Author's response to reviews

Title: Self-reported prevalence of atherothrombosis in a general population sample of adults in Greece; A telephone survey

Authors:

Nikos Maniadakis (nmaniadakis@esdy.edu.gr)
Georgia Kourlaba (kurlaba@hua.gr)
Vasileios Fragoulakis (yfragoulakis@esdy.edu.gr)

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Author's response to reviews: see over
Reply to Reviewer's report
Reviewer: Demosthenes Panagiotakos

This is a well written paper by a respectable group of authors; congratulations for your efforts! Presentation of prevalence data is always important for any population, thus I believe that your work deserves publication following minor revisions.

Reply: We would like to thank Prof. Panagiotakos for considering our work interesting. Moreover, we would like to thank him for his extremely useful comments. These comments help us improve and enrich our manuscript.

1. In general, pls correct several grammar and syntax errors throughout the paper, i.e., However, for the evaluation of the economic burden of atherosclerotic disease in the country, …Table 3 presents … a Table does not present anything, it should be …in Table 3 … are presented.

Reply: We have corrected several errors.

2. Abstract / Methods … please report mean age+/-SD (using the weighted mean, since you have recorded age in classes), % of males of the study’s sample, participation rate (responders)

Reply: We have provided these data in the abstract of the revised manuscript.

3. Abstract / Conclusion … report the limitation of telephone reporting of clinical conditions, i.e., Despite the limitations may occur due to the sampling procedure, atherothrombosis affects a large portion of the …

Reply: We have assessed this comment.

4. Methods … Pls report 3007 people out of ??? (i.e., participation rate)

Reply: For the purposes of the specific research 100,000 distinct phone numbers from Greek households were loaded in our phone centre. From those 89,526 phone numbers were used and only 41639 were handled calls (communications) the rest being rejected due to various reasons (No answer, Busy, …). From those 41639 calls that got handled by a research agent only 3007 resulted to a completed questionnaire the rest were either denials or were unsuitable for the specifications of the survey. Therefore, the participation rate regarding the communications can be estimated as \( PRe = \frac{3007}{41639} = 7.2\% \). If we consider only the communications that were valid to participate in the survey then only completed and denials will be included so the \( PRv = \frac{3007}{(3007+15751)} = 16.0\% \).

5. On what basis the sample size was decided

Reply: The initial planning requested that a maximum error of 2% is permitted in estimating proportions with probability 95%. This translates to a sample size of 2400 questionnaires. However, further discussions pointed out the need of having a bigger data base for better estimating smaller regions of Greek population. So, a new planning was made for 3000 completed questionnaires.
6. Was it computer-assisted telephone numbers selection? Pls explain.

Reply: The whole project was implemented in a C.A.T.I. environment. Telephone numbers were loaded in a phone centre and were distributed to agents on availability basis. When a call resulted to an answer the questionnaire appeared to the agent and the communication was initiated. All agent and campaign activities were monitored by supervisors through performance – monitoring software. Additionally, all agent and campaign activities were stored on a server from which data gathered from all agents were drawn and analyzed using statistical software.

7. Any info about the non-participants (i.e., regional profile; reasons for not participating? etc); how long was the interview?

Reply: Examining the characteristics of the non-participants was beyond the purposes of the project. However, from the initial planning, minimizing the non-response rate was taken into big consideration using available C.A.T.I. tools. For that purpose several routines were implemented during the dialling process to minimize that error. The main routine can be summarized as follows:

1. Dial a specific number.
2. If the number is “Busy” dial it again after 1 hour up to a maximum of four times per number for that specific reason.
3. If the number is “No Answer” dial it again after 4 hours up to a maximum of two times per number for that specific reason.
4. If in total 4 additional dialling attempts where made, regardless of the reason, reject the number.

The average time of completion of a questionnaire was 3 minutes and 21 seconds.

8. More details on the measurements are needed, i.e., you mention smoking habits were recorded i.e., smoker or non-smoker?, current, former? … diagnosis of clinical conditions was self reported due to the nature of the study, but did the investigators asked about signs / symptoms / person who clinically diagnosed the health status? Was the definition of health status based on established guidelines? I assume yes, but it should be reported … .

Reply: We have provided more details regarding the definitions used for the investigated health status.

9. The statistical analysis although correct, needs more advanced approaches to be followed, i.e., I suggest to the authors following a multivariate analysis, i.e., to cluster RFs by gender, age group, region etc and to compare these clusters based on their associated costs to the community …

Reply: We have provided results of more advanced statistical methods in the revised manuscript.

10. It is not surprising that the reported figures are in accordance with the results of the National Health Survey (Ref #4), since this was a telephone survey, too, with similar limitations. Thus, more discussion should be made based on this study and not on the EPIC, ATTICA, MetS etc that were based on direct clinical evaluation. So, my last, but not least comment is a strong prompt to the authors to re-arrange their discussion based on the differences observed in surveys that followed procedures
similar to the one presented here vs. face-to-face surveys … there are a lot of differences observed in the reported rates that could be explained by several behavioural mechanisms observed in telephone surveys, but also these differences could be modeled in order to provide a methodological basis for future similar studies. For example, the paper by A White on “Response rate calculations in RDD telephone surveys”, as well as similar methodological works on RDD telephone surveys should be included in a “good” methodological paragraph in the Discussion section. By this way the authors are encouraged to moderate their discussion about the actual rates of CVD RFs, which based on the sampling method could be misleading.

