Reviewer's report

Title: Quality of life is predictive of relapse in schizophrenia

Version: 1 Date: 3 April 2012

Reviewer: Pratap Sharan

Reviewer's report:

Relapse is a major negative outcome of schizophrenia and delineating predictors (in addition to noncompliance with medication) would be useful in determining intervention strategies to prevent its occurrence. This prospective study addresses the issue of predicting relapse of schizophrenia in a large sample of subjects from 3 countries.

There are, however, a few limitations that the authors should either discuss or address.

Major compulsory issues to be addressed

1. The authors should mention why they did not consider the following parameters that have been assessed in the EuroSC for the analysis (variables related to these parameters [mentioned in brackets] have been reported to predict relapse in schizophrenia): employment [employment], GARF [partnership], SOFAS [functional status], Calgary Depression Scale for Schizophrenia (depression), and number of previous hospitalizations? Also, why did they not use the EuroQOL EQ-5D as another QOL predictor of relapse?

2. How was objective compliance to treatment assessed? If it was not assessed specifically, in how many patients were the non-compliance items of ROMI (applied to patients who have not taken their medication for at least one week for any part of the past month) applied. A re-analysis of the data with the inclusion of objective compliance (rather than attitude towards compliance measured by ROMI) may change the results of the multivariate analysis.

3. The limitations of SF-36 as a measure of QOL (vs. overall health status) and particularly for schizophrenia (Papaioannou et al. How valid and responsive are general health status measures such as EQ-5D and SF-36 in schizophrenia? A systematic review. Value health 2011; 14: 907-920) should be discussed. Specifically, general health status measures may overlap with depression in schizophrenia, hence controlling for it (Calgary Depression Scale of Schizophrenia) may have charged the results of the multivariate analysis.

4. During analysis (Cox proportional hazards models), how were the issues of multiple relapses, attrition (which could be considered an alternative measure of relapse) and constancy of hazards ratio over time addressed?

Minor essential issues
1 The sample from United Kingdom differs on certain social parameters (Babington et al, 2005) that may have a bearing on quality of life assessment. A country-specific sub-analysis may inform interpretation of results.

2 There was a moderately high attrition rate (43%) over a 2 year period and a moderately high relapse rate (53%) despite this attrition. The authors should discuss the attrition and relapse rates in companion to other studies.

3 Issues related to precision of assessment of relapse over 6-12 months period without specific assistance of a instrument detailing the life course of schizophrenia; and of assessing relapse in naturalistic setting (e.g. relapsed patient may seek treatment elsewhere) should be discussed. Details of training of assessors and formal assessment of reliability of recording relapse (if any) should be mentioned.

Discretionary revisions

1 The authors use the results of the same study (Ascher-Svanum et al 2011 & Almond et al, 2004) in different ways in their introduction (more accurate) and discussion.

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 am a Principal Investigator for a multi-centred clinical trial sponsored by Eli Lilly. Also I collaborate with World Health Organization on various projects.