Author's response to reviews

Title: Public Perceptions and Attitudes towards Thalassaemia: Influencing factors in a Multi-racial Population

Authors:

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Version: 2 Date: 7 September 2010

Author's response to reviews: see over
Dear Sir,

Thank you for your resent email asking for revision and resubmission of this manuscript. I have pleasure in submitting the revision. All the comments by the reviewer have been very useful and indeed the revised manuscript has improved greatly. As much as possible, I have addressed all the comments and clarification needed by all the reviewers. However, in some cases, I have responded to their comments without inclusion in the manuscript.

Also enclosed the Manuscript with correction tracks that illustrate in full details all the changes recommended by the reviewers. In the feedback to reviewer’s comment file, the detail responses to reviewer comments were highlighted in blue.

Please do not hesitate to contact me again if any further changes or amendments needed, I am very much willing to revise this manuscript again if necessary.

Once again, thank you very much for considering and reviewing this article.

Looking forward to your reply.

Thank you.

Sincerely,

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Referee 1
Reviewer's report
Title: Public Perceptions and Attitudes towards Thalassaemia: Influencing factors in a Multi-racial Population
Version: 1 Date: 13 July 2010
Reviewer: Peyman Jafari
Reviewer's report:
The study is well-conducted and the findings are of interest. I have outlined some areas where the manuscript could be improved:
Major compulsory revisions:
Abstract
The “Method” section should mention that the score of knowledge for each patient is recorded as a value between 0 and 21 where higher scores indicate better knowledge.
Amended Abstract
Mean knowledge score was 11.85 (SD±4.03), out of a maximum of 21, with higher scores indicating better knowledge.
Also amended the results section, pg 6
“For each question, a correct response was given a score of one, and an incorrect or 'don't know' was scored as zero, for a total possible score of 0-21, with higher scores indicating better knowledge.”
In the “Results” section the last sentence (Thus, this clearly indicates...) should be deleted since it is appropriate for the Conclusion section.
The sentence has been moved to Conclusion in Abstract
Conclusion: Study shows that carrier and premarital screening programs for thalassaemia may be more effective and culturally acceptable in the reduction of pregnancies with thalassaemia major.

Body of the article
Introduction
Page 4, line 16:
The sentence “studies on knowledge, attitudes and practices related to thalassaemia are relatively scarce in Asia” needs reference. Here is an example:
Removed Asia and replaced with Malaysian context
“Studies on knowledge, attitudes and practices related to thalassaemia are relatively scarce in Malaysian context.”

Methods
Page 5, line 5:
The sample size cannot be calculated with the information presented in the method section. It is unclear how the total sample size was drawn. Please elaborate.
Amended, pg 5
“The sample size required for an approximately 10 million of population aged 18 to 55, for an accuracy level of 0.95 with a confidence interval of ±2.0% was 2400. For the estimate response of only 10% (due to invalid and inactive phone numbers, unreachable, refuse to participate), 24,000 numbers were randomly generated for inclusion in the study from over 2.6 million numbers registered in the 2008 telephone directory.”

Page 7, line7:
Moreover, the authors have mention that internal consistency was considered satisfactory if the coefficient was at least 0.6. However, in literature values of at least 0.7 for Cronbach’s alpha coefficient indicate acceptable internal consistency. Therefore, 0.6 should be changed into 0.7.

Changed to 0.7

Page 7, line 10 & 12- page 12, line 9- page 25 Table 2:
Multivariate and multiple regression: These two terms are not exchangeable (a common mistake in the literature). Multivariate regression is the analysis which deals with many dependent variables, while in multiple regression there is one dependent variable. Therefore, the word of “multivariate” should be changed into “multiple”.

Replaced all “multivariate” with “multiple”

Results
Page 23, Table 1;
It was better if the authors used the multiple logistic regression for computing odds ratios in table 1.

Table 1 is the demographic characteristics of participants, we viewed that it is not necessarily to use multiple logistic regression to compute ORs. Additionally, as suggested by Reviewer 2, even univariate ORs is unnecessary. We therefore removed the univariate ORs column.

