Author's response to reviews

Title: Mobile phone use and stress, sleep disturbances, and symptoms of depression among young adults - a prospective cohort study

Authors:

Sara Thomée (sara.thomee@amm.gu.se)
Annika Härenstam (annika.harenstam@av.gu.se)
Mats Hagberg (mats.hagberg@amm.gu.se)

Version: 2 Date: 6 September 2010

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

Please find a revised version of our manuscript (with the new title): *Mobile phone use and stress, sleep disturbances, and symptoms of depression among young adults – a prospective cohort study* submitted for publication in BMC Public Health.

Thank you for the constructive and valuable comments from the Associate Editor and two Referees! We have carefully considered and revised the manuscript according to the comments, presented point-by-point below. We believe that the manuscript has been much improved owing to the comments.

We hope our responses and revisions satisfactory addresses the issues. The alterations can be seen with “tracked changes” in the documents. All authors have read and approved of the final manuscript.

Kind regards,

Sara Thomée

Occupational and Environmental Medicine
Department of Public Health and Community Medicine
University of Gothenburg
Gothenburg
Sweden

The Associate Editor:

- Provide rationale for age range 20-24.

We wanted to study young adults, which is a group on the verge to work life and societal life. It is also a group with high ICT usage as well as a reported increase in mental ill health. The age range 20-24 corresponds to the UN definition of young adults, which is now added to Methods – Study population and data collection.

- How likely is there a bias due to the high non-response?

We know that women and native-born Swedes are over-represented in the study group. There is probably a healthy participation selection bias, including a tendency toward lower mobile phone use. This should have more effect on the cross-sectional results, than on the prospective results. The probable gender bias is handled by analyzing men and women separately. Possible biases are mentioned under Methodological considerations in Discussion.

- Page 8: 4156 or 4163?

There were 4163 respondents to the 1-year follow-up questionnaire. For this particular study, those who had not responded to either question concerning frequency of mobile phone calls and SMS use at baseline were excluded (n=7), leaving 4156 participants in the study group. This is described on page 8 and in Figure 1 (former Figure 2).

- Why Cox regression? Why not logistic regression?
The Cox proportional hazards model can be used “technically” to obtain PRs in cross-sectional studies, when analyzing multiple variables. When the prevalence of the outcome measures is relatively high, as in our study (16-48%), the OR obtained from logistic regression is likely to be higher than an actual PR (Coutinho, Scazufca et al. 2008). The OR can be more difficult to interpret and there is a risk for over-interpretation of the size of associations. Thus, we think it is more appropriate to compute PRs than ORs in this context. It is recommended that the Cox model with the robust variance option is used in cross-sectional studies, to correct for overestimation of the variance, due to the fact that there is no time to follow-up, or the CIs will be too wide. We have now used the robust variance option (proc phreg covs) in SAS for the cross-sectional analyses (Deddens and Petersen 2008), and have corrected the CI’s in Table 4 (former Table 6). However, in prospective analyses the CIs are still conservative. The procedure has been added to the Analys section as well as references (Coutinho, Scazufca et al. 2008; Deddens and Petersen 2008) for the choice of method, and is mentioned in Discussion.

-What is the validity of the outcome measure? Please discuss.

The stress variable is based on a single item which has shown satisfactory content, criterion, and construct validity for group-level analysis (Elo, Leppänen et al. 2003). The sleep disturbances variable is a non-validated item, constructed by including the most common primary sleep disorders (insomnia, fragmented sleep and premature awakening) into a single-item, adapted from the The Karolinska Sleep Questionnaire. Responses were divided based on clinical significance, i.e. reporting sleep disturbances several times per week or more, compared to reporting sleep disturbances a few times per month or less. The PRIME MD depressive items have been validated in several studies, and the probable high sensitivity/low specificity in our study, is discussed in Methods and in Discussion. Information about the outcome variables has now been added to Methods in text (instead of as footnotes to former Table 3 (now Table 2)), and the validity of symptom-reports is discussed in Methodological considerations.

-Reduce both the number of Tables and the length of the Discussion.

Table 4 (Study group characteristics at baseline) has been omitted and is instead described in text under Results - Study group characteristics. We have merged Table 1 (Mobile phone exposure variables) and Table 2 (Mobile phone use at baseline) into one (Table 1). Thus, we now have 4 tables instead of 6.

The discussion has been restructured and shortened. However, additions to the discussion have also been made in accordance with reviewer comments.

-Report on Tables in the right order: 1, 2, 3... etc. (Results Section).

The Tables are now reported on in the right order in the text. Table 1 is both a methods’ table and a results’ table, while Table 2 is only a methods’ table. Thus, the order of the tables referred to in the Results’ section will be 1,3,4,5.

-Please consider the possibility of chance findings due to multiple testing, but simultaneously consider the pattern and direction of effects across tests, without focusing too much on p-values. This pattern and consistency across tests might also provide confidence in the findings (and thus might indicate robustness).
We agree that there is a risk of chance findings when performing multiple tests and that it sometimes is appropriate to correct for this. However, in our study, the variables we test are not chosen by random, but are deliberately chosen (hypothesized) because of previous findings. They are all within the aim of the study.

