Reviewer’s report

Title: Use of aspirin for primary and secondary prevention of cardiovascular disease in diabetic patients in an ambulatory care setting in Spain

Version: Date: 16 June 2007

Reviewer: Jun Ma

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General
This study aims to evaluate the use of aspirin for primary and secondary prevention of cardiovascular disease (CVD) and the achievement of therapeutic goals for major CVD risk factors in 4,140 diabetic patients in an ambulatory primary care setting in Spain. The literature abounds with evidence of under-use of aspirin, particularly for primary prevention of CVD, and evidence of suboptimal control of major CVD risk factors in both diabetic and non-diabetic populations. The contribution of this study to the existent knowledge is unclear. The quality of the study is in question because of several concerns about some of the methodologies used. In addition, the manuscript needs thorough editing and proofreading.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The Introduction pays inadequate attention to numerous studies already published on the same subjects and does not address why this study is needed and how it advances the scientific knowledge.

Aspirin is contraindicated in individuals < 21 years because of increased risk of Reye's Syndrome, yet the study sample included patients >= 18 years. It is also unclear how patients with other known contraindications to aspirin were handled in the analysis. These contraindications include: aspirin allergy, bleeding tendency, anticoagulant therapy, recent gastrointestinal bleeding, and clinically active hepatic disease.

The definition of “regular use” of aspirin is unspecified, yet it is critical to the understanding and interpretation of the study findings. Also, in certain passages it is stated “aspirin was prescribed” whereas in other passages it is stated “aspirin was taken.” These two phrases imply entirely different measurements and implications. The former is medical prescription data and measures physician prescribing behavior, whereas the latter is typically by patient self-report and measures patient adherence.

No data are provided regarding the representativeness of the primary care centers and the patients in the study. As a result, no judgement may be made regarding the generalizability of the findings. In the Discussion, it is stated that "...the sample size achieved in our study, among the largest in the reviewed series, suggests that the results found should not differ too much from the actual results." It must be noted that sample size alone does not guarantee representativeness or generalizability.

A number of statistical methods are listed for bi-variate analyses. But, it is unclear which methods were used for what variables and the rationale is not provided. For example, why is it necessary to perform a correlation with polynomial trend when visual inspection and simple statistics would sufficiently show that most PP patients have 2 or 3 risk factors? Also, it is interesting that diabetes was included as one of the risk factors in Figure 1 when the entire sample had diabetes to begin with. In Figure 2, the PP and SP groups showed quite similar patterns. The reason that the trend test did not reach statistical significance for the SP group could very likely due to lack of power associated with a much smaller sample size compared to the PP group. The value of Figures 1 and 2 is not apparent and this reviewer recommends their omission.

The forward (or backward) stepwise logistic regression method utilizes the likelihood ratio test (chi-square difference) to determine automatically which variables to add or drop from the model. This brute-force method runs the risk of modeling noise in the data and is considered useful only for exploratory purposes. Selecting model variables on a theoretic basis and using the “Enter” method is preferred. However, problems of overfitting the model to noise in the current data may be mitigated by cross-validation, fitting the model to one a test subset of the data and validating the model using a hold-out validation subset.

Authors are recommended to consult a qualified statistician.
The thresholds quoted in the text and for statistical analysis were different from those enumerated in Table 1 for several clinical parameters (e.g., total cholesterol and HbA1c) and no justification is given.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

The manuscript needs thorough editing and proofreading.

Discretionary Revisions (which the author can choose to ignore)

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What next?: Reject because too small an advance to publish

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.