Author's response to reviews

Title: Prevalence of Psychological Distress and Associated Factors in Tuberculosis Patients in Public Primary Care Clinics in South Africa

Authors:

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Version: 2 Date: 9 May 2012

Author's response to reviews: see over
Editors comment:

- Thank you for submitting this paper to BMC Psychiatry. Your manuscript has now been reviewed by both myself as the handling editor and two reviewers. As you will see from the reviewers' comments, there was a general consensus that your study was addressing an area of public health importance, but there were a number of significant concerns regarding both the methodology of your analysis and the way in which your results are presented. As a result, I cannot recommend publication of your manuscript in its current form. However, I think the results of your study are important and I would like us to be able to re-evaluate your manuscript again following some revisions. I would like to emphasise that I think you will need to make quite major revisions to this paper for it to be able to be considered for publication and that this will almost certainly involve some re-analysis of your data. If you do choose to resubmit a modified version of this manuscript it will need to go through the review process again and publication cannot be guaranteed.

I have attached the reviewers' comments for you look and attempt to address. However, in addition to addressing the concerns raised by the reviewers, may I suggest some broad points which I think need to be addressed in a revised version of this paper:

1. At present the manuscript includes a lot of analysis which does not seem necessary and does not fit with your stated aims. In particular, it is not clear why you are wanting to test for differences between men and women in tables 1 and 2 and why the analysis in table 3 is needed at all.

Response (R): Table 2 no longer has gender differences and Table 3 has been removed

2. I wonder whether you should consider looking at alcohol misuse (AUDIT) as a mental health outcome in addition to common mental disorders. Not only would this make sense, but it would also allow you to differentiate your study from the previous studies looking at just CMD in a TB population.

R: The aim of the study was to focus on common mental disorders, which has been done

3. As noted by both reviewers, I think the way you have used the K10 in the current analysis is a major limitation. Within your manuscript you have quoted a previous study which validated the use of the K10 in a similar population (Spies et al). However, the ROC curve analysis in this study suggested that much higher cut off scores (around 28) were needed for your patient group. Given this result, your use of a much lower cut off value seems surprising. I would suggest you and your co-authors need to consider the issue of what cut off score you use again and consider using either a different or additional cut off value in line with Spies et al's findings or provide more detailed justifications for the approach you have taken.

R: We have two validation studies of the K-10 in South Africa, 1) with some 460 HIV patients, and 2) with a large representative population; the former suggests 28 as K-10 cut-off and the latter suggests 16 as the best cut off. As suggested, now prevalence and the regression model/outcome is now presented for both cut offs separately.
4. I think the paper would benefit greatly from the analysis being conducted and presented in a more logical approach. Obviously, it is up to you and your co-authors to decide what is best, but I feel I should make a suggestion of one way in which this could be achieved:

a. Firstly the sample should be described (one the reviewers has suggested how table 1 could be simplified)
b. The prevalence of mental illness (CMD and alcohol misuse) could be presented

**R:** In Table 1 sample characteristics and the prevalence of mental illness, using two cut offs are now presented.

c. The ways in which sociodemographic and health factors are associated with mental illness could be tested

**R:** In Table 2, predictors for mental illness, with two cutoffs are presented separately.

d. You could then, as a separate analysis, look at the treatment consequences of co-morbid mental illness - specifically the impact this appears to be having on treatment compliance Such an approach would allow you to present to the reader a more stepped story; mental health problems are common in this group, then these are the factors which seem to be associated with an increased risk of mental health problems and then finally, what effect does mental illness have on treatment compliance.

**R:** In table 1 treatment adherence is analysed as covariate, and not found significant.

5. As noted by both reviewers, the language used in this paper is at times difficult to follow. In making these revisions I would encourage the authors to find someone with experience in writing academic papers in English to assist them with the final editing.