Pattern: In the cross-sectional analyses all but one of the PRs were larger than 1.0 (although all CI's were not) and all the high categories of exposure generated a higher or equivalent PR compared to the medium categories, indicating a consistent pattern and even a dose-response relationship between the exposure variables and mental health outcomes (if only looking at PRs). In 38 of 40 prospective analyses the high category generated a PR above 1.0. All in all, 7 of 80 PRs (medium included) were under 1.0 (none statistically significant). In a majority of the prospective analyses (32/40) the high category of the exposure variable generated a higher PR compared to the medium category. Eight of 80 PRs were under 1.0 (ns). The consistency of pattern is now commented under Discussion.

-Page 15: Please clarify or re-formulate or re-consider: "It can of course be argued that this variable........... how we react to it".

We have omitted this passage while shortening the discussion.

As the 2nd reviewer also indicates, please clarify, perhaps throughout the whole text, the extent to which this manuscript is about "psychosocial exposure" and/or "biophysical exposure". Could there not also be a biological pathway? How likely or unlikely is that?

We predominantly take a psychosocial perspective on mobile phone exposure in the study. We have clarified this in the introduction and aims and where needed in the manuscript. We have also added a few references to biophysical research in the introduction and discussion, to contrast our perspective.

**Referee 1:**

**Minor Essential Revisions**

1: The authors divided responses into three categories, as shown in page 9 and Table 1. How did they categorize variables from frequencies of mobile phone usage and psychiatric symptoms? Do they have any statistical explanation about categorization?

The exposure variables were categorized into high, medium, and low, based mainly on the frequency distributions. We did not aim to analyze extreme portions of exposure, and so wanted the high category to contain about 25% percent of the study group. For the overuse variable categorization could only be based upon the two items concerned (high=3% and 7% for the men and women, respectively). The mobile phone use variable was constructed by merging the Calls and SMS variables. To do this we made a cross-table of the two items, to oversee how categories could be merged with a contrast between the categories. The high and low categories’ content (number of calls and messages) do not overlap. However, there was no obvious way to create the medium category without some potential overlapping, which is also mentioned in the discussion. We might want to point out that the categorization was performed before analyses of outcomes. We have described categorization in text in the Methods and added the categories to Table 1 (former Table 2). The overlap and possible misclassifications are mentioned in Methodological considerations in Discussion.

The mental health outcomes were categorized 1 or 0. The categorization of current stress was based on frequency distribution in combination with taking into account the content of the response sets. This categorization has also been used in Elo et al. Sleep disturbances
was categorized based on clinical significance, where the cut-off was set at reporting sleep disturbances several times per week the past month. The depression symptoms were based on the two items from the PRIME-MD screening form (Patient Questionnaire). We formed three categories: No items, one item, and two items. In a clinical setting it is sufficient if one of the two depressive items is confirmed to go forward with a clinical assessment of mood disorder according to the manual. However, the sensitivity with this procedure seems to be very high in our population, considering that more than 50% confirm at least one of the two items. The categorization of the mental health outcomes is now described in text in Methods, instead of as footnotes to Table 2 (former Table 3) and discussed in Discussion.

2: Limitations seems too long in Discussion. The authors should shorten it.

The discussion has been restructured and limitations have been shortened. The limitations’ heading is changed to Methodological considerations. However, as mentioned above, additions to the discussion have also been made in accordance with reviewer comments.

3: The authors should show statistical significance level $p<0.01$ as well as $p<0.05$ in Table 5.

Significance levels ($p<0.001$, $0.01$, $0.05$) are added to Table 3 (former Table 5).

Referee 2:

Major comments:

The authors present tables of association of exposure and mental health at baseline and of exposure at baseline and incidence of symptoms at follow-up. It would be good to see an additional analysis that looked at it the other way around: What happens to the people who report symptoms at baseline and who decrease their exposure? Does their mental health improve? It would considerably strengthen the conclusions if this effect could also be shown.

We definitely agree that this type of analysis would be of interest. However, it was not in the aims of the present article to explore the effect of change in exposure. We have considered this for future articles.

In the analysis, adjustments are made for some potential confounders. Please explain what the effect of these confounders was on the effect estimates.

We tested all confounders separately. The confounders were not consistently significant ($p$ value of 0.10 or less) over all analyses. However, instead of adjusting for different factors in different analyses, we preferred to use the same confounders in all analyses. The general effect of adjusting for the potential confounders was a lowering of the PRs, and several analyses lost statistical significance. In the prospective analyses of depression (2 items), the PRs actually increased slightly for men (though no increase of statistical significance).

In addition, accessibility stress (as well as other categories of exposure) might be related to other, as yet unmeasured factor, such as personality traits. These traits could also be related to developing symptoms over time. This issue should be discussed as a limitation of the study.

This is now discussed in Methodological considerations.
While I don’t think that the use of Cox proportional hazard models is fundamentally wrong in this context, I wondered about the reasons to use it. The authors might wish to reconsider and use e.g. logistic regression, where it is no problem that there is no person time to follow up at baseline, and exactly the same interval of follow-up time for every study participant. Also, the associations would be expressed simply as OR which is sufficient in the context of this analysis.

