Author’s response to reviews

Title: Post-hospitalization course and predictive signs of suicidal behavior of suicidal patients admitted to a psychiatric hospital: A 2-year prospective follow-up study

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Version: 2 Date: 10 October 2012

Author's response to reviews: see over
Dear Ms. Catherine Olino,

We are very much grateful for reviewer’s valuable comments and suggestions, and the opportunity given to us to revise the submitted manuscript. Major amendments are attaching descriptions of hypotheses and an outline of this study to the latter part of Background section, providing descriptions concerning the nomenclature of suicidal behavior, and expanding Conclusions subsection.

Please find below our detailed response to the reviewers’ comments and amendments we made in the revision. The amendments are also presented with red letters in the response and the revised manuscript. We hope our revision will meet with your approval criteria.

Sincerely yours,

Naoki Hayashi, MD, PhD

Reviewer 1: Michael Anestis

Comment 1: Reviewer 1 proposed that the background section be extended by (A) moving a substantial portion of the citations in the discussion section to build a case for the incremental value of the present study, and by (B) describing the study hypotheses and briefly discussing the implications of data supporting those hypotheses.

Response to Comment 1-(A): At the start of this study, we did not think that so many subjects died of suicide within the follow-up period. The unexpected number of victims forced us to use the substantial volume to discuss this issue in the manuscript. However, the number was not so large as to produce significant results in the survival analyses that sought the predictive factors. Consequently, descriptions concerning suicide are to be seen as an additional part of the manuscript.
Basically, the aim of this study was to seek predictive factors for suicidal behavior (or suicide attempt) (SB) recurrence of the discharged psychiatric patients. Therefore, in the former part of Background section, we put the focus on citations concerning the predictors of SB (suicide attempt) (while a few citations concerning suicide predictors were moved to Background section), and added the descriptions concerning suicide in the latter part of Background section that presented the aims, hypotheses (general ones in nature) and an outline of the present study.

Amendments: The latter part of Background section (page 6) has been replaced with the following paragraphs.

The present study aimed to investigate the post-hospitalization course of psychiatric suicidal patients while putting the focus on recurrence of SB. The studied sample was characterized by a predominance of involuntarily admitted patients and the majority diagnoses of mood disorders, anxiety disorders and PDs as shown in the cross-sectional study [32] that we had conducted as the former stage of the investigation on hospitalized suicidal patients, most of whom subsequently participated in this study. In the follow-up stage, a series of assessments were performed during the 2-year study period at 6-month intervals.

This study addresses the following questions about the discharged suicidal patients: what characteristics are predictive of SB recurrence, what are essential in SB prediction among the characteristics, and whether there are short-term (3-month) predictors of SB other than the predictors of within 2-year SB recurrence. In the analyses, suicide attempt (SB accompanied with suicide intent (SI)) was included in target variables since the presence or absence of SI would be of importance in classifying SB types [33, 34]. In addition, clinical characteristics of subjects who died of suicide within the 2-year period were examined. It is expected that predictive characteristics of SB that this study attempts to identify in the clinical course be usable for contriving SB and suicide prevention programs for this high-risk population.

Response to Comment 1-(B): Descriptions of study hypotheses are added in the latter part of Background section as shown above in the underlined part. The additional discussions corresponding to the hypotheses are also presented later in the response to Comment 6.

Comment 2: The reviewer 1 emphasized that use of the term, suicidal behavior (SB)
was problematic. “It encompasses an extremely broad variety of behaviors, including non-suicidal self-injury (NSSI). Likewise, the outcome variable was overly vague, lumping behaviors that share some similarity with suicidal behavior but differ in important ways. The broadness of terms that lump in such a range of disparate outcomes into a single variable might cause problems within the field of Suicidology. If the authors are to include NSSI within their definition of suicidal behavior, their background section needs to include a discussion of research relevant to that outcome and they must justify its inclusion in this manner while acknowledging findings that make that decision somewhat problematic.”

Response to Comment 2: We started this study with the concept of suicidal behavior (SB) by De Leo et al. (1999), in which suicide attempt and self-harm without suicidal intent (SI) (Silverman et al., 2007) or non-suicidal self-injurious behavior (NSSI) (Muehlenkamp, 2005) are not clearly distinguished. However, the SBs immediately prior to index admission of the studied subjects were in fact suicide attempts, as was suggested by Reviewer 2. The majority (88%) of the subjects confirmed the presence of SI component in Suicidal Intent Scale (SIS) Item 13. Though the remaining 13 subjects denied accompanying SI in the assessment interview, their family members or other people around them reported that SI was heard from them prior to admission. Even if they exhibited self-harm without SI (NSSI) before index admission, the SB immediately prior to admission should be seen as a suicidal attempt overridden on self-harm without SI (NSSI).

