validity of the price weights can be assessed meaningfully the table needs to be checked for errors and amended appropriately with each item checked to ensure the correct base year has been used.

**Level of interest:** An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests