PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Variation in minimum desired cardiovascular disease-free longevity benefit from statin and antihypertensive medications: a cross-sectional study of patient and primary care physician perspectives
AUTHORS	Jaspers, Nicole; Visseren, Frank; Numans, Mattijs; Smulders, Yvo; van Loenen Martinet, Fere; van der Graaf, Yolanda; Dorresteijn, Jannick

VERSION 1 – REVIEW

REVIEWER	stephen fitzgerald The Royal Adelaide Hospital Australia
REVIEW RETURNED	26-Jan-2018

GENERAL COMMENTS	This is an important addition to the literature indicating a mis-match between patient expectations and values and medical guidelines and treatments. I suggest some improvements. The title is not quite accurate- i suggest for example-' Variation in the magnitude of the estimated cardiovascular-disease-free life expectancy benefit from statin and antihypertensive therapy considered to be worthwhile.' The current title suggests a paper examining the actual variation in benefit. I am a little concerned about the example calculation (page 31). The calculated gain in CVD-free-life expectancy is 2.5 years. This does not lead to the next line where 38.5 years is quoted as the remaining CVD-free-life years on treatment. The onset of CVD may be well before the estimated death .The individual for example may have the onset of CVD delayed from age 60 to age 62.5 and there may be less effect on total life expectancy than on CVD life expectancy. Please check that there has not been an error here. Figure 3 legend discusses blood pressure lowering rather than statins? Both figure 3 and figure 4 would be improved if rather than just having orange for what is thought worthwhile ,there was a comparison between what guidelines recommend and what individuals think is worthwhile, squares could be coloured to indicate treatment as per guidelines and or meaningful benefit.. This could be fed into the discussion. In this context it should be remembered that when mean values are used there is still a large proportion of individuals who do not think that level of benefit is satisfactory. this compares with guidelines that imply that ALL patients at this level should be treated. The discussion point that guidelines need not be adapted to views of meaningful therapy might be justified. Extending this argument to measurements of quality of care might also be included.

REVIEWER	Peter Pype Ghent University Belgium
REVIEW RETURNED	05-Feb-2018

GENERAL COMMENTS	Dear authors, I liked reading this original paper describing an important issue. I have some questions I would like to see answered: 1. There is a lot being published on 'risk communication'. Bottom line is that the way you present your question describing a certain risk, influences heavily the way people answer. Can you describe some of these principles in the introduction or method section? 2. Can you explain why the questionnaire has been pretested with physicians and not with patients? It seems to me that the understandability is a bigger concern with the latter. 3. The fact that median threshold did not differ between patients on and off-therapy or between patients without versus with CVD requieres a bit more elaboration in the discussion as this is (to me at least) somewhat unexpected. 4. similarly I would like to see a reflection on preventive medicin in general. Literature sometimes raises questions about the overall benefit of prevention (with or without comments on pharmacy-guided research or guidelines) especially in primary prevention. The fact that current medication does not seem to be able to deliver what patients expect might feed this discussion.

REVIEWER	Emily Atkins The George Institute for Global Health, University of New South Wales AUSTRALIA
REVIEW RETURNED	13-Feb-2018

GENERAL COMMENTS	The manuscript describes the conduct and results of a survey conducted with primary care physicians and people with - or at high risk of - cardiovascular disease to determine the desired gain in healthy-life-years from both a decade and a lifetime of treatment with statin or blood pressure lowering therapy. A multiple-choice questionnaire was used to gauge how much additional life expectancy was perceived to make primary or secondary preventive pharmacotherapy worthwhile. The authors then compared the desired benefit against calculated 'clinically attainable' benefits expected from lipid-lowering or blood-pressure-lowering therapy and illustrated theses in risk factor charts. The authors reported a 10-minute introduction to individual therapy-benefit for participants to ensure informed and comparable responses, but it is not clear what the content of this talk was, or how it may have influenced the results. The language is generally clear and the paper is well structured. The concepts of desired benefits from treatment for patients and their doctors is important, and it is interesting to see here how the perceived disutility of taking cardiovascular medicines translates into hypothetically sacrificed months of healthy life. However, it is possible a lack of understanding in what is an achievable benefit from these therapies is what is leading to such high expectations.