**R:** Corrected

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**Reviewer's report**

**Title:** Prevalence of Psychological Distress and Associated Factors in Tuberculosis Primary Care Patients in South Africa  
**Version:** 1  
**Date:** 3 April 2012  
**Reviewer:** Amare Deribew

**Reviewer's report:**

Title: Prevalence of psychological distress and associated factors in tuberculosis primary care patients in South Africa  
Author: Karl Peltzer et al  
Reviewer: Amare Deribew  
Minor essential revisions:  
1. Title: shall be corrected as ‘Prevalence of …...in TB patients in primary health care clinics in South Africa’
2. Abstract:
# Methods: one month of initiating shall be replaced by one month of initiation of anti-TB
R: Changed

# ‘The demographic characteristics of TB were’ is not a correct sentence and should be corrected
R: Reworked

# please use the word anti-retroviral therapy
R: Changed accordingly

# Please merge the last two sentences together in the method section. Data on socio-demographic variables, health status, alcohol……were collected using a structured questionnaire
R: Changed accordingly

# Results: Please include the OR in the result section
R: added

# Conclusion: the last sentence is not clear: what do you mean structural Interventions
R: Financial

3. Background:
# The third paragraph should be revised for clarity and grammatical errors.
…..Pakistan: 43% depressed, 80% hospitalized etc……..is not attractive and interesting and has many errors. Please make them short by category (e.g mental illness in TB patients, the mental illness in co-infected patients).
R: Changed to below

Few studies have investigated common mental disorders in TB patients in low and middle income countries (LMICs), finding high rates of common mental disorders, in Pakistan 46.3%-80% [11-13], in Nigeria 27.7%-30% [14,15], in Ethiopia 64% [16], in India 76% [17], in South Africa 46% [18,19 ] and in Turkey 19%-26% [20].

# Please put ‘full stop’ after reference 6. There are also similar errors elsewhere
R: Added

4. Methods:
# Please replace method by methods
R: Changed

# When was the exact duration of the study (study period)?
R: The interview was conducted by trained external research assistants for a period of 6 months from mid April to mid October in all 42 clinics in 2011.

# This score was should be replace by these scores
R: Changed

# as recommended by [31] is not correct and please properly make citation (e.g name of authors)
R: added

5. Results:
# The first paragraph should be revised for clarity: final sample included 4900, 54.5% men and ..... is not attractive
R: Changed

# Please omit ‘insert table in the text’
R: Removed

# Use punctuations properly. E.g from total samples, 76.6%
R: added

# Under TB-HIV co-infection, please split the long sentence into 2. The second sentence can be ‘Younger age (OR=, 95%CI:), being female (OR=, 95%CI), ..... were associated with TB/HIV co-infection. Please avoid unnecessary words like in the multivariate analysis. This is already discussed in the method section.
R: The section on TB-HIV infection has now been removed.

# Under predictors of stress, please also split the sentences and include OR
R: Changed, and added

# Please include title for the variables in table 4 (e.g Sex: male and female, poverty level: low, medium, high etc....)
R: added

Major compulsory revisions:
1. Methods:
# How was the K-10 validated? What type of validation? Did you use the same language with the validated instrument?

R: In previous studies the K-10 was validated in South Africa, explaining the type of validation, as in below. In this study the two K-10 cut offs 16 and 28 as found in previous validation studies were used. We report high internal consistency of the K10
The K-10 scale in this study. The languages used in this study is now added, and there is considerable overlap between the languages in this study with the 2 validation studies.

This scale is increasingly used in population mental health research and has been validated in multiple settings [27] including HIV positive individuals in South Africa [28] and in a population-based survey in South Africa [29]. There was significant agreement among HIV patients between the K-10 and the MINI-defined depressive and anxiety disorders, with the best screening cut off of 28 [28]. A receiver operating characteristic (ROC) curve analysis indicated that the K-10 showed agreeable sensitivity and specificity in detecting depression (area under the ROC curve, 0.77), generalized anxiety disorder (0.78), and posttraumatic stress disorder (PTSD) (0.77), with the best cut off of 28 [28]. Further, the K10 demonstrated moderate discriminating ability in detecting depression and anxiety disorders in the general population in South Africa; evidenced by area under the receiver operating curves of 0.73 and 0.72 respectively, with a cut off of 16 [29]. We examined the K-10 scale using two cut offs (16 and 28), as found in validation studies in South Africa [28,29]. The internal reliability coefficient for the K-10 in this study was alpha = 0.92.

# In the analysis, did you check multi-collinearity? E.g education and poverty may have multi-collinearity?

R: Multi-collinearity was checked, as below:
Interaction between predictor variables was examined; none of the variables had a Variance Inflation Factor (VIF) value above 2.5

# Since income is included in the poverty scale, why did you use it separately in the analysis?

R: Income is removed now from the analysis.

