Reviewer's report

**Title:** Cardiovascular disease prevalence in patients with inflammatory arthritis, diabetes mellitus and osteoarthritis: a cross-sectional study in primary care

**Version:** 1  **Date:** 23 March 2012

**Reviewer:** Marissa Lassere

**Reviewer's report:**

Reviewers report
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**Major Compulsory Revisions**

The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical mistakes, errors in interpretation.

This paper describes the prevalence rate of non-fatal cardiovascular in patients with inflammatory arthritis, diabetes and osteoarthritis compared to patients without these disorders in the setting of primary care. The authors have published three papers on this in 2009 (see authors publications 8, 9 and 10)

Diagnoses are recorded using an electronic medical record used by GPs. A classification system is recorded when the general practitioner issues a prescription.

Individuals are classified within these diagnostic groups. The diagnosis and was recorded in 2006 and up to 2004. I'm not entirely certain what this means.

1. What is the exact period?
2. How often was the diagnostic classification reviewed?

The controls would be a combination of positive and negative risk factor groups combined.

3. Is there any more information about them? Major diagnostic groups, medications used?

4. How accurate is this diagnostic system. What validation has been done regarding this in general and specifically for this group of GP practices. My experience with electronic software used by GPs in Australia suggests that for some diagnoses it is very accurate and for others less so. Essentially the prescription is often a surrogate for the underlying condition that is being evaluated. There are classifications that are specifically important – the study factor classification – i.e for inflammatory arthritis, diabetes, and the outcome factor i.e cardiovascular events. Both study and outcome factor must be robust for the conclusions to be valid.
Study factor: Unfortunately the diagnostic code is not specific so that rheumatoid arthritis (RA) and ankylosing spondylitis (AS) two very different conditions, are combined.

5. How was RA and AS validated. As a rheumatologist, I am aware of misclassification of these conditions. (see authors publications 9 and 10)

6. How many patients with RA were on disease modifying agents? 7. 7. Also diabetes populations differ by duration of disease and severity, control and its management (ie need for insulin or not). Is there any information on this? (see authors publications 9 and 10)

Outcome factor: Conditions such as myocardial infarction and transient ischaemic attack are not always straightforward diagnoses. These are conditions that often require adjudication within the research setting, and clearly the accuracy of the data may not be sufficient in some administrative databases. ICD-10 codes allow for the various ischaemic heart disease conditions. No information is provided regarded how the accuracy of these diagnoses was evaluated.

8. Could the authors also provide information in the manuscript regarding this? (see authors publications 8, 9 and 10)

9. If there is misclassification bias – is it differential or non differential? We cannot say because there is no information within the manuscript. Can the authors please comment?

Hypertension and hypercholesterolaemia based on blood pressure readings and blood chemistry results – there would be more GP documentation. Cholesterol could be total or LDL-cholesterol alone.

The statistical analysis uses multivariate logistic regression. Patients were clustered within practices presumably to look for practice differences. Patients had multiple disorders; therefore, each group exceeded the total number of patients. Table 1 shows the population characteristics. I note that the controls mean age 51 versus OA mean age of 69 is a 20 year difference. Inflammatory arthritis falls in between at 60 years. There was also a female preponderance in the study factor group. More objective data such as the use of the prescription antihypertensive agents and the use of statins shows that these are much higher in the osteoarthritis groups than in the inflammatory arthritis groups. I would have restricted the dataset to patients with age greater than 50, as the authors did in reference 8, and provided results by decade strata, again as per reference 8.

Study Design: When determining OR the study design including the comparator/reference groups is the most important determinant of the result. If the hypothesis is that inflammatory arthritis has a greater cardiovascular risk then noninflammatory arthritis osteoarthritis should be the comparator control/reference rather than the non-specific controls (noted above). Then some other factors such as use of NSAIDS and prednisone are shared, particularly if the hypothesis is inflammatory burden rather than its management.
10. Could the authors provide this analysis. Without this I do not believe that the authors add much more to the state of knowledge over and above their publications from 2009, furthermore, this would be a better evaluation of their hypothesis.

The results are shown in table 2, model three (adjusting form some risk factors. This shows an increased odds ratio of cardiovascular events in the inflammatory arthritis and diabetes groups as compared to controls.

If the authors’ intentions are to draw conclusions about inflammatory processes and risk of cardiovascular events then I would also suggest the following:

11. Please separate the results by cardiovascular events and not report just total cardiovascular events. The readers can decide how much confidence there is about the accuracy of the diagnostic codes for myocardial infarction, transient ischaemic attacks, strokes with neurological deficits etc (as the authors did in reference 8)

Furthermore ankylosing spondylitis is a very different condition to rheumatoid arthritis, but these cannot be separated in their classification system.

12. Is smoking information known therefore included in the model?

The medications that are used in patients with inflammatory arthritis such as the non-steroidal anti-inflammatory agents and prednisolone are important risk factors are for cardiovascular morbidity and these are not included in the analysis.

13. The administrative database would also have this prescription data and so it could also be described and used to validate diagnostic codes.

Discretionary Revisions

For example clarifications, data that would be useful but not essential.

14. Another analysis that would add to the robustness of the results and therefore strengthen the conclusions would be to take a second snapshot to see whether the results are reproducible within these set of GP practices. I note that this appears to be the same snapshot of time as reference 8.

If the above analyses are undertaken then we would be more confident about the results and authors conclusions regarding management in general practice, and this may have an influence on future GP management of these conditions.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests