Reviewer’s report

Title: Prevalence of peripheral arterial disease in subjects with moderate cardiovascular risk: Italian results from the PANDORA study

Version: 1 Date: 3 June 2011

Reviewer: David P Brasil

Reviewer’s report:

BMC Cardiovascular Disorders: Review of manuscript
Prevalence of peripheral arterial disease in subjects with moderate cardiovascular risk: Italian results from the PANDORA study
Data from PANDORA (Prevalence of peripheral arterial disease in subjects with moderate CVD risk, with no overt vascular diseases nor diabetes mellitus)
Sanna G et al.

Comments, questions, and considerations:

1) Discretionary suggestion: The “abstract” mentions “A range of cardiovascular risk factors were significantly associated with asymptomatic PAD (p<0.0001)”. This sentence may be rephrased as: Suggested version: “A range of risk factors comprising smoking, hypertension, low HDL-C, family history of CHD, and habit of moderate-high alcohol intake were significantly associated with asymptomatic PAD”. This will help readers who did not have access to the entire publication to get to know the specific risk factors positively associated with asymptomatic PAD

2) Comment: The chi-square test was used to compare frequency of different groups of independent categorical variables. The authors tested the relationship of three variables: the ABI, lifestyle habits, and CV risk factors. In order to test whether two of the variables were independent of each other the Cochran-Mantel-Haenszel hypothesis test was performed. Finally, logistic regression was proposed to assess relationship between PAD and other categorical variables. The statistical analysis sounds consistently planned.

3) Discretionary suggestion: In the section “results” (top of page 8) the sentence below may be rephrased, targeting a more clear approach of the paragraph: “The most recurrent exclusion criteria were: less than 80% of CRF fields completed (2.45%), unmeasurable ABI (2.36%) and the lack of fatty serum (?) data collected within the previous 12 months (0.68%)”.

4) Discretionary suggestion: In the section “results” (middle of page 8) the sentence may be rephrased. Suggested version: “Among the 6 participating countries of the previous PANDORA study, a higher prevalence of PAD was observed in Greece (28.0%) and Italy (22.9%), rather than in France (12.2%), Belgium (7.0%), the Netherlands (8.1%) or Switzerland (12.2%). Multiple logistic
regression analysis confirmed that following Greek subjects, Italians had a greater risk of PAD. (Figure 1)."

5) Discretionary suggestion: In the section “results” (top of page 9) the sentence may be rephrased. Suggested version: “Multiple logistic regression did not yield any difference regarding gender, race, physical activity, elevated waist circumference, dyslipidemia, high LDL-C levels or BMI. Variables significantly associated with PAD are shown in Figure 3”.

6) Discretionary suggestion: In the section “results” (top of page 9) the sentence may be rephrased. Suggested version: “In addition to age, most subjects (with or without PAD) presented 2 or 3 CVD risk factors (Figure 4A). Whenever subjects were evaluated for the presence of #2 or >2 risk factors, frequency of PAD was higher above 2 risk factors (Figure 4A, inset).”

7) Discretionary suggestion: In the section “results” (bottom of page 9) the sentence may be rephrased. Suggested version: “However, statin therapy was significantly associated with absence of PAD (Figure 3).”

8) Revision: In the section “discussion” (first paragraph of page 10). Please elaborate and explain the sentence: “The present study is in agreement with findings from the original PANDORA study in that (in which?) it (is?) confirms (confirmed?) that the prevalence of a low ABI is not eligible (?) in patients who would otherwise be classified as intermediate and even low risk.”

9) Discretionary suggestion: In the section “discussion” (page 10). Long sentence - consider shortening it as it follows. Suggested version: “Limited use of statins in the total cohort of Italian subjects (10.5%) was also confirmed within the subgroup of dyslipidemia (24%). Other participant countries had higher percents of patients on statins.”

10) Revision: In the section “discussion” (page 10). Needs correction. “Subjects without symptoms of the lower limbs and overt CV diseases, who are defined by current guidelines as at risk of PAD, include (including?) those less than 50 years old with diabetes and one (additional?) atherosclerosis risk factor (smoking, dyslipidemia, hypertension, or hyperhomocysteinemia) or subjects aged 50 to 69 years with a history of smoking or diabetes, or subjects aged 70 years and older.”

11) Discretionary suggestion: In the section “discussion” (page 11). Long sentence - consider breaking it up in two sentences as it follows. Suggested version: “This frequency is in agreement with results of the present study, even though in the Get ABI study 2.8% of the subjects with low ABI had PAD symptoms. In addition, risk profile in the Get ABI population showed differences from that of PANDORA, which was due to fewer previous cardiovascular events or diabetes”.

12) Discretionary suggestion: In the section “discussion” (page 11) sentence may
be rephrased as it follows. Suggested version: “Nevertheless, as evidenced by PANDORA, the Get ABI also confirmed the usefulness of expanding measurement of ABI over to other risk categories beyond those indicated by guidelines”.

13) Discretionary suggestion: In the section “discussion” (middle of page 11), instead of using e.g. (exempli gratia, or “for instance”) perhaps a better fit would be i.e. (id est, meaning “that is”). Suggested version: “Furthermore, demographic and clinical characteristics of this Turkish population were similar to the Italian cohort (i.e., age, gender ratio, associated risk factors, etc.), suggesting that a relatively high prevalence of PAD can be observed in other Mediterranean-like lifestyles”.

14) Revision: In the section “discussion” (page 11). Difficult understanding of sentence. Please consider rewrite it. “The marked differences between these results and those of the PANDORA study results where, even in countries with minimal prevalence of low ABI, reported frequencies of over 3%, thus emphasizing the need to apply this issue in many risk-groups that should be submitted to the periodical measurement of ABI”.

15) Revision: In the section “discussion” (bottom of page 11). “This finding showed the uncertain role of cholesterol in the pathogenesis of dyslipidemia, as a relevant risk factor as also reported in other studies.”… uncertain role of cholesterol in the pathogenesis of dyslipidemia? What does this mean? Please elaborate on this sentence.

16) Revision: In the section “discussion” (page 12). “It is also worth highlighting the association between marital status and the presence of low ABI, with unmarried or widowed subjects more likely affected by low ABI than married subjects”. This data is presented as demographics for no PAD versus PAD: unmarried 4.9 vs 4.5; married 79.7 vs 68; widowed 11.4 vs 13.5. The PANDORA is an exploratory observational (cross sectional) study, whose aim is to predict systematically the relationship among two or more variables. The marital status data above does not infer that unmarried subjects are more likely affected by low ABI, but otherwise presumes a “real world” inclusion of subjects, which is typical of observational studies. Indeed, it looks like marital status may be a confounding variable in this case. Confounders are imbalances between groups that can affect real estimation of results. Thus, some statistical methods are required to adjust the imbalance and control for observed confounders. Two examples of statistical methods to control for possible confounders are the logistic regression (for categorical data) and a propensity matching analysis (AKA as propensity score). In the case of the present study the methods section on page 5 describes that “the relationship between PAD … and the features of patients admitted … was assessed by multivariate logistic regression …”

17) Revision: In the section “conclusion” (page 13). “Moreover, the finding of a relatively high prevalence of asymptomatic PAD among Italian subjects was
paradoxical, given the recognised lipid-lowering benefits of the so-called “Mediterranean diet”. There is no evidence that the present study tested the specific benefits of the “Mediterranean diet” on asymptomatic PAD patients so data does not support this conclusion. This is a mere speculation rather than a confirmed fact and should not be part of the conclusion.

18) Revision: In the section “conclusion” (page 13). “Although compared to other countries (from the original PANDORA study) this Italian population showed a restricted statin medical prescription and treatment, although it is unlikely that this effect may alone account for this increased prevalence”. The use of “although” twice in the sentence is confuse. Consider rephrase it.

19) Tables and figures miss the legends that can help readers navigate through the results.

20) In conclusion, the data presented in the manuscript may be largely interesting, but would benefit from a more consistent “discussion” and “conclusions” to support the authors’ hypothesis.

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 do not have any conflict of interest relating to the present activity. I have more frequently acted as a speaker for LIBBS and MSD, and have occasionally acted as a speaker for Novartis and AstraZeneca in 2004. I do not hold shares in pharmaceutical or device companies. I have no financial or non-financial competing interests related to the present activity.