Author's response to reviews

Title: Poly-substance use and antisocial personality traits at admission predict cumulative retention in a buprenorphine programme with mandatory work and high compliance profile.

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Version: 4 Date: 24 March 2011

Author's response to reviews:

Dear Dr. Krampe;

• We were very grateful for all the work you put into the review and the very exacting comments you provided. We have done our best to follow your advices and answer to your suggestions. We hope we are more adequate in responding this time.

• We also felt you did not find a sound clinical stance in the previous draft and we agree with your position and have made some alterations in a clinical direction this time.

• We also suggest a somewhat more appropriate title after discussing your
comments:

• Poly-substance use and antisocial personality traits at admission predict cumulative retention in a buprenorphine programme with mandatory work and high compliance profile.

K: According to my understanding of survival analyses, it is cumulative retention probability. Maybe I am wrong; please definitely consult a statistician.

• We have nothing against the term "probability". It is somewhat self-evident that what is predicted is a probability, since this is a statistical estimation, just as the probable mean value of a variable can be estimated in linear regression. We have since searched for the term “survival probability” in the literature. In Pubmed.gov, there are seven instances where researchers have used the term “cumulative survival probability” along with “cox regression or “cox proportional hazards” and 203 instances where researchers have used the term “cumulative survival” along with “cox regression or “cox proportional hazards”, so the omission of the term “probability” is more common (checked on February 27, 2011). Similar numbers were found in Scopus.

General comment: Definition of outcome variable: Dr Krampe suggests relapse and in a way this would be easy to understand, but there mostly was at least a week delay before excluding a patient from treatment and we do think involuntary discharge is therefore the best outcome measure, but regrettable, less easy to grasp for the reader.

K: Background, page 4, paragraph 2, 3: "One potential predictor ... SOC ..." Sense of coherence is introduced in a quite promising way but afterwards completely dropped in the aims, methods, results. What happened?

• Keeping it was an error. SOC was not predictive and was omitted in the forthcoming analysis.

K: Background, page 4, paragraph 4: "The aim of this study ..." Why are age and gender not mentioned?

• Age and gender were kept because they are variables that it is customary to check for. In this context, there is the additional rationale that some of the important co-variates (conduct disorder, psychiatric symptoms) vary considerably by gender. This has now been mentioned in the statistical analyses section.

K: Methods, Assessments, page 7: What happened to the description of the SOC Scale?

• We dropped the SOC in the subsequent analysis.

Methods, Statistical analysis, page 9:

- It is very good to restrict the number of covariates. However, based on the literature, the selection of predictors could have been different, too, e.g. number of symptoms of avoidant PD, SOC etc. Please explain why you chose age,
gender, number of drugs in urine at baseline, as well as criteria count for conduct disorder.

• We kept those variables as the most feasible based on the literature. Avoidant PD was not included, but instead anti-social was focused upon also from our own earlier findings. The SOC has been studied in only a few samples as well but was dropped.

• In this paper we chose to follow your notion on personality test. We write briefly on (SSP) even though it was not possible to make any specific hypothesis on this test. It has not been used before in this context. We just chose to note that it did not discriminate between completers and relapses and was not included in the regression model.

K: - Which statistical software was used for analyses?

• Stata 11 for Windows.

- By the way: (1) stepwise inclusion does not have to be "statistical stepwise inclusion" One can also in a first step calculate univariate analyses, and in a second step include those covariates in the multivariate regression that exceeded in the univariate regression an a priori defined strength of association.

• The inclusion of variables based on observed univariate associations still capitalizes on chance. We agree with the reviewer that our model contained too many variables in the first place, so we chose the four clinical variables and the two “demographic” that we felt had the strongest base.

K: (2) When I had the idea of adjusting the personality disorder counts to the maximum number of potentially reachable symptoms, I did not suggest standardizing all predictors. There must have been a misunderstanding leading to the worries of "meaningless comparison". As the current regression model includes only one of the SCID-II screening modules (number of conduct disorder symptoms) the issues seems to be solved, anyhow.

• That is fine with us. We can do much better next time thanks to your comments.

Results, page 11, paragraph 4: "The observation period ranged from one week to 64 months."

• Five cases who dropped out early (one week), and were not part of the study. With only two or three persons dropping out after the first two it was maybe unfair to ourselves to exaggerate the time span since patients dropping our early, were not part of the sample.

The variation should more correctly be stated as two weeks up to 64 months.

K: As far as I have understood survival analyses, the concept of censoring cases is especially used in order to correct for varying follow-up times. This is why
Kaplan–Meier estimates of cumulative abstinence probabilities (or survival probabilities) are calculated. I might be wrong. Please consult a statistical expert.

- This is exactly what we thought. Survival models make no assumptions about follow-up time, except that follow-up time should be unrelated to predictor variables (or to the processes whereby predictor variables are assumed to work). Of course, follow-up ends when the event occurs. We have gone through some of the statistical literature, and in important assumption is the assumption of proportional hazards. That is, that the influence of covariates is independent of the time variable. We did test this for all individual variables in the model, and found no indications that any variables varied over time in their influence on risk of dropout. This has been added, and is an improvement.

K: Results, page 11, paragraph 5: Why is the effect of age not mentioned?
- This was an erroneous omission. It has now been added to the text.

Discussion, page 13, conclusion: "Patients who are not able to bring their drug use under some degree of control before entering treatment, and patients who experience high levels of anxiety or report many indicators of conduct disorder before age 15 may need additional support."

K: To which result refers the conclusion that patients with high levels of anxiety need additional support?
- This was an error, and has been corrected.

Minor Essential Revisions

K: Title: "Illicit drug use and antisocial personality traits at intake to treatment predicts cumulative retention"

Shouldn't this be "predict" instead of "predicts"?
- Yes, has been corrected.

Abstract: "Symptoms Checklist 90 (SCL-90)". The issue is minor but still open: correct name is 'Symptom Checklist-90-Revised (SCL-90-R)'. Please check throughout the text.

- SCL-90: We did not use the revised version. Sorry, we forgot to put this in the response last time, and we have added this to the text, along with an explanation (the normative data are for the original instrument).

Methods, Assessment, page 9, SCL-90-R, AUDIT: "For the present study, only the Global Severity Index, the mean of all scales, was used ...gender-adjusted T-scores..." This issue is also still open: Which scales are you referring to with "all scales"?

- In practice, the GSI is the mean of all items or all sub-scales. Since all nine sub-scales of the SCL-90 have the same number of items, and all items have the
same potential values, the mean value of all items and of all sub-scales will be the same. We have replaced scales with items.

Were gender-adjusted T scores used for Cox regression analyses? Why not using raw scores? Gender and age are analyzed as specific predictors in this study, so why gender-adjusted T-scores should be used? The same holds true for the AUDIT? Why using gender and age adjusted T scores when including the variables age and gender in the analyses? For the SCID-II screening questionnaire symptom counts, no adjustment to gender and age was performed. Shouldn't this be consistent?

• After reading this comment, we decided that it was more consistent to use the unadjusted scores, and did so in the now submitted analyses.

Level of interest: An article of importance in its field

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.