Author's response to reviews

Title: To screen or not to screen for peripheral arterial disease in subjects aged 80 and over in primary health care: a cross-sectional analysis from the BELFRAIL study

Authors:  
Stein Bergiers (stein.bergiers@ugent.be)  
Bert Vaes (bert.vaes@uclouvain.be)  
Jan Degryse (jean-marie.degrye@uclouvain.be)

Version: 2 Date: 27 April 2011

Author's response to reviews: see over
To the Editor of BMC Family Practice

Brussels, Belgium, 27th April 2011

Dear Editor,

We would like to thank you for considering our manuscript ‘To screen or not to screen for peripheral arterial disease in the oldest old in primary health care: a cross-sectional analysis from the BELFRAIL study’ for possible publication in BMC Family Practice.

Herewith we would like to submit our revised manuscript. In the rebuttal we addressed all the Reviewers’ comments point by point.

We hope you will consider our revised manuscript for publication in BMC Family Practice.

On behalf of all authors,

Yours sincerely,

Dr Bert Vaes
Answer to reviewers

Reviewer 1 report - Bruno Rushforth

Reviewer's report:
This paper from Belgium reports a cross-sectional study embedded within the BELFRAIL study. In the ‘oldest old’ (those aged 80 years or older) the authors looked to: (i) examine the prevalence of reduced ABI (ankle-brachial index); (ii) determine the accuracy of the medical history and clinical examination for reduced ABI; (iii) investigate the difference in functioning and physical activity between patients with and without reduced ABI. The authors can be commended for attempting to develop an evidence-base to help guide intervention decisions within this under-researched group (the oldest old) and from keeping the exclusion criteria limited to try and make the study results meaningful for everyday primary care practice (although see comment below regarding consent issues). The paper is well written and well presented. However, there appear to be a number of issues that need further clarification and / or discussion, which as currently stand detract from the impact of the paper.

Major Compulsory Revisions / Clarifications

1. The title of the paper is ‘to screen or not to screen for PAD…’ but the study appears to describe using medical history and clinical examination as a screening test for reduced ABI, the implication being that reduced ABI can be seen ‘as an indicator of PAD’. However, it’s unclear to the reader if an asymptomatic ABI of, for example, 0.89 meets the diagnostic criteria of PAD. If it does, then the question arises about the benefit from identifying those aged 80 or over with asymptomatic PAD given that very few will progress to limb ischaemia. If it does not, then it’s unclear whether the medical history and clinical examination can be seen as a screening test for PAD, or whether it is more accurately being used as a screening test for reduced ABI (which may be asymptomatic). It is noted that in the conclusion the authors state that ABI ‘correlates well with arteriography findings’. Perhaps these issues would be clarified by making the diagnostic criteria of PAD explicit in the paper.

Answer: We thank the Reviewer for this important remark. The diagnostic criteria of PAD were added to the Background section. In agreement with the approach followed by Fowkes et al (Int J Epidemiol. 1991;20:384-392) and by Schroll and Munk (J Chron Dis. 1981;34:261-269), PAD was considered present when the ABI was lower than 0.90 in at least one leg, a threshold value used in most studies.
PAD, and thus a low ABI, is considered a manifestation of generalized atherosclerosis, and life expectancy in patients with PAD is reduced compared with subjects without PAD. This is mainly attributable to an increased incidence of cardiovascular disease in patients with and without complaints of intermittent claudication. This issue is described in paragraph 2 of the Background section.

2. The key issue around the (accepted – e.g. last sentence of abstract) lack of known effective interventions for those patients aged 80 or over identified from the screening test requires further discussion, in that the usual purpose for having a screening test is to enable patients found as ‘positive’ to the screening test to have further investigation and / or treatment which improves outcomes.
Answer: The authors fully agree with the Reviewer. The authors believe they already discussed this issue in the first version of the paper, but added an extra sentence about promising results of endovascular interventions. In the discussion section we state: “The effectiveness of possible interventions after finding a low ABI in patients aged 80 and over remains unclear. The treatment of PAD consists of an optimal treatment for classic cardiovascular risk factors, such as hypertension, hyperlipidaemia, diabetes mellitus, and stopping smoking, including the use of antiaggregants and walking exercises. These measures have a proven beneficial effect on younger patients up to the age of 75; however, no intervention studies currently exist for patients aged 80 and over. On the other hand, advances in endovascular interventions have expanded the options available for the invasive treatment of PAD the last few years. Although no causal link has yet been established, major lower extremity amputation rates have fallen by more than 25% during this time period.” Furthermore, we concluded a screening strategy for PAD using the determination of ABI could be considered only if effective interventions resulted from further research for those aged 80 and over with a low ABI.

