Identifying Some Risk Factors of Time to Recurrent Relapses in Bipolar I Disorder Patients using Frailty Model of Survival Analysis", Psychiatry-15-284 for Journal of Psychiatry: Open Access.

Objective: Bipolar I disorder patients often experience relapse once and even more with no limit on number of relapses. The time to relapses of these patients are rarely studied particularly considering heterogeneity across individuals. The aim of this study was to identify some risk factors of time to recurrent relapses in bipolar I disorder patients with a recurrent event model in survival analysis.

Methods: In a retrospective longitudinal study, data of medical records of 526 bipolar I disorder patients who had referred to Razi Psychiatric hospital in Tehran from 1993 to 2011 with at least one relapse, with-out relapse in other hospitals or home in this duration, were investigated and time to recurrent relapses were collected in months. Semi-parametric penalized frailty model which consider whit-in subject correlation and heterogeneity across individuals, was applied to identify the risk factors of recurrent time to relapses.

Results: Significant frailty parameter (p<0.001) prove presence of heterogeneity among data. In frailty model the effects of substance abuse (p=0.041), regular fluctuation (p=0.002) and marital status (p=0.009) were significant on the hazard of recurrent times to relapses but other variables showed no significant effect.

Conclusions: Substance abuse, marital status and RF are important risk factors in order to plan for postpone the time to next relapses. More studies are required to clear out the effect of other covariates with this model.

Comment: I commend the authors for the choice of the robust methodology (semi-parametric penalized frailty models) to detect risk factors to relapse in a large sample of BD patients, interviewed from 1993 to 2011. The findings are worth being published and will have important implication for public health policy and clinical practice. Considering these strengths I would recommend that the authors improve their introduction and expand their discussion and conclusions to highlight the clinical relevance and future directions of these findings.

1. Overall the writing style is appropriate for a book/memoir but is not written as a scholar manuscript. In particular, the description of bipolar disorder and of the statistical methods is extremely lengthy. While a book is all about content, a manuscript is about critical thinking and critical appraisal of evidence. Please narrow down what you want to study, define the research problem, rationale, and hypotheses in a succinct way. In terms of methods, please refer to handbooks or other manuscript instead of describing in details the statistical methods used here. Rather provide a description of the clinical population (demographics, education, clinical course of the disease, IQ, employment, comorbidities,etc. and refer to summary tables).
2. In your discussion show how your manuscript offers a contribution to the field. Use direct and straightforward sentences to compare results to conclusions.
3. In the results please describe more thoroughly what the figures display and mean.