Discussion:
The author should compare their results with those of other similar studies in details in discussion section. Page 12, line 5 and page 16, line 4:
In the first paragraph of the “Discussion” section authors have mentioned that “Ethnic disparities in awareness of thalassaemia are not known and this warrants further investigation.”
Also in the last paragraph of the “Discussion” section they have stated: “The study is unique because the sample is multi-ethnic, which has not been reported elsewhere.”
However, the following citation shows that this work is not the only multi-ethnic study in this area.

The sentence has been rephrased, cited study by Armeli et al 2005 as reference 12 (pg 12)
Disparities across the three main ethnic groups (Malay, Chinese, and Indian) in awareness of thalassaemia are not known and this warrants further investigation. Educational efforts are needed to raise awareness, particularly among the Indian groups, to bridge the awareness gaps between people of different ethnic backgrounds in Malaysia. It has been suggested that community-based education program work best to address the knowledge disparities in multiethnic country [12].

(pg 16)
The study is unique because the sample is multi-ethnic, encompassing the three main ethnic groups (Malays, Chinese, and Indians) in Southeast Asia, which has not been reported elsewhere, thus offers many insights that have practical relevance to other Southeast Asia countries.
Page 13, line 20:
The author stated that: “In general, termination of pregnancy is not a consideration in the Asians because of a complex web of moral, cultural and traditional religious values of the family and community. A number of studies showed religious beliefs to be associated with refusal for prenatal diagnosis and termination of affected fetuses among high risk couples [10,17,18].” They have cited studies from Cyprus and Britain to support this argument. However, the authors unfortunately ignored some relevant related work in this area. I recommend the authors include the following very relevant reference whose study subjects share religious beliefs with Malaysian population. Here is two examples:

Added the paper by Christianson et al 2004 and Karimi et al 2007 as reference 20 & 21

Pg15
“Premarital screening to identify carrier couples and subsequently provision of counseling in Iran has resulted in a 70% reduction in the annual birth rate of affected infants and a large amount of medical expenses [21,22].”

This is associated with perceived cultural and religious restrictions on abortion among the Muslim [23]. In this context, premarital screening program coupled with antenatal diagnosis and legalization of abortion before the 16 weeks of gestational age are recommended [22].

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:
No

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Referee 2
Reviewer's report
Title: Public Perceptions and Attitudes towards Thalassaemia: Influencing factors in a Multi-racial Population
Version: 1 Date: 20 July 2010
Reviewer: Manju Mantani
Reviewer's report:
Summary: This is an interesting paper in which the authors have reported knowledge, attitude and practices towards Thalassaemia in the multi-racial Malaysian population.
Major Compulsory Revisions
1. Table 1 – The OR column is both unnecessary and confusing. In a descriptive epidemiological study the authors are better advised not to indulge in statistical testing of hypotheses not defined a priori.

Removed ORs column

Minor Essential Revisions
The mean and median age of the study participants was 35.0 (SD±9.9).

   Replaced ‘unnecessarily’ with ‘unnecessary’

4. Table 1 – I think there is a typo in the percentage of Ever married category: 2510 (32.6). It should be 2510 (67.4).
   Corrected Table 1

5. Table 2 – Under the socio-demographic variable – employment – Please replace ‘In employment’ with ‘employed’ and ‘Not in employment’ with ‘unemployed’.
   Replaced ‘In employment’ with ‘employed’ and ‘Not in employment’ with ‘unemployed’.

Discretionary Revisions
6. Please improve the overall usage of English language and refrain from over-generalization of the results. In that regard, the authors may be benefitted by a professional editing of the manuscript.

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

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

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

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

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Referee 3

**Reviewer’s report**

**Title:** Public Perceptions and Attitudes towards Thalassaemia: Influencing factors in a Multi-racial Population

**Version:** 1 **Date:** 29 July 2010

**Reviewer:** Jenny Hewison

**Reviewer’s report:**

Major Compulsory Revisions

1. Analysis plan and description of results. The multiple regression analysis should be omitted, together with all reference to its results. Only a minute amount of explanatory power is achieved, and the reported statistical significance simply reflects the large sample size. Drawing policy conclusions on the basis of these analyses is misguided and likely to mislead. The same applies to the correlational analyses. **Removing the multiple regression analyses, and correlation analyses would result in reporting only descriptive findings, which may not meet the journal standard. We believed readers will interpret the findings with cautious, based on the reported power and level of significance, as well as other study limitation as indicated in manuscript.**

2. The authors overstate and misinterpret the literature on attitudes to termination in Muslims. The problem is similar to the one above: group differences have to be interpreted in the context of very substantial within group variation, so any policy targeted at groups, or any conclusion based on beliefs about group differences, is not reflecting the more complex reality.
Revised final paragraph of page 15 the issue of termination of pregnancy as suggested by reviewer 4.

Rephrased last sentence in the paragraph
“In short, given the diversity in attitudes towards termination of foetuses within different religions, thalassaemia prevention programmes should consider the beliefs and preferences of individuals in multiethnic society [10].”

3. The termination of pregnancy question in Table 3 is very poorly worded (multiple components, does not distinguish personal views from views of what others should do) and that will certainly have influenced the results. If this was the actual question used, the results must be interpreted with considerable caution.

We regret the limitation of the question, we believed readers will interpret the findings with cautious.

4. More information on source and content of knowledge questions, plus justification for believing they tap all the important knowledge domains.

Enclosed the questionnaire as required by the Editor. Added the following in pg 7.

“The questionnaire was adapted and modified from previous published literature [7,10,12,13].”

Further the questionnaire was reviewed by expert to assess the face and content validation as indicated in Pg 7
“Before data collection, the questionnaire was reviewed by expert to assess the face and content validity.”

5. A much shorter version of the paper, presenting only simple descriptive statistics, and acknowledging throughout the similarities as well as the differences between groups, as well as data limitations, might be acceptable.

Reporting only descriptive findings, which may not meet the journal standard. We believed readers will interpret the findings with cautious, based on the reported power and level of significance, as well as other study limitation as indicated in the limitation section.

Conclusions would need to be tempered accordingly.

Minor Essential Revisions
1. Some of the knowledge questions are difficult to follow in translated English, eg p9 line 6 – what does “either one parent” mean?
“Either one parent” means either father or mother

2. Is “Chinese” a spoken language? Cantonese perhaps, or Mandarin?

Pg 7, replaced “Chinese” with “Mandarin”

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 that I have no competing interests.

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Referee 4
Reviewer's report
Title: Public Perceptions and Attitudes towards Thalassaemia: Influencing factors in a Multi-racial Population
Version: 1 Date: 4 August 2010
Reviewer: Nadeem Qureshi
Reviewer's report:
Review of Public Perceptions and Attitudes towards Thalassaemia,
Authors Li Ping Wong, J A Mary Anne Tan
I enjoyed reading this manuscript and suggest re-submission with appropriate amendments (major compulsory revisions).
Going through each specific sections:
INTRODUCTION
There was a good introduction to the size of the problem in Malaysia.
Major compulsory revisions:
• At the end of the section it would be useful to state more explicitly the objectives of the study (e.g. to identify the understanding about the condition)
  Rephrased and included statement of objective of the study (pg 4)
  “Our study, the first nation-wide survey in Malaysia, aimed to determine differences in Malaysian public awareness, perceptions and attitudes towards thalassaemia and thalassaemia screening practices.”

Rephrased Abstract to include statement of objective
This study, the first nationwide population based survey of thalassaemia in Malaysia, aimed to determine differences in public awareness, perceptions and attitudes towards thalassaemia in the multi-racial population in Malaysia.

• On page 4 “Control of pregnancies” please be more explicit what is meant by this.
  Rephrased
  “Prevention of the birth of children with thalassaemia major is, therefore, important to reduce the prevalence of this disorder.”