Reply: We would like to thank Prof. Panagiotakos for this useful comment that help us improve our discussion section. Following this comment, we have re-arranged our discussion section emphasizing on the comparison of our results with those provided of similar studies. We have not removed at all the results of the previous large epidemiological studies taking into account the comment of Prof. Athyros that reported that our results indicate that the prevalence of CVD risk factors and CVD is much lower than those reported from other studies. However, we have mentioned that our results are not in accordance with those of previous studies mainly due to different study design. Moreover, we have provided a paragraph discussing the methodological issues related to RDD studies compared to face to face studies.
Reviewer: Vasilios G Athyros

We would like to thank Prof. Athyros for his useful comments that help us improve and enrich our manuscript. We have modified our manuscript following his comments and we are prompt to do any other change if it is considered necessary.

2. Are the methods appropriate and well described?
The use of random telephone interview is not probably the best method to find a representative sample of general population. There might incur a patient selection bias.

Reply: We agree with Prof. Athyros that the current study design is not the most suitable one for finding a representative sample. We have emphasised on the discussion section that although RDD surveys are vulnerable to response bias that may affect the representativeness of the study, based on the initial planning of the study, individuals were unsuitable for interviewing if they belonged to a combination of age group-gender-region (i.e. strata) for which the necessary number of participants had been enrolled, in order to ensure the age-gender-region representativeness of sample.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
No. The paper reports very low prevalence of CVD risk factors and overt CVD cases. In other studies from Greece (ATTICA, EPIC, and MetS-Greece) the prevalence of these CVD risk factors and overt CVD cases are much-much higher.

Reply: We agree with Prof. Athyros that the prevalence of CVD risk factors found in the current study is lower compared to that reported in ATTICA, EPIC, and MetS-Greece. However, the current figures are in accordance with those reported in the National Health Survey which is a telephone survey, too. The differences identified between our results and the results of ATTICA, EPIC and MetS-Greece are attributed to the different study design of these studies. Moreover, it should be highlighted that our results are more close to the proportion of the participants of other studies that were found to be aware of their conditions and/or they are treated. We have clarified this topic in the revised manuscript.

4A. Panagiotakos DB, et al. Status and management of blood lipids in Greek adults and their relation to socio-demographic, lifestyle and dietary factors: the ATTICA Study Blood lipids distribution in Greece, Atherosclerosis 173;2004:351-9 ATTICA included 1128 men and 1154 women, and 46% of men and 40% of women had total serum cholesterol levels >200 mg/dl. Of them, 40% of men and 30% of women were unaware of their condition. Twenty-one percent of men and 7% of women had HDL–cholesterol levels <35 mg/dl.

Reply: We have provided these findings in the revised manuscript in Table 6. It is clear that the prevalence of hypertension and hypercholesterolemia is higher in ATTICA study, however the percentage of hypertensive and hypercholesterolemic participants that are aware of their condition is similar with those finding in the current study (Table 6).

**Reply:** We have provided these data on Table 6.


The prevalence of hypertension in 26,913 adults is 40.2% for men and 38.9% for women (age-adjusted to the adult Greek population of 2001). In the sample examined, awareness among hypertensives is 54.4%, pharmaceutical treatment among those aware is 83.9%, and effective control among hypertensives is 15.2%.

**Reply:** We have provided these data in the revised manuscript and it is clear that the percent of awareness is similar with this reported in the current study (Table 6).


The fully adjusted prevalence of vascular disease in those with the MetSyn (n = 984) was 29.4%, significantly higher than in those without (n = 3169, 9.6%, p < 0.0001), while subjects without both the MetSyn and DM had the lowest vascular disease prevalence (n = 3035, 8.9%). Subjects with the MetSyn but no DM (n = 674) had a vascular disease prevalence of 24.1% (p < 0.0001 vs. those without the MetSyn), which was similar to that in subjects with DM without the MetSyn (n = 134, 25.4%), but lower than in those with both the MetSyn and DM (n = 310, 40.7%, p < 0.0001 vs. all).

**Reply:** We have provided the findings of this study in the revised manuscript (Table 6). It is true that the prevalence of vascular disease in the present study is a little lower compared to the study of Athyros VG et al. However, this difference could be attributed to the different study design of the two studies (i.e. the sample of the study of Athyros et al was obtained by the hospitals and not in the general population).

4E. Thus, it seems that data reported in this paper were those that patient knew. This is self reported prevalence and can not be used as a basis to evaluate treatment costs (to evaluate the economic burden of the disease in this country) as stated by the authors. This is because real the prevalence of CVD risk factors and the real number of patients with overt CVD are much higher. Therefore, even the title should change and say (Self reported prevalence of atherothrombosis in a general population sample of adults in Greece; An observational study).

**Reply:** We agree with Prof. Athyros that self-reported data underestimate the prevalence of these conditions/diseases. However, the actual direct health care cost at a national level is estimated based on the utilization rate of health care resources (i.e. outpatient visits, hospitalization, medications, interventions etc). Therefore, the percent of population that is aware of a condition/disease and use health care resources is the appropriate proportion in order to provide an accurate estimation of the direct health care cost. We have provided this information in the introduction of
the revised manuscript. Of course, the use of self-reported prevalence may lead to an underestimation of indirect cost due to productivity loss and this limitation will be reported in the ongoing paper presenting the economic burden of atherothrombosis in Greece. Finally, we agree with the suggestion of Prof. Athyros to change the title and we have addressed this comment accordingly.

5. Are the discussion and conclusions well balanced and adequately supported by the data? Yes, but some greater emphasis should be put on study limitations.  
Reply: We have provided the limitation of our manuscript in more details in the revised manuscript, giving greater emphasis in the limitations of the RDD.

6. Are limitations of the work clearly stated? Some greater emphasis should be put on study limitations.  
Reply: We have provided the limitation of our manuscript in more details in the revised manuscript, giving greater emphasis in the limitations of the RDD.

8. Do the title and abstract accurately convey what has been found? The title must be changed (please see above).  
Reply: We have changed the title of the manuscript following Reviewer’s suggestion