Author's response to reviews

Title: Adherence to antidepressant therapy for major depressive patients in a psychiatric hospital in Thailand

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Version: 2 Date: 23 April 2010

Author's response to reviews: see over
April 22, 2010

The Editor
BioMed Central Psychiatry

Dear Sir/Madam:

We have addressed the reviewer's comments in the revised manuscript entitled “Adherence to antidepressant therapy for major depressive patients in a psychiatric hospital in Thailand”. It contains 2,168 words (excluding abstract and references), 27 references and 3 Tables. Please also see the point-by-point response to the concerns attached.

Please note, the address for correspondence has changed since the initial submission. New details are:

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Thank you for your consideration. I am looking forward to hearing from you.

Yours sincerely,

Benjamas Prukkanone, M.D.

Enclosures: a point-by-point response to the reviewer's comments (7 pages)
Reviewer's report 1

Title: Adherence to antidepressant therapy and pattern of prescriptions for major depressive patients in a psychiatric hospital in Thailand

Version: 1 Date: 13 February 2010

Reviewer: Churn-Shiouh Gau

Reviewer's report:

The main purpose of this article is to provide the adherence data to antidepressant therapy for major depressive patients based on the pharmacy data set from a psychiatric hospital in Thailand. The authors used the well-defined medication possession ratio (MPR) to measure the adherence rate. However, the data presentation is quite disorganized and the discussion is poor that the manuscript may need some revision. Following are comments on the manuscripts:

1. In the sentence “…is calculated by multiplication of the number and strength of pills dispensed and dose per day.” (Page 3, 3rd paragraph), it is not clear how the days’ supply was calculated.

Response: We have changed the sentence to “The days of supply was calculated as dosage strength divided by daily dose and multiplied with the number of pills dispensed. For instance, a prescription for fluoxetine 40 mg/day, sixty 20-mg tablets, was calculated as (20/40) x 60 = 30 days’ supply” (page 4).

2. It looks like the data in Table 2 was calculated based on the percentage of total patients that certain antidepressants have ever been prescribed to the patients. If this is the case then the heading of Table 2 should be modified.

Response: This table shows the percentage of patients who have ever been prescribed each drug type. The table heading has been changed to “Percentage of patients ever prescribed each drug type”.

3. There is a mistake in the data calculation in Table 3. The number in parentheses after 588 for “Total for those visiting more than one” shouldn’t be 100 since the data in parentheses for the other set of data in the same column were calculated by dividing the total number (1058) of eligible patients in this study.

Response: Table 3 has been re-structured and the text on pages 5 and 6, describing the table’s results has been changed accordingly.
4. In the discussion section 2nd paragraph on page 7, the authors claimed that “combination antidepressant therapy is widely used by specialists” according to experts in Thailand. However, the data (12% in Table 2) in this study did not support above observation, authors should give comments or explanation on this discrepancy.

**Response:** See the changes in table 3 and accompanying text mentioned in response to comment 3. We also have changed the statement to ‘combination antidepressant therapy is commonly used by specialists’ in the discussion section 3rd paragraph on page 8.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being Published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.

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**Reviewer's report 2**

**Title:** Adherence to antidepressant therapy and pattern of prescriptions for major depressive patients in a psychiatric hospital in Thailand

**Version:** 1 **Date:** 14 March 2010

**Reviewer:** Manit Srisurapanont

**Reviewer's report:**
Overview:
This retrospective study found poor adherence to antidepressants treatment in depressed outpatients of a psychiatric hospital in Thailand. The research question, methods, and data are sound. The results and discussion are appropriate but may need some improvement (see below). The study limitations are clearly defined. Previous studies are cited appropriately. In my opinion, the term of ‘pattern of prescriptions’ should be excluded from the title because only the percentages of antidepressant prescriptions, which are a small part of prescription pattern, were presented. The abstract and writing are acceptable. In my opinion, the evidence obtained from this study, which was carried out in low
and middle income countries, increases our knowledge in this area.

Discretion revisions:
1. Title, page 1: the term of ‘pattern of prescriptions’ should be excluded from the title. In this study, only the percentages of antidepressant prescriptions, which are a small part of prescription pattern, were presented.

   Response: We have changed the title to ‘Adherence to antidepressant therapy for major depressive patients in a psychiatric hospital in Thailand’

2. Background, page 2: For the sentence of ‘In the Thai burden of disease study in 2004, it ranked as one of the top ten causes of Disability Adjusted Life Years (DALYs), the authors should give a reference.

   Response: Reference added in 1st paragraph of Background, page 2.

3. Background, page 2: For two sentences of ‘Adherence of between 40% and 70% is reported for antidepressant therapy in developed countries [3]’ and ‘Only one study shows the pattern of prescriptions for antidepressants in clinical practice in Thailand [6], the authors should give some more details of the studies or reviews, e.g., study designs, the sample sizes, settings.

   Response: Please see Background, page 2: The first sentence has been changed to ‘According to a review of non-adherence with antidepressant therapy, values of between 40% and 70% have been reported for antidepressant therapy in developed countries[4]’ and the second sentence ‘Only one retrospective study shows the pattern of prescriptions for antidepressants in 53 new cases of major depressive disorder in the out-patient psychiatric department of Siriraj Hospital [7].’

4. Methods, Study Population, page 2: The authors should reconsider about including the data of patients with the diagnosis codes of F38 and F39. Because these codes are not specific for depressive disorders, the data of bipolar patients may be included in the analysis.

   Response: We agree that the use of F38 and F39 diagnostic codes may include some people with bipolar disorder. We considered it most likely that these codes were used for unspecified major depression. As it involves only 3% of patients, we don’t think it is a crucial assumption.