Please see our response to the Associate Editor, above.

This would also make terminology slightly simpler (because what is now called prevalence ratio at follow-up is actually the incidence ratio).

It is true that the estimates from the prospective analysis could be considered incidence ratios. However, the mental health outcomes are not definite such as chronic illness or death. The time span of the items is “currently” or “the past 30 days”, i.e. the mental health symptoms could come and pass in the latency time. Hence, we prefer to use the term prevalence ratios.

Tables 6 and 7 list the total n of the groups and percentages of the symptomatic population. It would be easier to understand if also the n of the symptomatic group was added.

We agree that adding the n of the symptomatic groups could increase understanding of the analytic process. On the other hand, the prevalence % is given and so it is quite simple for the reader to calculate the symptomatic n. Taking into consideration that the tables are rather large already, we think it might not be necessary to add the column.

Also, some of the numbers do not add up. For example, the n in Table 7 should be n of Table 6 minus symptomatic group (minus some missing data). This is fine for the women with current stress (second line), where 2695 minus 29% (=782 persons) symptomatic population equals the 1913 women in Table 7. However, the same calculation for the symptoms of depression yields 692. Either there are some bigger mistakes in the Tables or the authors should explain and discuss in some more detail where this difference comes from and what 61% of missing data means for the interpretation of the results.

We realize that we have not been clear in our description of how the analysis of Symptoms of depression was performed. The reason for the numbers not adding up was that we had excluded all 1-item responses from analysis (due to the probable high sensitivity/low specificity discussed above). This was described in footnotes to the tables. Now, instead of excluding the 1-item responses, we account for them as Symptoms of depression – 1 item. Hence, we now have 4 outcome variables, which is described in Methods and accounted for in Results. Furthermore, to simplify Tables 4 and 5 (former 6 and 7), we have omitted the rows containing the prevalence of mental symptoms and describe the data in text instead under Results – Study group characteristics.

We hope that this satisfactory addresses the problem with missing data.

The main conclusions in the manuscript relate only to mobile phone use. The way it is written now it could be misinterpreted to be related to the biophysical aspects of exposure (non-ionising radiation dose). This should be rephrased to make it clear that only psychosocial aspects of mobile phone use were assessed.
Please see response to Associate Editor, above. It is very important that misinterpretation of results is avoided. We have now clarified in introduction, aims, and discussion that we take a psychosocial perspective on mobile phone exposure.

In addition, accessibility stress had a more consistent effect on symptoms. This could be presented in the conclusions in a more balanced way.

We have added this to the conclusions. (The risk for reporting mental health symptoms at follow-up was greatest among those who had reported that they perceived the accessibility to be stressful).

Minor comments:
Figure 1 could be omitted from the manuscript as it does not add to the understanding of the context.

Figure 1 is now omitted.

In its current form, the presented data do not inform about changes about exposure and outcome reporting at the two time points. How many persons change their exposure status? It would be nice to see such a table added.

We agree that that information could be of interest. However, the Associate Editor has requested a decrease in number of tables, and since analyzing changes of exposure is not within the aims of the study we have not added this data.

The drop out analysis could be moved to the results part.

We have moved the drop out analysis to Results.

Reduce the length of the introduction. Some parts of the introduction could instead be used in the discussion section.

We have shortened the introduction.

The discussion section could benefit from some shortening and restructuring, for example into the more conventional form of a short sub-summary of the main results, the strength and limitations, the comparison with other studies, the mechanisms that might be at work, and the conclusions.

We have restructured and shortened the discussion. However, as mentioned above, additions to the discussion have also been made in accordance with reviewer comments.

The manuscript might benefit from some English language editing. Currently there are some sentences where the meaning is somewhat unclear (e.g discussion section p15: "It can of course be argued that this variable is close to the outcome. We find the variable of interest, though, since how we value the exposure probably has an effect on how we react to it”).

We have omitted the passage (as mentioned above) while shortening the passage. We have also edited the language and so hope that meaning over-all is clearer.

The wording “mental symptoms” is unclear. Maybe change to “symptoms of reduced mental health”.
We agree that “mental symptoms” is unclear. There is a need to summarize the outcome variables now and then, e.g. in the text and tables. We have changed to “mental health symptoms” and “mental health outcomes”. “Mental health symptoms” was suggested in connection with professional copy-editing of the manuscript, and we define what we mean with mental health symptoms in Methods. Furthermore, we have replaced “mental symptoms” in the title with stress, sleep disturbances, and symptoms of depression.

The headers of Table 6 and 7 are misleading since these tables deal with psychosocial aspects related to mobile phone use including frequency of use.

We have changed to “mobile phone variables” in the headings. There is a limit to number of words allowed in the table headings which makes it difficult to be more specific. We hope that the statements in the introduction and aims sufficiently explain that we do not take a biophysical perspective on mobile phone exposure.

In Table 2, the “overuse of mobile phone” is the only category that does not include the n for the reference (low) group.

The no-item (low) category has now been added to the table. Also, data in the cells have been corrected and the order of the high, medium, and low category is now switched to match the rest of Table 1 (former Table 2).