In the follow-up assessment, we tried to discriminate suicide attempts from self-harm without SI (NSSI) by inquiring whether SI accompanied SB or not. However, the method to distinguish the SB types might not be sufficient, and would fail to identify some of suicide attempts in SBs as a whole during the follow-up period since the inquiry was very simplistic, and was conducted when a considerable time period (6 month at the maximum) had lapsed after SB. Furthermore, many studies have evinced that self-harm without SI (NSSI) are closely related to suicide and suicide attempt. Therefore, instead of omitting SB that occurred without clear SI, we used “SB as a whole” and “SB with (certain) SI (suicide attempt)” as target variables of the survival analyses. (Resultantly, the findings of this study appeared to indicate that SB as a whole had richer clinical implications than suicide attempts (SB with SI).)

In order to clarify the nature of SB types in this study, we added the following descriptions.
Amendments: The following sentences are inserted in the revised manuscript.
(In page 7, after descriptions of the definition of SB by De Leo et al. (1999)).

This concept might cause a problem in the investigation since it included various related concepts such as suicidal attempt and self-harm without SI [33, 34] or non-suicidal self-injurious behavior [36]. To minimize the problem, the level of SI that accompanied SB was consistently to be taken into account in this study.

(In Page 14 in the descriptions of the subjects’ clinical characteristics)
Particularly, 93 (88%) of the subjects reported the presence of SI component (SIS Item 13). From 13 subjects who denied SI in the entry assessment, SI that accompanied SB immediately prior to index admission was heard by family members or others around them. Therefore, the SBs could be understood as suicidal attempts.

(In Page 22, limitations of this study, Discussion section)
Third, some measures used in the follow-up assessments might be too simplistic. Future studies should apply well-validated measures, particularly for social support, quality of treatment and distinguishing various SB types.

Comment 3: Reviewer 1 posed a question why the authors did not utilize survival analysis. Length of time to reoccurrence, which seems highly relevant to the purpose of this paper, should be presented.

Response to Comment 3: Our main research question is not to estimate intervals of SB reoccurrence, but to seek predictive signs of SB. Therefore, Cox proportional hazard regression analysis is a more suitable survival analysis method than Kaplan-Meier method. The median of length of time to recurrence of SB as a whole is to be additionally presented in the manuscript (page 16).

Comment 4: Given the nearly universal global tendency for females to attempt far more often than men and for men to die by suicide at a much higher rate than do women, the authors should spend more time discussing the potential impact of biological sex on the results of this study, as they had an almost evenly divided sample.

Response to Comment 4: We included a univariate Cox proportional hazard regression analysis to examine the predictive value of female gender. However, it did not produce a
significant result. Considering the importance of gender, we have included “gender female” in the SB predictors the previous studies showed in Background section of the revised manuscript. However, this issue is not dealt with later in Discussion section since the finding is far from conclusive because of the small sample size of this study.

Comment 5: The authors need to discuss other variables not measured in their study that might have had an impact on the results (e.g., variables from Joiner’s theory, access to means, etc.)

Response to Comment 5: Since Joiner’ theory is dealing with development stages of suicide, and is a rich sources of productive ideas for many people who are engaged in suicide prevention activities, we cited “Why people die by suicide (2005)” in Background and Discussion sections, by which we stressed that some SB predictors could be suicide-driving moments in Joiner’s theory.
Regarding access to SB means, we tested SB predictive values of SB methods, which gave no significant result. Consequently, it would be quite unlikely that access to SB means has some predictive value for SB recurrence.

Amendments: A phrase shown below about Joiner’s interpersonal-psychological theory of SB is inserted in Background section. Another citation is also made in Conclusions subsection (page 23).
(In Page 5, Background section)

Consequently, SB evidently comprises a critical part of the processes that lead to suicide completion, which is known as “a pathway to suicide” [12], “suicidal process” [13] and acquisition process of “the capability for suicide [14]” in many cases.

Comment 6: There was very little discussion regarding potential mechanisms driving the findings. In other words, the authors noted a number of relatively stable characteristics associated with reoccurrence of a maladaptive behavior, but did not discuss why that relationship might be there and how interventions might mitigate that risk. Given that the list of variables predictive of the outcomes (e.g., particular diagnoses and demographic variables) was consistent with prior research, this study really needs to provide a firmer theoretical basis for the findings to really justify incremental validity for the findings.
Response to Comment 6: We attempted to enrich discussions of the new manuscript. However, it was not easy for us. The results obtained in this study that dealt with a very specialized sample of discharged suicidal patients, are not far-reaching in nature. Additionally, compared to thickly accumulated literature on predictive factors of suicide, the number of studies on SB predictive factors is so limited. Therefore, we suppose that the studies of this type remain in a developing stage where their results need further accumulation of related findings for validating or denying them.

