Author's response to reviews

Title: Insights into the clinical management of the syndrome of supine hypertension - orthostatic hypotension (SH-OH): The Irish Longitudinal Study on Ageing (TILDA)

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Version: 4 Date: 1 July 2013

Author's response to reviews: see over
1 July 2013

Dear Prof. Mitnitski

Insights into the clinical management of the syndrome of supine hypertension - orthostatic hypotension (SH-OH): The Irish Longitudinal Study on Ageing (TILDA). MS: 8945419719442233 (Revision 2)

Please find below a point-by-point response to the reviewer.

We look forward to hearing from you,

The Authors.
Reviewer: Ruth Peters

Major Compulsory Revisions

1: Given the postulated sequence of pathophysiological steps on page 20 (OH → OI → fainting) it would be helpful to explore the role of age and particularly sex further. At present, those who are female and older are significantly more likely to have MOH3, (table 3) however, when OI is the dependent variable and MOH3 membership a covariate being female and older are significantly less likely to have OI (table 4). When MOH3 and OI are both included in a model with blackouts or faints as the dependent variable being female is once again significantly associated with increased risk. It would be helpful if this could be discussed further alongside the presentation of the sequence model in the discussion.

Reply: two new paragraphs have been added to the discussion (pages 19, 20):

“Although the age and sex effects are non-modifiable, they could be relevant in terms of the postulated sequence of pathophysiological steps (OH → OI → fainting). In short, female and older participants were more likely to have an MOH-3 pattern (Table 3); however, when OI was the dependent variable and MOH-3 membership a covariate, being female and older were significantly less likely to have OI (Table 4). And when MOH-3 and OI were included in a model with blackouts or faints as the dependent variable, being female was once again significantly associated with increased risk (Table 5). The differential effects of age and sex are difficult to explain in our cross-sectional design. However, in terms of the age effect, it is plausible that advancing age may lead to an impairment of both the orthostatic hemodynamic response (i.e. more MOH-3) and the awareness of the latter (i.e. less OI). Indeed, we know that awareness of orthostatic hypotension is influenced by age: in younger subjects it is
usually brief but symptomatic whereas in older individuals the situation is reversed (2 new references).

In terms of the differential effects of sex in the pathophysiological sequence OH → OI → fainting, it is difficult to explain why women had more MOH-3, more history of faints, but less OI. OI is much more common in young women relative to men, children or older women (2 new references), and women in our sample were middle-aged and older. Another possibility is the presence of sex differences in the self-report of OI; for example, a previous study showed that symptoms of vertigo, dizziness or unsteadiness may be more related to psychological factors in men (new reference). The full understanding of this sex effects requires purpose-designed research.”

2: Thank you for the flow chart - is it possible to add information as to those lost to these analyses? Eg what made participants not complete each stage etc: If this information is not present then it could be discussed as a limitation?

Reply: On page 23 (paragraph 1), we have added: “Precise information as to what made participants not complete each stage of the participants’ flow chart (Figure 1) is not available, but frailty-related reasons are very likely. It is known that frailty is associated with missing data in research designs that involve the collection of physical performance measures (i.e. as required in the active stand) (new ref)”.
Discretionary revisions

1: thank you for table 1 - it would be helpful to have an additional column detailing the characteristics of the remainder of the population.

Reply: we appreciate the suggestion, but we have opted not to add a third column as in our opinion it would make more difficult to read the results of the statistical comparisons between the two existing groups.