3. It is unclear how the third aim of the study, investigating the difference in functioning and physical activity between patients with and without reduced ABI, sits with the paper title question around screening. Further clarification would be welcomed. Particularly, the finding that the LAPAQ score was significantly lower in the group with reduced ABI may simply be due to factors such as cardiac morbidity which was significantly greater in those with reduced ABI.

Answer: We thank the Reviewer for this important comment. Lower-extremity function is an important predictor of future disability, mobility loss, and nursing home placement. As PAD is frequently asymptomatic, a low ABI may identify persons whose high risk for mobility loss and nursing home placement might otherwise go unrecognized. This suggests interventions to prevent mobility loss and nursing home placement might be appropriate for persons with low ABI. This was added in the Discussion section.

4. The authors report participating patients were examined ‘after informed consent’, yet they also note that those with an MMSE of 15 or more could be eligible for inclusion. In Figure 1 the refusal number for the main study is given as 19/591 (=3%), although Figure 1 also shows that the number of participants drops from 246 to 239 in the penultimate stage of the flow chart. It would be important for the authors to discuss the issue of the low refusal rate and the fact that participants with significantly reduced MMSE scores were potentially eligible for the study.

Answer: The protocol has been described in detail in BMC Geriatrics (BMC Geriatrics 2010, 10:39). The initial cohort of subjects that accepted to participate in the BELFRAIL study consisted of 593 subjects. However, 19 refused to continue and five died before the examinations were started. Therefore the definitive cohort consists of 567 subjects that underwent at least one study visit (echocardiography, GP visit, CRA visit or blood test). This refusal rate only refers to the number of patients that refused to continue after inclusion. No data on initial refusal was recorded. This was added in the Methods section. The Hoeilaart population drops from 246 to 239 because only the patients selected from the group practice of Hoeilaart were used for this study. The seven other subjects were included in another GP centre in the municipality of Hoeilaart. We used only three exclusion criteria for the BELFRAIL cohort: urgent medical need, palliative situation and known serious dementia (MMSE < 15/30).
MMSE < 18 informed consent was given by the patient and the caregiver. This was added in the Methods section.

5. The first sentence of the discussion states that, ‘This study was carried out on a representative sample of people aged 80 or over in a large group practice in Belgium.’ However, the selection criteria for participants involved attempting to recruit those aged 80 or over who consulted a doctor (either home visit or who attended for a consultation) between March and July 2009. Discussion would be welcomed on how representative this group is (doctor-consulters).

Answer: In Belgium general practitioners (GPs) have a prominent place in the health care system. More than 95% of the population is reported to consult the same GP or practice (duo or group) in case of health problems. More than 90% of people aged 65 and older have at least one contact with their GP every year, with an average of 11.9 contacts per year at the age of 75 and older. This was added in the Discussion section.

Minor Essential Revisions

1. It would be helpful to know if the clinical research assistant was a medical practitioner or a nurse or some other health professional.

Answer: The CRA was a nurse, a psychologist or a biomedical scientist and performed an extensive examination including performance testing and questionnaires following a standardised protocol. This was added in the method section.

2. Please clarify how many of the non-measurements were due to ‘failed oscillometric BP reading’

Answer: We performed only a qualitative registration of failed measurements, but did not register the percentage of non-measurements due to failed oscillometric BP reading.

Discretionary Revisions

1. First sentence of Background section: is PAD appropriately described as an ‘illness’ given that ‘PAD is often a subclinical disease in which the patient […] experiences no symptoms.’

Answer: The first sentence of the background section was changed to: ‘Peripheral arterial disease (PAD) refers to atherosclerotic occlusive disease of the arterial system distal to the aortic bifurcation and is a relatively common disorder in older persons.’
Reviewer: Frances Mair

Reviewer's report:
This is a useful paper relating to a common problem and addresses the issue of PAD in relation to older people (those over 80yrs) who are so often excluded from studies. It is clearly written and includes a clear acknowledgement of the study limitations. My view is that this paper should be accepted for publication but I have made a number of comments below.

Major compulsory revisions

1. I'm afraid I have problems with the term: "the oldest old". I think that wherever this term is used... e.g. title of paper, abstract, text of paper that it should be amended so that it is clear what is meant. e.g. those over 80yrs or similar... The term is ambiguous and should not be used.