METHODS
It is very impressive offering the structured interview in three languages in such a large cohort.
Major compulsory revisions:
• On page 5 it states, “If more than one eligible person is found in the household one person will be selected randomly” How was this done?
  Our enumerator first ask respondent how many adults 18-55 yrs in the household, if N>1, then only one will be randomly sample among all eligible participants.
  Rephased (pg5)
  “Only one person per household was surveyed. If more than one eligible person is found in a household, one person will be selected in a separate random drawing from among all eligible participants.”

• For sample size what was the predicted prevalence measure (stated as +/- 2%) and what measure was assessed for this sample size.
  As also indicated to elaborate by the Reviewer 1, revised.

“The sample size required for an approximately 10 million of population aged 18 to 55, for an accuracy level of 0.95 with a confidence interval of ±2.0% was 2400. For the estimate response of only 10% (due to invalid and inactive phone numbers, unreachable, refuse to participate), 24,000 numbers were randomly
generated for inclusion in the study from over 2.6 million numbers registered in the 2008 telephone directory."

- What was the design of the questions e.g. Likert scale/visual analogue scale. Answer options were “true”, “false” and “do not know” and was read out to all the participants after statement of questions.

Discretionary revisions:
- I assume there is a risk of selection bias as only individuals with phone access were sampled. Was there any socio-economic information on people who did not have phones? I note there is a brief comment about this in the discussion section.

Unfortunately, we do not have the socio-economic information on household who do not registered in the telephone directory.

- How was the survey instrument validated (at least for face validity)?

Yes, the questionnaire was face validated.

Added the following in pg 7

“Before data collection, the questionnaire was reviewed by expert to assess the face and content validity. Changes to the questionnaire were made as recommended.”

- How was it ensured that those who answered small red blood cells or shortage of blood (page 5-6) were thinking of thalassaemia as opposed to another cause e.g. iron deficiency anaemia?

The interviewers were informed not to provide information other than “Thalassemia is a disease with low numbers of red blood cells or shortage of blood”, as the detail will be assessed in the knowledge section.

Nevertheless, all the interviewers were university students and they were comprehensively briefed about this genetic disorder. They were also enlightened that in case respondents erroneously think that thalassaemia is anaemia, they would further informed participants that thalassaemia is NOT anaemia but it causes anaemia due to a defect in haemoglobin production.

Furthermore, interviewers were informed to cite the disease in different languages, Malaysia national language, Mandarin and Tamil, to respondents of respective ethnicity, thus, participants completed the interview were those that have heard or aware of thalassaemia.

**RESULTS**

There are several very interesting findings in the results, specifically:

- Misconceptions (page 9)
- Cultural differences in attitude and practice (page 10-11)

- In particular, the highly significant finding that nearly 23% state that they would be willing not to continue on with their partner if they were both carriers (page 11). In the discussion it would be worth considering these findings in relationship to other studies like this (e.g. Scrivers work in Montreal).

Added studies by Scrivers as Ref 24 and 25

“It was reported that the majority of carriers identified in a high-school screening program remembered their status, favourable of knowing the status of their partners, and willing to take options for reproductive counseling and prenatal diagnosis [24]. Likewise in this study, among the young unmarried participants, near 23% indicated not willing to continue to be with their partners if both are thalassaemia carrier, and 32% indicated willingness to abort their baby if the child has been diagnosed with thalassaemia major. An earlier study in Montreal showed that high-schools students have high level of interest in thalassaemia screening, with participation rate of near 80% [26]. This again indicates that school-based carrier screening may lead to favorable outcomes.”
Major compulsory revisions:
It is important when performing multiple analyses that care is taken in interpreting findings. On page 8, Knowledge section, I would be careful commenting on the significance of several characteristics in table one.
The significance analyses in Table 1 has been removed as suggested by Reviewer 2

Discretionary revisions:
• It would have been interesting to compare the responses between individuals who recognise a diagnosis of thalassaemia and those who specified a non-specific diagnosis (small blood cell/shortage of blood). We are not able to compare the responses as those who did not recognize thalassaemia did not proceed to answer the questions.
• Any information on 45% of sample that were non-responders. If there was no information on age or sex perhaps information on the locality of the phone (more likely not to respond if they have lived in a deprived area?). We have only the information about the ethnicity of non-responders, unfortunately the gender and age of non-responders were not recorded.