5. Methods, Definition and Measurement of Adherence, page 3: The first paragraph started with ‘A definition of adherence ...... is comparing multiple methods [9].’ should be moved to ‘Background’ section.

   Response: As the definition is closely linked to our choice of method we believe it fits in the methods section.
6. Results, Table 3, page 5: This table is difficult to understand. It is understandable that there are two groups (one visit only and at least two visits) for ‘1. Used only one drug’, but why there are no two groups for ‘2. Ever received 2 drugs at the same date’ and ‘3. Switched from initial drug to a different one’. Does it mean that no patient who received 2 drugs at the same date or switched from initial drug to a different one came back only once? To make this table more understandable, the authors break the patients into two groups first, which are one visit only and at least two visits. After then, the authors break the groups with at least two visits into three subgroups, which are ‘used only one drug, ever received 2 drugs at the same date, and switched from initial drug to a different one’.

**Response:** The table has been re-structured and the text on page 5 and 6, describing the table’s results has been changed accordingly.

7. Discussion, page 5: Should the paragraph started with ‘Numerous direct and indirect methods …improve medication adherence [18].’ be moved to ‘Introduction’ or ‘Methods’ sections?

**Response:** This paragraph explains the advantages of MPR and to justify the use of this method in our study, hence its inclusion in the discussion section.


**Response:** Please see Discussion, page 7: ‘The adherence in our study among patients attending at least twice is similar to the MPR results from a national database including data from patients who participate in 30 different health plans reported in US studies [12] [21].’

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:** I declare that I have no competing interests.
Reviewer’s report 3

Title: Adherence to antidepressant therapy and pattern of prescriptions for major depressive patients in a psychiatric hospital in Thailand

Version: 1 Date: 24 March 2010

Reviewer: Michael Moore

Reviewer's report:
This is a well written and clear article describing estimated adherence to antidepressant medication (using a validated measure) in an outpatient population treated by a psychiatric hospital in Thailand. In order to fully appraise the validity of the data presented an international reader will need at least some description of the health delivery system in Thailand, ie how many patients will be treated in primary care with depression and how many in institutions such as that described. The data are severely limited as it seems feasible that patients initiated on antidepressant medication may obtain continued supplies from primary care providers. Without more information about the health set up we are unable to estimate whether this is unlikely or likely. If large proportions are likely to receive medication from primary care then the data have little intrinsic value. (essential)

Response: See changes in background section on page 2: ‘In Thailand, most general practitioners are not confident with the diagnosis of mental health conditions including major depression. The majority of depressive patients that treated in psychiatric hospitals and treatment coverage is low. According to an estimate from the Health Information Technology Center of the Department of Mental Health in Thailand only 3.4% of depressive patients in 2005 received treatment from the Ministry of Public Health including psychiatric hospitals and general hospitals.’

Abstract
The results are incomplete, I think the the overall adherence should be presented first and a description of the measure (i.e. MPR>80%) (essential)

Response: We have changed this to: ‘1,058 were eligible for study inclusion. The overall adherence (MPR>80%) in those attending this facility at least twice was 41% but if we assume that all patients who attended only once were non-adherent, adherence may be as low as 23%’.

Study population
It would help if we knew more about the patients treated ie some estimate of depression severity in those treated? Is this a mixed group similar to that treated in primary care or a more severe group similar to those treated in secondary care in other countries. (desirable)

Response: There is no information available in Thailand regarding the severity of patients treated in psychiatric hospitals and outpatient clinics. However given the
majority of patients are treated at this level, we believe it reflects accurately the mix of depressive patients that are present across Thailand.

Results
It is impossible to interpret these without some estimate of prescriptions received elsewhere as mentioned above. The authors imply that if only one attendance then they assume that patients receive ongoing prescriptions from their regular healthcare facility. (essential)

Response: Please see in the discussion section on page 7: ‘According to mental health experts in Thailand, the majority of cases are treated by psychiatric services with only few patients being treated in primary care. We do not know how many of the 44% of patients who attended only once, got further drug supplies elsewhere but it is likely that many of them did not. This means that the lower estimate of 23% adherence is a more likely estimate than the 41% based on more regular visitors. That would put adherence in Thailand at quite a lower level than reported elsewhere.’

I could not get the figures regarding adherence from table 3 which is poorly set out. (essential)

Response: Table 3 has been re-structured and the text on page 5 and 6, describing the table’s results has been changed accordingly.

Discussion
It is plausible that those attending only once simply discontinue medication, in the UK nearly 50% of those first prescribed discontinue medication in less than 2 month (GPRD data in preparation for publication) In the same data set there are clear differences in adherence between antidepressant classes and I suspect there is a lack of power in this study to show this, the authors should provide an estimate of the adherence difference this study is powered to show- if as I suspect it is underpowered then this section becomes redundant and a statement regarding lack of power to show adherence differences between medications would suffice. (essential)

Response: Please see in the discussion section on page 7: ‘Given the large proportion of patients who switch between drug types, or are on multiple drug types, we cannot calculate adherence for individual drugs.’

The authors also selectively quote the meta analysis (22) which did show differential adherence with SSRI and TCA and a separate comparison to heterocyclic TCAs was equivocal. (essential)

Response: Please see in the discussion section on page 7: ‘One meta-analysis found a higher dropout rate for TCAs compared with SSRIs [23][21], whereas another showed that no significant difference in the discontinuation rate between SSRIs and TCAs
Recently, there has been contrasting evidence whether there is a difference in tolerability between those antidepressants’.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being Published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare I have no competing interest