Answer: The authors agree the term “the oldest old” is ambiguous. Therefore, the term was deleted throughout the paper and replaced by “subjects aged 80 and over”.

2. In the abstract the authors state that: "A general practitioner (GP) centre, located in Hoellaart, Belgium, recruited 239 participants." It is important to add details about participant selection at this point. So what were the inclusion/exclusion criteria for participants?

Answer: We thank the Reviewer for this important remark. The inclusion and exclusion criteria for participants were added in the abstract.

3. The authors then go on to say that a researcher performed questionnaires with patients. But what questionnaires were used. The methods section of the abstract should contain such basic details.

Answer: Agree. The different questionnaires performed, were written down in the abstract.

4. Within the methods section I think it would be helpful to address GP training to measure ABI...was there testing to check inter-rater reliability....if not should this be a limitation?

Answer: We thank the Reviewer for these important remarks. The fact that participating GP’s were trained to standardise the ABI measurement was added in the method section. Since the ABI was measured fully automatically by the oscillometric application and was not operator dependent, and the GP was only trained to standardise the placement of the patient and cuffs, the authors believe an inter-rater reliability was not needed. Therefore, this was not added as a limitation.

5. I would also be interested to know what the researchers did with those individuals identified as having PAD?

Answer: The treating GP’s received the ABI measurements of their patients. This was added in the method section.
Since the BELFRAIL study is an observational study, the GP decided what further happened with this information and no specific treatment or strategy was put forward by the study organizers. However, all participating physicians were referred to existing guidelines (reference 2).

6. The discussion section makes no mention of existing guidelines in relation to PAD screening e.g. Guideline Title. Screening for peripheral arterial disease. Bibliographic Source(s) U.S. Preventive Services Task Force. Screening for peripheral arterial disease: recommendation statement. Am Fam Physician 2006 Feb 1;73(3):497-500. It would be helpful if the authors could interpret their findings in relation to this literature. At present I feel this is a bit of a gap.

Answer: We thank the Reviewer for this suggestion. The findings of our study were related to this literature and described in the discussion section (see also point 7).

7. Generally the authors have been very measured in their claims...for e.g. stating that screening should be considered in the future if beneficial treatments are discovered. However, at one point in the discussion they say, "Considering the high prevalence of low ABI in the aged population, the asymptomatic early stages and the simple method of determining ABI, a screening program for PAD in the elderly should be considered." I think this comment needs to be removed or modified because the results from this study do not lead to one drawing this conclusion. The study shows that if you measure ABI you will detect lots of PAD in the elderly. However, as the authors acknowledge elsewhere one needs to have a worthwhile treatment before one can recommend screening. So this suggestion in the discussion is unwarranted and needs to be removed or modified.

Answer: The authors fully agree with the Reviewer. This section was removed from the discussion section. As already suggested in point 6, the USPSTF guidelines were integrated in the discussion section and the following paragraph was inserted: “The U.S. Preventive Services Task Force (USPSTF) recommends against routine screening for PAD among asymptomatic adults in the general population because the prevalence of PAD in this group is low and because there is little evidence that treatment of PAD at this asymptomatic stage of disease, beyond treatment based on standard cardiovascular risk assessment, improves health outcomes. The present study, however, showed a high prevalence of PAD, symptomatic or asymptomatic, in a selected population of subjects aged 80 and over. The identification of the presence or absence of a low ABI on the basis of known cardiovascular morbidity and a clinical examination appeared to be difficult. Moreover, it appeared that 80% of patients with a low ABI were not yet diagnosed with PAD, probably due to the great number of patients at a sub-clinical stage. Furthermore, an oscillometric ABI measurement is simple to carry out, has been validated in several studies, and could easily be integrated in a GP consultation. Therefore, a screening program for PAD among people aged 80 and over could be considered, if effective interventions resulted from further research.”

Minor essential revisions

1. When using abbreviations for the first time (e.g. LAPAQ score) in abstract please write out in full on the first occasion.

Answer: Agree. This was done.
2. INTRODUCTION: claudicatio intermittens should be intermittent claudication.

Answer: Agree. This was corrected.

3. Reference 13 has a spelling error: assesing instead of assessing.

Answer: This was corrected.

4. The authors have placed details of the study limitations at the very end of the paper in the conclusions section. I think this would be better placed earlier within the discussion section.

Answer: The authors agree. The limitations were removed from the conclusion section and a specific subheading “strengths and limitations” was made within the discussion section.