PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cross vascular risk for first and recurrent hospitalised atherothrombosis determined retrospectively from linked data
AUTHORS	Briffa, Thomas; Nedkoff, Lee; Knuiman, Matthew; Hankey, Graeme; Norman, Paul; Hung, Joseph; Thompson, Peter; Hickling, Siobhan; Bremner, Alexandra; Sanfilippo, Frank

VERSION 1 - REVIEW

REVIEWER	Mark Harris University of New South Wales School of Public Health and Community Medicin School of Public Health and Community Medicine UNSW Sydney NSW New South Wales 2052 Australia
REVIEW RETURNED	09-Oct-2013

GENERAL COMMENTS	This data linkage study examines first even and recurrent hospitalisations with atherothrombosis in the cerebrovascular, coronary and peripheral arterial bed in Western Australia. This is an important study which emphasises the importance of secondary prevention. The abstract is appropriately structured. The statement in the conclusions that first-events predominate is true for cerebrovascular events but for coronary and peripheral events only just over half were recurrent. In the results page 8 second paragraph it is knotted that only 6% of first even coronary events had a prior admission compared to a much higher proportion for first ever brain and periphery. Can the authors calculate how much of this is due to the fact that coronary events dominate hospitalisations (and are therefore likely to occur first) rather than the fact that they lead to cerebral or peripheral events (eg by embolization)? What contribution does an other vascular history in the periphery have on cerebral events (compared with OVH in the heart)? The implications of the rapid rise in risk of first ever events in the 45-54 age band deserves more comment. In Australia 45-49 is targeted for health checks in general practice. These provide an opportunity for risk assessment and planning of more active primary and secondary prevention.

REVIEWER	Jay Cohn University of Minnesota United Kingdom
REVIEW RETURNED	14-Oct-2013

- The reviewer completed the checklist but made no further comments.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

1. The statement in the conclusions that first-events predominate is true for cerebrovascular events but for coronary and peripheral events only just over half were recurrent.
Response: We agree. We have reworded the focus of the conclusion in the abstract to read “This population study of hospitalised atherothrombosis suggests that rates of recurrence are substantially higher than first-events independent of vascular territory, age and sex. These findings accentuate the necessity for early and sustained active prevention”.

2. In the results page 8 second paragraph it is noted that only 6% of first ever coronary events had a prior admission compared to a much higher proportion for first ever brain and periphery. Can the authors calculate how much of this is due to the fact that coronary events dominate hospitalisations (and are therefore likely to occur first) rather than the fact that they lead to cerebral or peripheral events (eg by embolization)?

Response: Our population findings support a real dominance of first-ever coronary over other vascular events in men and women aged 35-84 years. This is evidenced by (i) first-ever coronary events occurred on average at least 5-years earlier in men and women than their brain and peripheral counterparts, and (ii) there were almost twice as many coronary events in men and women aged 35-54 years as for each of the other disease subtypes. Finally, to offset the contribution of elective hospitalisations, restricting the analysis to acute coronary or cerebral infarction, the proportions with other vascular history were unchanged (6.6% and 26.2%, respectively) from those reported in the text and Table 1.

3. What contribution does an other vascular history in the periphery have on cerebral events (compared with OVH in the heart)?

Response: The proportions of first-ever brain and coronary events with a history of peripheral disease are around 2% for each disease subtype. For recurrent events, the corresponding proportions are approximately double this proportion. Thus, even with likely under-reporting of peripheral disease, its contribution to events in other vascular territories is modest.

4. The implications of the rapid rise in risk of first-ever events in the 45-54 age band deserves more comment. In Australia, 45-49 is targeted for health checks in general practice. These provide an opportunity for risk assessment and planning of more active primary and secondary prevention.

Response: We agree. We have inserted the following text on p13 line4 “The nationally funded health checks in general practice for 45-49 year olds are an ideal opportunity to effect comprehensive risk assessment and more active primary and secondary prevention in this group.”

5. Linkage of this data to national pharmaceutical data would be useful in modelling the extent of and effectiveness of secondary preventive pharmacotherapy.

Response: In a separate dataset, from 1994 to 2006, we linked national pharmaceutical benefits data in 28-day survivors of a first ever myocardial infarction and showed long-term survival benefit. [Gunnell et al. Improved long-term survival in patients on combination therapies following incident acute myocardial infarction: a longitudinal population-based study. Heart online 25 July 2013].

Reviewer 2

6. The obvious weakness of this analysis is that it is limited to hospitalization data and does not control for deaths, which obviously would compete with re-hospitalization.

Response: We agree. We have inserted the following text under study limitations p10 line21; “A weakness is that the analysis is limited to hospitalisation data and does not control for out-of-hospital deaths”.