Results:
# In table 1, you did cross tabulation (chi-square). E.g marital status and sex. In this case there should be one p-value and one X2 value. Where did you get the other p-values in each category (for married, separated etc..)? Unless you did OR, you can’t have many p-values in one variable like marital status or education.
R: This is now removed

# The purpose of table 2 is not clear. Why did you stratified by sex (men and women ). This makes the table complex? Unless sex is an effect modifier, better to include sex like other variables. If you have clear reasons to know differences
among sex, you can explain in the result section. In the current version, nothing is said about all those p-values in table 2? You can simplify the table as sample Variable Number (%) Sex Level of psychological distress Others........

R: Reworked accordingly

In table 4, non-significant values as taken as significant. E.g grade 8-11, the 95% interval indicates that the variable is not statistically significant. R: Corrected

Discussion:
# The discussion is short and pleased try to add logical explanation on association between variables (why is some important variable not significantly associated? What could be the reason?

R: Totally reworked, as below:
A high overall prevalence of psychological distress (32.9% and 81% according to the K-10 score ≥28 and K-10 score ≥16, respectively) was found in this large sample of tuberculosis public primary care patients in South Africa. Caseness of psychological distress or common mental disorder was assessed using two different cut-offs (K-10 score ≥28 and K-10 score ≥16), as found in two different previous validation studies in South Africa [28,29]. Several studies showed that the K-10 had good psychometric properties [27,28] and can discriminate between cases and non-cases reported in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [16,35]. The finding of 32.9% to 81% (depending on the cut offs) psychological distress in this study is in line with the prevalence rate of depression or common mental disorders in most other studies with tuberculosis patients 46%-80% in LMICs [11-13,16,17,18,19]. The differences in prevalence of common mental disorders could be attributable to several factors including the population being studied, the study periods during TB treatment and the diagnostic tools [16]. It is possible that increased rates of psychological distress were found in this study because the assessment followed within a short time (within one month) of the TB diagnosis which might not have persisted at a later stage or completion of TB treatment. Further, Andersen et al. [29] have suggested that the Kessler scales had significantly lower discriminating ability in regard to depression and anxiety disorders among the Black African than among the combined non-Black African population group in South Africa, and they attribute this to differential item
biased measurement. The Black African population group has been having the lowest socioeconomic status often lacking basic necessities among the different population groups in South Africa, and therefore may be more likely endorse K-10 items such as “How often do you feel that everything is an effort?”[29] However, we did not find differences in psychological stress rates between Black African and Indian or Asian or Whites population groups in this study. Spiess et al. [28] also did not find a significant difference in validity of the K-10 in detecting depression and anxiety disorders among HIV infected South Africans across gender, age, education, or ethnicity categories.

In multivariable analysis the study found that lower formal education and poverty were associated with psychological distress. Low socioeconomic status has also been found in other studies to be associated with common mental disorders in TB patients [14,15,16]. Most studies in developing countries showed an association between indicators of poverty and the risk of mental disorders, the most consistent association being with low levels of education [4, 36,37]. Many patients in low and middle income countries suffer from common mental disorders because of stress caused by poverty [4,16,38] and factors such as the experience of insecurity and hopelessness, rapid social change and the risks of violence and physical ill-health may explain the greater vulnerability of the poor to common mental disorders [36]. Financial empowerment of patients may reduce depression in them, improve the compliance rate to anti-TB medication, and could furthermore bring an improvement to their quality of life [14].

Further, older age was in this study associated with psychological stress, which was in agreement with some other studies with TB patients [14,15] but not with general population studies [39]. This increased prevalence may be due to increased responsibilities such as child care, care or other family members, employment and economic responsibilities as well as having to cope more likely with more chronic illness conditions including HIV in the older age group [14]. Marital status (being married or cohabitating) has been found in this study, in agreement with other studies [40,41], a protective factor from psychological stress (K-10 ≥28). Being married or cohabitating provides social support reducing psychological distress [41]. In contrast with some [12, 14] but in agreement with other studies [42], we did not find a significant association between gender and psychological distress.

General: please make thorough editorial revisions??
R: Corrected
Reviewer's report
Title: Prevalence of Psychological Distress and Associated Factors in Tuberculosis Primary Care Patients in South Africa
Version: 1 Date: 12 April 2012
Reviewer: John Joska
Reviewer's report:
The authors have investigated an area of critical public health concern. The sample size is substantial, and the methodology overall is sound. I have some queries around interpretation of the findings regarding the measure and the related findings.
Major comments:
1. I feel that more discussion of the utility and validity of the K10 for this population is needed. Specifically, the authors use a low cut off score to define distress, which results in a very high prevalence. What have other studies found with regard to cut off scores and case ness? For example, the Spies study found that a cut of about 30 was most suitable to define case ness. Also, the Andersen study was less enthusiastic about the K10 for assessing for mental disorders.