Added the following in pg 8.
“The Chinese have the highest non-response rate (56.5%), followed by the Indians (40.4%) and the Malays (39.1%).”

DISCUSSION
The authors had a thoughtful description of the implications with respect to low educational status. They highlight the importance of improving the genetic health literacy of the population. Also on page 14 there is a good discussion of the public health implications of their findings.

Major compulsory revisions:
• Page 12. In the first paragraph, the principal findings is really dependent on the specified objectives. I would suggest that the findings related to attitude and practice (see my comments in the results section) are the most relevant. Further, description of mean scores as a principal finding is perhaps not that relevant, particularly considering this is not a validated instrument.

As indicated in pg 7 of Method section, the questionnaire underwent face and content validation by expert of the field. Further, the knowledge score had a Cronbach’s alpha reliability coefficient of 0.86, indicated high reliability of the set of question.

Reporting only the findings of attitude and practice would be merely descriptive and may not meet the standard of the journal

• On page 13, participants stating pre-marital screening as unnecessary is described as a concern. Please elaborate why this is a concern.

Added the following, pg 14
“Of concern is a considerable minority of participants that perceived premarital screening as unnecessary for the general public. The current quantitative study limits in-depth exploration of the reasons for refusal. The reasons participants perceived premarital screening as unnecessary warrant further investigation in future studies. Literature reports have also indicated that when extended family members were approached to identify carriers in the family tree, the responses were usually unfavourable due to the fear of being stigmatised and in particular, concerns about possible implications in future marriage prospects [7,17]. Religion is also believed to have a significant impact on decisions about screening [10].”
• In the final paragraph of page 13 the issue of termination of pregnancy is described. It would be useful to give some societal perspective on the acceptability of termination (e.g. forbidden by government legislation). The societal norms would impact on how individuals perceive termination.

Added the following in pg 14
“Under the section 312 of the Penal Code (Amendment) Act 1989 of Malaysia, an abortion is only permitted if the pregnancy is likely to result in danger to the mother’s physical and mental health. Unfortunately there are very few studies looking at societal perspective on the acceptability of termination of pregnancy in Malaysia context.”

• Limitations are described in some detail, but very limited information on the strengths of the study. I would suggest that having the participants complete a structured telephone interview is far more likely to have an appropriate completion rate than a self-administered survey.

Added the strength of the study in pg 17
“Another advantage is that the high response rate of 54.9% was achieved, with 3723 completed survey over 6777 contacted household, compared to self-administered survey [30].”

• On page 16 the demographics of the participating population are described as similar to the general population. No data is provided to support this statement.

Other demographics, beside proportion of ethnicity, of the participating population are similar to the proportion in the recent Social Statistics Bulletin Malaysia, 2008.
“The proportion of ethnic, highest educational achievement, and average household income of the sample matches the proportion in the general population [29], suggesting that these results may be reflective of national trends.”

Discretionary revisions:
• On page 13 there was a good point about facilities for pre-marital and pre-natal diagnosis, but I am unclear how this comes out of the results.

Added reference citation to the statement.
“Facilities for premarital and prenatal diagnosis to confirm the molecular mutations involved, and genetic counseling services will contribute to a reduction in the numbers of babies born with thalassaemia major [1,8,9].”

• On page 15 the cross-sectional design is described as a limitation. I am not sure if this really is an issue when you are carrying out a knowledge and attitudinal survey.

Removed the cross-sectional design.

ABSTRACT
A key point in the results is the nearly 14% of married participants that have not been screened. Also see comments in Results section.

Major compulsory revisions
At the end of the results section indications for carriers and premarital screening are described. Firstly, it is not appropriate to put this in the results section and secondly, I am not sure how this comes out of the results.

The statement has been moved to conclusion, as also suggested by reviewer 1

Discretionary revisions:
In the conclusions, educational interventions are suggested but this again is not mapped directly to the results of your study.

Educational interventions are suggested due to lack of knowledge and knowledge disparities among ethnicities and other socio-demographic characteristics indicated in the results section.

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.

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