Reviewer's report

Title: Cost-effectiveness of family psychoeducation to prevent relapse in major depression: Results from a randomized controlled trial

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Reviewer: Nicholas Breitborde

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Major Compulsory Revisions

1) The mean age of participants in this study was 59.2 for the intervention group and 60.9 for the control group. Do the authors feel that the results would be consistent for younger individuals with depression?

2) The authors note that costs were calculated by summing “NHI bills for the duration of the study.” They also note that in Japan, 70% of medical services are covered by NHI and 30% are paid for by patients themselves. Based on this information, I am unclear if the costs reported in the manuscript refer to the 70% covered by NHI or the total cost (i.e., the 70% covered by NHI and the 30% covered by patients directly). If it is the former, what is the rationale for not including the 30% paid for by patients directly in the cost-effectiveness analysis?

3) In other studies which have examined depression free days (DFDs), this variable was defined as the number of days for which the subjects was below a symptomatic threshold (e.g., Hamilton Depression Scale <7) for the entire follow-up period (e.g., Lave et al., 1998, McCrone et al., 2004). Conversely, in the current study, DFDs was defined as the number of days until a relapse of depressive symptoms occurred. As such, the authors' definition appears to be more consistent with the construct of “time to relapse” rather than DFDs. In fact, in their previous paper (Shimazu et al., 2011 Brit J Psychiatry), the authors appear to use this same operational definition to define “time to relapse. As these two constructs (i.e., DFDs and time to relapse) are not the same, what is the authors' rationale for using this definition of DFDs?

4) The authors calculated the cost-effectiveness acceptability curves using three costing scenarios (i.e., ¥0, ¥5,000, and ¥10,000). Why were these particular values selected? Do they have any practical significance?

5) In the subsection “Cost outcomes,” the authors report that there was not a statistically significant difference between the intervention and control group when family psychoeducation was priced at ¥0. Later, in the subsection “Cost-effectiveness” they state that the family psychoeducation was “superior to the control group both in terms of effectiveness and the cost when family psychoeducation was priced at ¥0.” This seems like a very strong conclusion given that there was no statistically significant difference in cost between the intervention and control group. Although the authors do note later that the
superiority was not statistically significant for cost, the earlier statement with regard to superiority still appears to be inaccurate.

6) In the Discussion section, the authors state that “one quality-adjusted life year (QALY) is often valued at ¥5,000,000 to ¥7,000,000” and cite a paper by McCrone et al as evidence for this point. Can the authors clarify how these values were determined from the information presented in that paper by McCrone and colleagues? Similarly, the authors report that “one fully depressed year is valued at 0.6 to 0.7 QALY” and reference a paper by Lave et al as evidence for this point. Can the authors clarify how these values were calculated based on the information presented in paper by Lave and colleagues? Finally, based on these data, the authors conclude that value of a depression free day is ¥4,100 to ¥7,700 greater than the value of a depressed day. Again, can the authors clarify how these values were calculated?

7) In the conclusion, the authors raise the possibility that the intervention may need to be changed if utilized outside of Japan. What changes would be needed and why?

Minor Essential Revisions

1) Although the follow-up period for this study is less than one year, I wonder if discounting of the costs is warranted. For example, current guidelines for cost-effectiveness analysis suggest that costs be discounted at a rate of 3% per year to account for time preference (e.g., Gold et al., 1996. Cost-Effectiveness in Health and Medicine).

Discretionary Revisions

1) In the introduction, the authors state that family psychoeducation has proven cost-effectiveness in schizophrenia. Although this may be true, I wonder if citing a single study (Mihalopoulos et al., 2004) is sufficient evidence for this point. As a comparison, the authors cite a Cochrane Review paper by Pharoah and colleagues which reviewed multiple studies in support of the conclusion that family psychoeducation is clinically effective for schizophrenia.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.