R: In the two previous studies the K-10 was validated in South Africa, optimal cut offs 16 and 28 (53.1% depressive disorder, HIV patients, Spies study) were found. Deribew’s study in TB/VIV co-infected patients in Ethiopia used a cut off of 16/7 and also found high prevalence of psychological distress (64%). Based on the two validation studies of the K-10 in South Africa, 1) with some 460 HIV patients, and 2) with a large representative population; the former suggests 28 as K-10 cut-off and the latter suggests 16 as the best cut off. Now prevalence and the regression model/outcome of psychological distress is now presented for both cut offs separately.

This scale (K 10) is increasingly used in population mental health research and has been validated in multiple settings [27] including HIV positive individuals in South Africa [28] and in a population-based survey in South Africa [29]. There was significant agreement among HIV patients between the K-10 and the MINI-defined depressive and anxiety disorders, with the best screening cut off of 28 [28]. A receiver operating characteristic (ROC) curve analysis indicated that the K-10 showed agreeable sensitivity and specificity in detecting depression (area under the ROC curve, 0.77), generalized anxiety disorder (0.78), and posttraumatic stress disorder (PTSD)
Further, the K10 demonstrated moderate discriminating ability in detecting depression and anxiety disorders in the general population in South Africa; evidenced by area under the receiver operating curves of 0.73 and 0.72 respectively, with a cut off of 16 [29]. We examined the K-10 scale using two cut offs (16 and 28), as found in validation studies in South Africa [28,29]. The internal reliability coefficient for the K-10 in this study was alpha = 0.92.

2. The manuscript needs more discussion regarding the implication of these findings. A paragraph on the background to distress And health outcomes is needed in the introduction. As it turns out, no association was found between adherence and distress in this study- so why screen? Other than to offer treatment? What will the operational outcomes be?

R: It seems the above is covered in below introduction, and also in the discussion

Factors associated with common mental disorders in TB patients included: male gender [12], age groups, young and elderly [12,14], low educational attainment [15], financial status, no source of income [14,16]; day labourers [16] an increase in the number of symptoms reported, more serious perceived consequences and less control over their illness [11,14]; TB/HIV co-infected [16], perceived stigma [16], poor perceived health status [16], adverse effect on drug compliance and TB treatment [12,21] and negative TB treatment outcome (death) [22].

In addition, more discussion added, as in below

A high overall prevalence of psychological distress (32.9% and 81% according to the K-10 score ≥28 and K-10 score ≥16, respectively) was found in this large sample of tuberculosis public primary care patients in South Africa. Caseness of psychological distress or common mental disorder was assessed using two different cut-offs (K-10 score ≥28 and K-10 score ≥16), as found in two different previous validation studies in South Africa [28,29]. Several studies showed that the K-10 had good psychometric properties [27,28] and can discriminate between cases and non-cases reported in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [16,35]. The finding of 32.9% to 81% (depending on the cut offs) psychological distress in this study is in line with the prevalence rate of depression or common mental disorders in most other studies with tuberculosis patients 46%-80% in LMICs [11-13,16,17,18,19]. The differences in prevalence of common mental disorders could be attributable to several factors including the population being studied, the study periods during TB treatment and the diagnostic
tools [16]. It is possible that increased rates of psychological distress were found in this study because the assessment followed within a short time (within one month) of the TB diagnosis which might not have persisted at a later stage or completion of TB treatment. Further, Andersen et al. [29] have suggested that the Kessler scales had significantly lower discriminating ability in regard to depression and anxiety disorders among the Black African than among the combined non-Black African population group in South Africa, and they attribute this to differential item biased measurement. The Black African population group has been having the lowest socioeconomic status often lacking basic necessities among the different population groups in South Africa, and therefore may be more likely endorse K-10 items such as “How often do you feel that everything is an effort?”[29] However, we did not find differences in psychological stress rates between Black African and Indian or Asian or Whites population groups in this study. Spiess et al. [28] also did not find a significant difference in validity of the K-10 in detecting depression and anxiety disorders among HIV infected South Africans across gender, age, education, or ethnicity categories.