Amendments: Conclusions subsection (page 22-23) was replaced with following paragraphs.

Conclusions
The present study elucidated that a very high SB and suicide risk persisted during the post-hospitalization period of psychiatric suicidal patients though improvement of some psychiatric symptoms was observed. It also identified patterns of predictive signs of SB as a whole and suicide attempt, which suggested that SB-predictive signs varied depending on types of SBs. The results indicated that SB as a whole was more strongly predicted by life-historical factors such as number of lifetime SBs and maltreatment in the developmental period rather than other factors such as relevant psychiatric disorders and socio-demographic factors. These findings justifiably lent support to some earlier processes in the suicide development theories [13-15]. From this viewpoint, the importance of clinical efforts to prevent SB as a whole should be emphasized to stop the processes leading to suicide. In contrast, depressive symptoms at entry were predictive of suicide attempts during the follow-up period, which suggested that to mitigate the symptoms promptly might be contributory of preventing later intensification of SI. Additionally, poor physical health was presented as a novel candidate of proximal SB predictors for the patients. The predictive signs and characteristics are to be applied for further deepening understandings of SBs and developing individualized suicide prevention programs for the patients. It should also be stressed that clinical and research efforts be directed to improving treatments and to examining their effectiveness for this patient population at extremely high risk of suicide.

The result of stepwise regression analysis is more clearly stated.

(in page 19, Predictive signs of SB subsection)
Moreover, the stepwise multiple regression analysis selected life-historical and demographic factors: number of lifetime SBs, maltreatment in the development and
younger age as more essential in SB prediction than psychiatric symptoms and diagnoses.

(in page 20, Predictive signs of SB subsection)

Regarding predictive signs of suicide attempt, however, depressive symptoms appeared to be predominant over socio-demographic characteristics, life-historical factors and psychiatric disorders.

Reviewer 2: Maurizio Pompili
Comment 1: The main problem with this paper is the nomenclature. Authors use through the paper the term “suicidal behavior” when in fact it’s “suicide attempt”. The definition they provide is correct and refers to suicide attempt but the use of the term suicidal behavior is misleading and incorrect. He suggested to keep the definition as it is, to change suicidal behavior with suicide attempt and to discuss the issue by citing the paper by Silverman et al, 2007 (Suicide and Life-Threatening Behavior; two papers) on the nomenclature in suicidology.

Response to Comment 1: As described before in the response to Comment 2 of Reviewer 1, we added to the new manuscript the following descriptions: SI that accompanied SB should consistently be considered in this study (in Page 7); and all SBs immediately prior to index admission were in fact suicidal attempts (in Page 14). We did not change the term “suicidal behavior” with “suicidal attempt” since the possibility that there were “self-harm without SI (Silverman et al., 2007)” or “(non-suicidal) self-injurious behavior (Muehlenkamp, 2005)” in SBs in the lifetime history and the follow-up period could not be neglected.

Comment 2: Reviewer 2 stressed the role of marital status on SB recurrence and suicide by citing a paper by Masocco et al (Suicide and Marital Status…, Psychiatric Quarterly 2008;79…).

Response to comment 2: We included “living with a partner” in the list of possible SB predictors in Background section, and presented the result of a univariate Cox proportional hazard regression analysis of living with a partner in Table 4. It did not produce a significant result. This issue is not discussed later in Discussion section since the finding might be derived from the small sample size of this study.

Reviewer 3: Matthew Large
Comment 1: Reviewer 3 kindly recommended to replace words in the manuscript with more pertinent ones: to replace "supposed" in page 5 line 1 with "usually considered", and "to remedy it proficiently is an urgent task" in page 5 line 2 with "managing SB is an important responsibility"

Response to Comment 2: We have applied all the recommendations by Reviewer 3 in the manuscript.

Comment 2: Reviewer 3 proposed use of the word “risk factor” instead of "predictor”.

Response to Comment 2: As stated before in the response to Comment 6 of Reviewer 1, the accumulation of studies on SB recurrence among patients with specific disorders or conditions is not enough. Therefore, we would like to chose “predictor” instead of “risk factor” hoping that some “predictors” will be ascertained to be “factors” in future studies.

Comment 3: Reviewer 3 stated that we ought to formulate clearly hypotheses at the end of Background section.

Response to Comment 3: We clearly showed the study hypotheses (general hypotheses) as shown in the response to Comment 1-(A) and (B) of Reviewer 1.


Response to Comment 4: We found that it was very useful to support some of our contentions (E.g., the importance of SB in the suicide development process). The study is included in References, and is cited in Background and Discussion sections.

We thank again all the reviewers for the very much constructive comments to improve the quality of our manuscript.