	Specific comments: Abstract: Is it the median reported before the IQR? This should be clearer. The outcome is defined as 'months gain of CVD-free life expectancy at which therapy is considered worthwhile' but described as 'meaningful benefit' in the abstract results. There should be consistency in the language used in the abstract. Methods: please consider adding further description of the introduction to individual therapy benefit, or perhaps providing in an appendix for interested readers. Results: The comparison of clinically attainable and meaningful benefit thresholds would benefit from more in-text reporting. Figures 3 and 4 are tricky to interpret (please check the descriptions, both mention statins, but one should be blood-pressure lowering therapy), and seem to contradict some of the discussion about treatment in older high-risk patients versus younger patients with high SBP or lipids. Also the results from the question about acceptable treatment duration for 1 year gain in healthy life do not appear to have been reported. Discussion and conclusions: Please check line 247, should this be patients and physicians? One of the potential limitations not discussed is the limitations of the calculator used to calculate the clinically attainable benefit. Also not discussed was the potential of the structure of the questionnaire to influence the reported preferences, was an anchoring effect at play? The concluding statement about avoiding a one-size-fits-all treatment strategy seems out of place with the rest of the paper. I believe the point made in lines 255 and 256 is an important point which could be emphasized instead. References: please check references 23 and 24 are complete.

VERSION 1 – AUTHOR RESPONSE

Dear Editorial Office, Assistant Editor Emma Gray, and Reviewers,

We are pleased to submit our revised manuscript (bmjopen-2017-021309.R1) to the BMJ Open:

Thank you very much for taking our manuscript into consideration. We have followed the suggestions of the reviewers and editors and made major revisions to the manuscript. In the attached point-by-point response we have responded to each comment sequentially. The point-by-point response also includes a specific response to the editor's suggestions on the first page. The changes may additionally be viewed in the track changes version of manuscript document.

As requested by the editorial office, we have added the separate section "Patient and Public Involvement" to the methods. Elements of this section had previously been incorporated into the other areas of the methods section, and we have altered the manuscript to avoid redundancies.

On behalf of all the authors I would like to thank you very much for your time and consideration, and for the numerous insightful suggestions made during the review process. We look forward to your opinion on our revised work.

Thank you for your time and consideration,

On behalf of the co-authors,

Frank Visseren, MD PhD

- The author provided a marked copy with additional comments. Please contact the publisher for full details.

VERSION 2 – REVIEW

REVIEWER	stephen fitzgerald the Royal Adelaide hospital ,Australia
REVIEW RETURNED	15-Mar-2018

GENERAL COMMENTS	The paper is fine. The title is still not quite right- ? try 'minimum' rather than 'minimal'. perhaps the difference between life expectancy and disease free life expectancy might have been commented upon. The onset of IHD does not necessarily make one 'unhealthy' in terms of daily life. The main messages however are sufficient.

REVIEWER	Peter Pype Ghent University, Belgium
REVIEW RETURNED	18-Mar-2018

GENERAL COMMENTS	Dear authors, All my questions and concerns have been addressed adequately.

VERSION 2 – AUTHOR RESPONSE

Response to Reviewer 1
Reviewer: Stephen Fitzgerald, the Royal Adelaide Hospital, Australia
Please state any competing interests or state ‘None declared’: none declared
Reviewer Comment:
1. The paper is fine. The title is still not quite right- ? try 'minimum' rather than 'minimal'. perhaps the difference between life expectancy and disease free life expectancy might have been commented upon.
The onset of IHD does not necessarily make one 'unhealthy' in terms of daily life. The main messages however are sufficient.
Author Response: Thank you for suggesting these improvements. We believe changing the wording has improved
the title. We additionally believe that differentiating between life expectancy and disease free life expectancy has
made it more clear. The title now reads as follows:
“Variation in minimumal desired cardiovascular disease-free longevity benefit from statin and antihypertensive
medications: a cross-sectional study of patient and primary care physician perspectives"