In multivariable analysis the study found that lower formal education and poverty were associated with psychological distress. Low socioeconomic status has also been found in other studies to be associated with common mental disorders in TB patients [14,15,16]. Most studies in developing countries showed an association between indicators of poverty and the risk of mental disorders, the most consistent association being with low levels of education [4, 36,37]. Many patients in low and middle income countries suffer from common mental disorders because of stress caused by poverty [4,16,38] and factors such as the experience of insecurity and hopelessness, rapid social change and the risks of violence and physical ill-health may explain the greater vulnerability of the poor to common mental disorders [36]. Financial empowerment of patients may reduce depression in them, improve the compliance rate to anti-TB medication, and could furthermore bring an improvement to their quality of life [14].

Further, older age was in this study associated with psychological stress, which was in agreement with some other studies with TB patients [14,15] but not with general population studies [39]. This increased prevalence may be due to increased responsibilities such as child care, care or other family members, employment and economic responsibilities as well as having to cope more likely with more chronic illness conditions including HIV in the older age group [14]. Marital status (being married or cohabitating) has been found in this study, in agreement
with other studies [40,41], a protective factor from psychological stress (K-10 ≥28). Being married or cohabitating provides social support reducing psychological distress [41]. In contrast with some [12, 14,] but in agreement with other studies [42], we did not find a significant association between gender and psychological distress.

3. A significant limitation / consideration was not made, namely the timing of the assessment. It is my experience that the early period of treatment (and by implication diagnosis- which is not assessed?) is associated with a spike in distress, which may or may not persist at 6 months and beyond. This needs to be discussed at least.
R: This is added in the discussion

4. The discussion should be revised. It is brief as it stands, which is not itself a problem, but a number of findings and statements need to be explored in more detail. For example, the case ness issue above, the clustering of SES associations (say more about why poverty is so strongly related) and why HIV coinfection is more distressing. These are important points which need to be spelt out, not assumed.
R: added

A high overall prevalence of psychological distress (32.9% and 81% according to the K-10 score ≥28 and K-10 score ≥16, respectively) was found in this large sample of tuberculosis public primary care patients in South Africa. Caseness of psychological distress or common mental disorder was assessed using two different cut-offs (K-10 score ≥28 and K-10 score ≥16), as found in two different previous validation studies in South Africa [28,29]. Several studies showed that the K-10 had good psychometric properties [27,28] and can discriminate between cases and non-cases reported in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [16,35]. The finding of 32.9% to 81% (depending on the cut offs) psychological distress in this study is in line with the prevalence rate of depression or common mental disorders in most other studies with tuberculosis patients 46%-80% in LMICs [11-13,16,17,18,19]. The differences in prevalence of common mental disorders could be attributable to several factors including the population being studied, the study periods during TB treatment and the diagnostic tools [16]. It is possible that increased rates of psychological distress were found in this study because the assessment followed within a short time (within one month) of the TB diagnosis which might not have persisted at a later stage or completion of TB treatment. Further, Andersen et al. [29] have suggested that the Kessler scales had significantly lower discriminating ability in
regard to depression and anxiety disorders among the Black African than among the combined non-Black African population group in South Africa, and they attribute this to differential item biased measurement. The Black African population group has been having the lowest socioeconomic status often lacking basic necessities among the different population groups in South Africa, and therefore may be more likely endorse K-10 items such as “How often do you feel that everything is an effort?”[29] However, we did not find differences in psychological stress rates between Black African and Indian or Asian or Whites population groups in this study. Spiess et al. [28] also did not find a significant difference in validity of the K-10 in detecting depression and anxiety disorders among HIV infected South Africans across gender, age, education, or ethnicity categories.

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Minor comments:
1. There are numerous grammatical errors, and places where it is not clear how phrases relate to each other. Examples include "demographic characteristics of TB" in abstract, lines 2 and 3 of the background, and the line 3 of para 3 in the background- how do these % relate to each other?

R: For the first part of above comment, we are not sure what this is referring to, and for line 3 of para 3, this has been changed to below:

Few studies have investigated common mental disorders in TB patients in low and middle income countries (LMICs), finding high rates of common mental disorders, in Pakistan 46.3%-80% [11-13], in Nigeria 27.7%-30% [14,15], in Ethiopia 64% [16], in India 76% [17], in South Africa 46% [18,19] and in Turkey 19%-26% [20].

2. Other outcomes in abstract? What about referral and treatment, in addition to "screening and brief psychological therapies"

R: is added

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.